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Lower Urinary Tract Symptoms and Benign Prostate Hyperplasia

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ABSTRACT

Objectives: This article's purpose is to review and discuss the relationship between urinary tract symptoms (LUTS) and renal damage, bearing in mind the epidemiology and pathophysiology of benign prostatic hyperplasia (BPH) and potential association.

Methods: Concerning the increasing number of elderly patients in urology clinics and the incidence of LUTS, the relationship between renal damage and LUTS should be an important issue. The authors searched literature in PubMed in order to correctly identify the pathophysiology and clinical correlation connecting these 2 entities.

Results: BPH is a common disease in adult men and its incidence is age related. Clinical BHP usually refers to the palpable enlargement of the prostate, which can be detected by physical or imaging examination, or by the presence of urinary symptoms loosely defined as LUTS. Despite the many possible causes of obstructive kidney disease, in studies of elderly patients with acute renal failure, the most common cause among all patients was BPH. Considering the high prevalence of BPH in older men with chronic kidney disease (CKD) it is invaluable to take into consideration the relationship between these 2 clinical entities.

Conclusion: Clinical and scientific findings show a worrisome and undiagnosed number of silent urinary obstruction symptoms that can lead to renal damage. This paper emphasizes that renal damage secondary to BPH, clinically manifested by lower urinary tract symptoms, is a preventable disease and must be under the care of physicians.

INTRODUCTION

TBPH is a highly prevalent clinical entity. Based on clinical criteria, the Baltimore Longitudinal Study of Aging found that the prevalence of BPH is approximately 25% in men aged 40 to 49 years, 50% in men aged 50 to 59 years, and 80% in men aged 70 to 79 years [1].

BHP is, theoretically, the detection of prostatic hyperplasia by histological study. However, histological studies for all men are unfeasible in clinical practice, so BHP usually refers to the palpable enlargement of the prostate, which can be detected by clinical or ultrasonographic examination or the presence of urinary symptoms roughly defined as lower urinary tract symptoms (LUTS) [25].

Chronic kidney disease (CKD) encompasses a spectrum of different pathophysiologic processes associated with abnormal kidney function and a progressive decline in glomerular filtration rate (GFR). Chronic renal failure (CRF) is the continuing significant irreversible reduction in nephron number normally resulting in end-stage renal disease (ESRD). Despite the many possible causes of obstructive kidney disease, in studies of elderly patients with acute renal failure, the most common cause among all patients was BPH [45,23]. Kumar et al. showed in their studies that acute renal failure in patients with obstructive kidney disease was due to BPH (38%), neurogenic bladder (19%), and obstructive pyelonephritis (15%) [23]. Attending to a high prevalence of BPH in older men with CKD, it is invaluable to take into consideration the relationship

KEYWORDS: Benign prostate hyperplasia (BPH), chronic kidney disease (CKD), lower tract urinary symptoms (LUTS), renal disease

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between these 2 clinical entities. However, despite the high prevalence of CKD and BPH in elderly men, there is limited knowledge on the association between these 2 conditions.

METHODS

The main objective of this review is based on the understanding of physiological and cellular mechanisms by which BPH can evolve into CKD. Thus, this paper results from a structured and comprehensive literature review. Searches were done at PubMed. Initial search terms were BPH and CKD. Based on the results of these initial searches, additional, separate searches were performed using the terms such as LUTS, renal disease, renal damage, and acute renal failure. The reference section in published articles was also examined and compared with electronic search results to maximize the review and inclusion of pertinent data. Other comorbidities (diabetes, hypertension) that can cause CKD, and others that can cause lower urinary tract symptoms (overactive bladder activity, neurologic diseases), were not evaluated in this paper.

RESULTS

Epidemiology: Benign Prostatic Hyperplasia

BPH is characterized by the non-malignant overgrowth of prostatic tissue surrounding the urethra, ultimately constricting the urethral opening and giving rise to associated LUTS [44,29,46], and defined by some authors as an important medical problem [5]. The diagnosis of BPH is made based on histologic examination of prostatic tissue (biopsy, surgery, or autopsy); however, surrogate measures, namely lower urinary symptoms, bladder outlet obstruction, and prostate enlargement are often used to define BPH as a clinical syndrome [9]. BPH is considered a disease of the aging male and can have a familial inheritance, especially if large prostate volumes and surgical intervention at a young age are seen in the pedigree [47]. It is striking that the age-specific autopsy prevalence is remarkably similar in all populations studied, regardless of ethnic and geographic origin [3]. Although BPH is not a life-threatening condition, the impact of BPH on quality of life (QoL) can be significant and should not be underestimated [29,8]. According to the World Health Organization, although the death rate attributable to BPH is negligible, the estimated DALYs (the sum of years of potential life lost due to premature mortality and the years of productive life lost due to disability) due to BHP are quite considerable. Most of the disability is probably due to severe clinical symptoms and/or late complications of BPH such as renal failure [32].

Benign Prostatic Hyperplasia and Chronic Kidney Disease

Although the exact etiology of BPH is not known, it seems (from recent studies and daily clinical practice) that the natural history and evolution of benign prostatic enlargement ends up in urinary obstruction causing the degradation of renal function over time [11]. In a retrospective study of 19 patients admitted for renal dialysis units for end-stage renal disease that was caused by BPH [38,39], the role of BPH as a cause for CKD was highlighted, and a more adequate screening of renal function in men with untreated LUTS was suggested [38]. More recently, a cross-sectional survey in Spain of 2 000 randomly sampled men showed a 2.4% prevalence of self-reported renal failure related to a prostate condition (9% reported renal failure from any cause) [19,34]. Another study [16] showed that men presenting for prostate surgery had a 7.7% prevalence of renal failure compared to a 3.7% prevalence in age-matched men presenting for non-prostate surgery. Other statistical studies revealed that 13.6% of men who presented for BPH treatment exhibited renal failure [27].

The Rochester Epidemiology Project found a significant association between signs and symptoms of BPH and CKD in their population-based sample of 476 white men [36,37]. More recently, evidence of association between BPH and CKD has also arisen in 2 different studies [18,48]. Bladder outlet obstruction (BOO) signs and symptoms (maximum urinary flow rate (Qmax); post-void residual volume, and obstructive LUTS) are significant predictors [36,48]. BOO probably makes the bridge between CKD and BPH [18]. Most likely this is the reflection of the etiology of CKD secondary to BPH.

As we consider all this data, one should consider that BPH is an almost ubiquitous condition in the older man. Thus, the low occurrence of CKD in BPH clinical trials should not be used to infer a weak association between the 2 disease processes.

BPH Physiopathology, Disease Progression, and Renal Failure

The exact etiology of BPH is unknown; however, the similarity between BPH and the embryonic morphogenesis of the prostate has led to hypotheses that BPH may result from a reawakening of embryonic induction processes in adulthood [29,30]. The most common renal pathology finding in men with obstructive nephropathy due to BPH is chronic interstitial nephritis [7,38], and 30% of cases have been attributed to obstructive kidney disease. Late or end-stage renal failure secondary to prostatic enlargement or BOO should be amenable to prevention if cases are recognized early; however, it is still difficult to recognize which men with BPH are at risk of renal failure and need close investigation.

Lower Urinary Tract Symptoms (LUTS)

LUTS are clinical criteria to define a urinary dysfunction. Most of the men with BPH have voiding dysfunction, and they complain of nocturia, urgency, weak urinary stream, increased urinary frequency, and a sense of incomplete bladder emptying

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after micturition. For many years some studies were done to achieve a scientific relation between LUTS and CKD [16,31]. A retrospective study did not find any relation between the duration of symptoms and serum creatinine levels [16]. Likewise, Gerber et al. did not achieve any success in linking serum creatinine levels and LUTS [12]. However, Hong et al. reported that obstructive symptoms were significantly associated with CKD status [18].

Patient perceptions are receiving greater emphasis as part of clinical decision-making [17,20,35] in daily clinical practice. The variability of the relationship between symptom severity and its impact in GFR requires further investigation [14]. It must take into account that the absence of LUTS in older men does not necessarily exclude BPH with urinary outlet obstruction, and that the severity of LUTS does not predict the degree of obstruction to urinary flow. However, when men with complete chronic urinary retention and severe symptoms needing surgical intervention were evaluated, the authors found as much as 30% of men with renal insufficiency [39]. Clinical practice shows us that many men with LUTS do not value their symptoms and do not seek medical care. Those older men often tolerate and disregard their lower urinary tract symptoms. As such, under-reported symptoms can induce a significant bias in most of studies already done.

Clinical Contributors for LUTS in BPH and Its Relation with CKD

Prostate Enlargement

BPH/BPE (benign prostate enlargement) first develops in the periurethral transition zone of the prostate. Prostate enlargement involves an increase in the number of glands, particularly the periurethral glands, and an increase in smooth-muscle and connective tissue in the periurethral region of the prostate [28,38,47]. Prostate size can be estimated by digital rectal examination (DRE) (underestimating true prostate size), but reliability across observers is, in general, considered [47]. For these reasons, in all cross-sectional studies, prostate volume is assessed by TRUS (transrectal ultrasound).

In the physiological point of view, as the prostate enlarges, it compresses the urethra, preventing the outflow of urine and contributing to the common lower urinary tract symptoms. Authors like Shapiro et al. emphasize the role of prostatic smooth muscle in pathophysiology of BPH [41]. Active muscle tone in the human prostate is regulated by the adrenergic nervous system [40], and α-adrenergic blockade leads to a significant down-regulation of normal protein gene expression, specifically smooth-muscle myosin heavy chain [4,47]. Recent studies related prostate size and LUTS in BPH. Hassanzadeh et al. found a significant correlation between urgency and prostate size [15], which can be considered a predictive factor for the disease and possible link between BPE and CKD. The prostate and its enlargement can contribute to outflow obstruction, not only by its static component (periurethral compression caused by a stromal component) but also its dynamic component (smooth-muscle cells and adrenergic pathway).

Post-voiding Residual Urine Volume: Chronic Urinary Retention

Chronic urinary retention is thought to be the dominant mechanism by which BPH can cause renal injury [36]. Rule et al. defined chronic urinary retention (CUR) as post-void residual urine (PVR) higher than 100 mL, and reported that CUR was significantly associated with CKD in community-dwelling men [37]. For years it has been described that large volumes (> 300 mL) affect renal function in advanced BPH [37,48], and PVR of the patients with CKD was significantly greater than that of the patients without CKD. Recent studies, however, demonstrate that the volume of residual urine (post void) necessary to impair renal function is not that elevated. Yamasaki et al. verified, in their study, a cutoff of 12 ml for PVR [48], and they confirmed PVR as a significant and independent risk factor for CKD. This study showed for the first time that patients with BPH could develop impaired renal function with small amounts of post-void urine (PVR < 100 ml). These findings indicated a higher prevalence of CKD in patients with BPH, acknowledging it as a risk factor for CKD.

Although, as Yamasaki et al. demonstrated, low post-void residual urine can cause the deterioration of renal function, and it is scientifically accepted that, in cases of renal function deterioration, a greater volume of residual post-void urine is observed [48]. PVR cannot be dissociated from changes in bladder remodeling and consequent changes in static component (as it is described in "Bladder Remodeling").

Acute Urinary Retention

Acute urinary retention (AUR) is defined as an acute complication of benign prostatic hyperplasia. AUR represents an immediate indication for intervention or even surgery. Between 25 and 30% of men who underwent transurethral resection of the prostate (TURP) had AUR as their main indication [47]. This complication is not exclusive for patients suffering from BPH. Other causes can trigger acute urinary retention such as surgery, anesthesia, trauma, medications, medical examination, and urinary tract infections (mainly prostatitis). Acute urinary retention is responsible for the majority of acute renal failure cases due to obstructive kidney disease [33] and for long-term tubular dysfunction [36,37].

Bladder Remodeling: A Response to Urinary Obstruction

The bladder has a central role in the pathophysiology of BPH and its complications.
Current evidence suggests that the bladder´s response to

obstruction is largely an adaptive one, although it is only partially adaptive. It is also clear for many authors and physicians that LUTS in men with BPH or prostate enlargement are more closely related to obstruction-induced changes in bladder function than to outflow obstruction directly.

There are of 2 types of bladder changes. First, ones that lead to detrusor instability (clinically associated with symptoms of frequency and urgency). Second, changes associated with decreased detrusor contractility (emptying symptoms: low urinary stream, hesitancy, intermittency, and increased residual urine) and detrusor failure [47]. The development of bladder-wall thickening (easily measurable by ultrasound) and trabeculation due to smooth-muscle hypertrophy and connective tissue permeation are responsible for increased bladder pressure in patients with high-pressure chronic retention [21,37,42]. Severe trabeculation is related to significant residual urine, suggesting that increased collagen in the bladder wall is probably responsible for incomplete bladder emptying rather than impaired muscle function [47]. Detrusor hypertrophy is one of the first modifications in the bladder. Obstruction also induces changes in smooth-muscle cell contractile protein expression, impairing cell-to-cell communication [24,26] that leads to detrusor instability, and, in some cases, to impaired contractility.

Cellular and physiological changes in bladder muscle and collagen contribute to a high-pressure bladder that perpetuates itself with worsening ability to empty, causing kidney lesions. These mechanisms of bladder remodeling develop in a hypofunctional bladder, with low compliance. Comiter et al. reported that in a series of men with symptomatic BPH, 78% of patients with low bladder compliance had renal failure [6]. Low bladder compliance and detrusor instability may be causal mechanisms for renal failure in men with chronic urinary retention [37].

Bladder remodeling is a response to continued bladder obstruction, and detrusor smooth-muscle cell is a key contributor to the complex symptoms associated with prostatic obstruction, namely in LUTS/BPH/BPE.

Ureterovesical Junction and Upper Tract Dilation

In general, ureterovesical junction obstruction caused by bladder remodeling in chronic urinary retention is a contributing mechanism for renal failure in BPH [37]. Upper tract dilation occurs because of continued bladder outlet obstruction and remodeling (detrusor hypertrophy and scarring), leading to anatomical ureterovesical junction obstruction [21]. Upper urinary tract dilation or hydronephrosis is consistent with chronic renal failure from obstructive kidney disease [43]. In men with BPH and increased serum creatinine, hydronephrosis is common (one-third), and it is found in 90% of men with BPH who are hospitalized for uremic symptoms [39]. A history of enuresis, painless chronic retention, and palpable bladder should suggest a diagnosis of high-pressure chronic retention with attendant risk of hydroureteronephrosis [39].

Other Causes

Recurrent urinary tract infections in men with chronic urinary retention due to BPH may also contribute to chronic renal failure [37]. Secondary hypertension due to chronic urinary retention is also a complication of BPH, leading to hypertensive kidney disease [13]. Nephrogenic diabetes insipidus caused by partial or chronic urinary obstruction can result in renal failure [22]. Other clinical entities such as diabetes and hypertension are independent factors that can lead to CKD [12]. Patients with BPH are probable carriers of these pathologies that are likely to seriously aggravate renal function and must be taken into account as likely precursors of conditioners of renal disease.

DISCUSSION

Benign prostate hyperplasia and chronic kidney disease are 2 common and prevalent entities in elderly men. It has been reported in several studies that threads of evidence suggest that BPH is a risk factor for chronic kidney disease. An average of 13.6% of patients presenting to urologic clinics for the treatment of BPH had renal failure. The low occurrence of CKD in BPH clinical trials should not be used to infer a weak association between these 2 disease processes [36]. However, a number of patients with BPH and some degree of renal disease can be higher, mostly because older men mostly ignore their micturition problems and seek clinical help while at a higher degree of BPH.

Although BPH is not a life-threatening condition, the impact of BPH on QoL is significant and should not be underestimated. Concomitantly, CKD can be a critical medical problem [10]. It has been well documented that BOO by an enlarged prostate can lead to renal insufficiency. Recent data suggests that the combination of several factors can lead to chronic and progressive urinary retention, high bladder pressure, and ureterohydronephrosis working together to cause progressive renal injury. Obstructive processes develop cellular and physiological changes in bladder muscle and collagen, contributing to a high-pressure bladder that perpetuates itself with worsening ability to empty, causing kidney lesions that lead to renal failure.

It must be emphasized that CKD secondary to BPH is a preventable disease, and early detection can prevent the heavy tolls of CKD treatment (hemodialysis included) with considerable economic and social savings. Primary physicians have a very important role in the diagnosis and management of men over 50 or 60 with lower urinary tract symptoms.

Nowadays, the number of patients seeking medical care later in life is increasing. Morbidities and complications of common diseases are growing, as we can observe day by day in urologic clinics. BPH is a prevalent urologic disease, and is a very good example of a treatable disease that is now appearing at clinics with serious complications. The correct evaluation of lower urinary tract symptoms, and their underlying causes, may prevent the development of serious diseases with effects on the patient's health. Most guidelines have abolished the screening of renal function for patients with BPH. The increasing number of patients with BPH complications may suggest a change in the evaluation that general physicians, internists, and urologists should take into account.

The findings mentioned suggest that progressive nephropathy caused by prostatic/bladder outflow obstruction (urinary outflow obstruction) might be averted by more adequate screening of renal function in men with untreated LUTS. It is important in the near future to characterize a clinical phenotype of BPH; measure disease severity and outcomes; design clinical trials; and study concepts for drug therapy, behavioral and lifestyle interventions, and additional intervention therapies [2].

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Correlation Between Gleason Scores on Prostatic Biopsies and Prostatectomy Specimens in 40 Patients Undergoing More Than 12 Core Biopsies

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ABSTRACT

Summary: The Gleason score obtained on prostatic biopsies is a key parameter in the management of localized prostate cancer.

Objectives: We conducted this study to evaluate the correlation between Gleason scores (GS) obtained on prostate biopsies and radical prostatectomy to establish the accuracy of biopsy grading in the prediction of final grades.

Materials and Methods: Forty patients with localized prostate cancer diagnosed between 2000 and 2010, and treated with radical prostatectomy, were included in this study. All patients underwent transrectal needle biopsies (TRNB) with at least 12 cores. Gleason scores on biopsies and radical prostatectomy specimens were determined and the concordance between the 2 scores was then evaluated. Histological grading using the conventional Gleason grading system (3 groups) and the modified Gleason grading system (5 groups) was also performed. The correlation between grades obtained on biopsies and radical prostatectomy specimens was also evaluated.

Results: The mean age of patients was 61.1 years, with a mean PSA value of 10 ng/ml. In 32.5% of cases, the biopsy's Gleason score correlated with the one obtained on radical prostatectomy. Using the conventional Gleason grading system, the correlation highly improved, with 62.5% of patients remaining in the same group after radical prostatectomy. However, using modified Gleason grading, the correlation was slightly improved and estimated at 37%.

Conclusion: In this study we have noticed that the accuracy of Gleason scores determined by transrectal needle biopsy in patients with prostate cancer seems unreliable. The classification of patients into 3 distinct groups (well, moderately, and poorly differentiated tumors) increases the concordance between the biopsy GS and the definitive GS, but the modified Gleason grading system seems to be more precise and better reflects the Gleason score.

INTRODUCTION

Prostate cancer is an increasingly frequent pathology, and it is considered the second most frequent urinary cancer in Tunisian men [1]. After the clinical or biochemical suspicion of prostate cancer, the diagnosis can be histologically confirmed on transrectal needle biopsy. Moreover, the degree of tumor differentiation is determined by establishing the Gleason score (GS). This score is obtained by combining the primary and secondary patterns for a number score from 2 to 10 [2,3]. It is one of the most powerful predictors of biological behavior, and it is one of the most influential factors used to determine treatment for prostate cancer and a choice of external radiotherapy, brachytherapy, cryotherapy, or radical

KEYWORDS: Prostate carcinoma, prostate biopsy, radical prostatectomy, pathology, Gleason score

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prostatectomy [5]. However, in some cases, the GS established on transrectal needle biopsy could be different from the one for radical prostatectomy, which has a very important impact on prognosis and therapeutic options [3-6].

In this retrospective study, we evaluate the correlation between Gleason scores obtained on prostate biopsies and radical prostatectomy to establish the accuracy of biopsy grading in the prediction of final grades.

MATERIALS AND METHODS

We retrospectively analyzed the medical records of 40 patients who had undergone radical prostatectomy for prostate cancer, from January 2000 to February 2010.

Exclusion criteria included patients who underwent prostate biopsies who showed a high or low PIN grade, patients using 5-alpha-reductase inhibitors, and patients with a positive biopsy for prostate cancer that were not candidates for/refused radical prostatectomy. Inclusion criteria included patients who underwent transrectal needle biopsy with at least 12 cores and were candidates for radical prostatectomy.

The diagnosis was made on transrectal needle biopsy (TRNB), which was performed on patients with elevated serum PSA and/or abnormal digital rectal examination findings. Patients underwent at least 12 core biopsies (from the apex, the middle, and the base of the prostate, with 4 cores for each site). Additional target biopsies were performed when needed (prostatic nodes; hypoechogenic lesions). The same senior pathologist examined all the biopsies. Various preoperative biopsy findings were recorded, including the primary and secondary Gleason pattern grade from each positive biopsy site. The Gleason score was then established by combining the highest Gleason score among all biopsy sites and the Gleason score from the site with the highest tumor volume on the needle biopsy. The tumor was then classified using the conventional Gleason grading system with 3 categories: Well-differentiated tumors (score: 2 to 4), moderately differentiated tumors (score: 5 to 7), and poorly differentiated tumors (score: 8 to 10) [2]. The modified Gleason grading system included 5 categories: Well-differentiated cancer (score: 2 to 6), moderately differentiated (score: 3 + 4 = 7), Moderately/poorly differentiated (score: 4 + 3 = 7), poorly differentiated (score: 8), and undifferentiated (score: 9 to 10) [7]. The 2002 TNM staging system of the American Joint Committee on Cancer (AJCC) was used for clinical staging.

All these patients underwent an open, retropubic radical prostatectomy. For each patient, we evaluated these parameters: Serum PSA level, clinical stages, biopsy data, and postoperative criteria (pathological TNM stage 2002, Gleason score). The highest GS established on the TRNB and radical prostatectomy specimens were compared. A "downgrade" was defined as the Gleason score for the prostatectomy specimen greater than that of the biopsy specimen, whereas an "upgrade" was defined as the opposite.

Table 1. Gleason score biopsy and after radical prostatectomy.

Biopsy/ Prostatectomy	4	5	6	7	8	9	Total
4	0	0	1	0	0	0	1
5	0	0	0	0	1	0	1
6	0	1	11	9	4	1	26
7	0	0	1	1	0	1	3
8	0	0	1	3	1	1	6
9	0	0	2	0	1	0	3
Total	0	1	16	13	7	3	40

Statistical analysis was performed using the Student *t* test for continuous variables, Pearson's chi-square test, and Fisher's exact test for categorical variables. The software used for statistical analysis was SPSS version 12.0 (SPSS Inc., Chicago, IL, USA). A *P* value of less than 0.05 was considered statistically significant.

RESULTS

There were 40 patients with a mean age of 61.1 ± 4.4 years (52 to 69) and a mean serum PSA level of 10 ± 6.3 ng/ml (1.9 to 26.3). For the TRNB, the mean GS established was 6.52 (4 to 9). Among the 40 patients, 1 (2.5%) had a GS of 4 (2 + 2), 1 (2.5%) had a GS of 5 (2 + 3), 26 (65%) had a GS of 6 (3 + 3), 1 (2.5%) had a GS of 7 (3 + 4), 2 (5%) had a GS of 7 (4 + 3), 6 (15%) had a GS of 8 (4 + 4), 1 (2.5%) had a GS of 9 (5 + 4), and 2 (5%) had a GS of 9 (4 + 5) (Table I).

For the radical prostatectomy specimens, the mean GS was 6.87 (5 to 9). One case (2.5%) had a GS estimated at 5 (2 + 3), 16 cases (40%) had a GS estimated at 6 (3 + 3), 13 cases (32.5%) had a GS estimated at 7 (9 patients exhibited a pattern of 3 + 4, and 4 patients exhibited a pattern of 4 + 3), 7 cases (17.5%) had a GS estimated at 8 (2 cases showed a pattern of 3 + 5 and 5 cases a pattern of 4 + 4), and 3 cases (7.5%) had a GS estimated at 9 (2 cases exhibited a pattern of 4 + 5 and 1 case had a pattern of 5 + 4) (Table I).

For the group of 26 patients with TRNB GS estimated at 6, 11 cases (42.3%) had identical Gleason scores on the needle biopsy and prostatectomy specimens, whereas 14 cases (53.8%) were under-graded (9 cases with radical prostatectomy GS of 7, 4

Table 2. Concordance results of the Gleason score biopsy/radical prostatectomy.

	Concordance	No Concordance	Total
Biopsy GS 4-5	0	2	2
Biopsy GS 6	11	15	26
Biopsy GS 7	1	2	3
Biopsy GS 8	1	5	6
Biopsy GS 9	0	3	3
Total	13	27	40

Table 3. Concordance results of the Gleason score biopsy/radical prostatectomy.

GS Biopsy/ Prostatectomy	Well	Moderate	Poor	Total
Well	0	1	0	1
Moderate	1	22	7	30
Poor	0	6	3	9
Total	1	29	10	40

Table 4. Concordance results for tumor differentiation: biopsy/radical prostatectomy (conventional Gleason grading system).

GS Biopsy/ Prostatectomy	Concordance	No Concordance	Total
Well	0	1	1
Moderate	22	8	30
Poor	3	6	9
Total	25	15	40

cases with a GS of 8, and 1 case with a GS of 9), and 1 case (3.8%) was over-graded (GS on radical prostatectomy estimated at 5) (Table 2). For the group of 7 patients with TRNB GS estimated at 7, concordance with radical prostatectomy specimen GS was observed in only 1 case. There was an under-grade in 1 case (GS estimated at 9 after radical prostatectomy) and an over-grade in 1 case (GS 6 after radical prostatectomy). For the group of 6 patients with TRNB GS estimated at 8, there was concordance with radical prostatectomy specimen GS in only 1 case, an over-grade in 4 cases (1 case with GS estimated at 7 and 3 cases with GS estimated at 6 after radical prostatectomy), and an under-grade in 1 case (GS estimated at 9 after radical prostatectomy). For the 3 patients with TRNB GS estimated at 9, there was an over-grade in all cases (2 case with GS estimated at 6 and 1 case with GS estimated at 8 after radical prostatectomy) (Table 2).

Overall, the preoperative biopsy predicted the prostatectomy Gleason score accurately in 13 cases (32.5%), with the highest accuracy rates obtained for Gleason scores of 6. The Gleason scores were discordant in 27 cases (67.5%), with an under-grade in 45% of cases and an over-grade in 22.5% of cases. The difference between the 2 GS in these cases was not significant (P = 10.6).

Using the conventional Gleason grading system to classify the results obtained on TRNB, this series accounted for 1 well-differentiated tumor, 30 moderately differentiated tumors, and 9 poorly differentiated tumors (Table 3). Comparing the results of TRNB using this classification to the results of radical prostatectomy specimens showed that the concordance highly improved, estimated at 62.5% (N = 25). There was an under-grade in 20% (N = 8) and an over-grade in 17.5% (N = 7) (Table 4). The difference between the 2 GS in different groups was also not significant (P = 1.0).

The majority of tumors were classified as moderately differentiated (score: 5 to 7) on TRNB (75%) as well as on radical prostatectomy specimens (72.5%). The highest accuracy rate was noted in this group (73.3%). Using the modified Gleason grading system for classification, the series of biopsies accounted for 28 well-differentiated, 3 moderately differentiated, 6 poorly differentiated, and 3 undifferentiated tumors (Table 5). The concordance according to the 5 groups was 35% (N = 14), under-staging in 20% (N = 8), and over-staging in 45% (N = 18) (Table 6). The difference between the 2 GS in the 5 groups was not significant (P = 0.40). The majority of patients using this new classification also had well-differentiated tumors (score: 2 to 6) on biopsy (70%) and prostatectomy specimens (45%). The highest accuracy rate was also noted in this group (46.4%) (Table 6).

DISCUSSION

In clinical practice, treatment decisions for prostate cancer depend on many factors, including prostatic biopsy GS, preoperative PSA, and clinical stages [8]. The Gleason score is a system based on tumor architecture. It is determined by adding the scores of the 2 most represented volumetric quotas. The course of action is based on the hypothetical correlation between Gleason score of the biopsy and that of the prostatectomy specimen. Gleason score represents the

Table 5. Tumor differentiation: Biopsy/radical prostatectomy (modified Gleason grading system).

GS Biopsy/ Prostatectomy	Well Differentiated Cancer	Moderately Differentiated (Score: 3 + 4)	Moderately-Poorly Differentiated (Score: 4 + 3)	Poorly Differentiated (Score: 8)	Undifferentiated (Score: 9-10)	Total
Well differentiated cancer (score: 2-6)	13	6	3	5	1	28
Moderately differentiated (score: 3 + 4)	2	0	1	0	0	3
Moderately-poorly differentiated (score: 4 + 3)	0	0	0	0	0	0
Poorly differeniated (score: 8)	1	3	0	1	1	6
Undifferentiated (score: 9-10)	2	0	0	1	0	3
Total	18	9	4	7	2	40

histological assessment of the different cellular differentiation degrees in prostate cancer. The most frequent tumor patterns are regarded as primary grade while those that are next in frequency are regarded as secondary grade. The sum of both patterns enables classification on the basis of differentiation and a good prognosis of patterns (a good prognosis and good cellular differentiation yields a GS of 2 to 5, a medium prognosis and moderate cellular differentiation a GS of 6 to 7, and a bad prognosis and bad cellular differentiation a GS of 8 to 10) [2,9]. Recent studies have focused on the discordance in GS between TRNB and radical prostatectomy specimens. Global discordance varies from 31 to 72% [3,5,6,9-18] (Table 5). Under-staging ranges from 26 to 46% [3,5,6,9-13,16,19,20]. Our results accord with those reported in medical literature.

Several factors could explain this discordance and must be taken into consideration when the treatment decision is based on Gleason score:

- The prostatic biopsies are heterogeneous and do not fully reflect the real tumor architecture.
- The reproducibility of the GS is low during iterative analysis by the same or by other pathologists [2,21].
- Other factors, including PSA level, prostate volume, size of the tumor mass, and preoperative clinical stage, are known to be associated with discordance of the GS between TRNB and radical prostatectomy [22,23].

The clinical implication of this discordance is very important.

Table 6. Concordance results and tumor differentiation: Biopsy/radical prostatectomy (modified Gleason grading system).

GS Biopsy/ Prostatectomy	Concordance	No Concordance	Total
Well differentiated (score: 2-6)	13	15	28
Moderately differentiated (score: 3 + 4)	0	3	3
Moderately-poorly differentiated (score: 4 +)	0	0	0
Poorly differentiated (score: 8)	1	5	6
Undifferentiated (score: 9-10)	0	3	3
Total	14	26	40

Indeed, an under-grade on biopsy should not have any impact on treatment decisions, especially if the patient does not change groups. However, in some cases, the therapeutic attitude may

be different between 2 very close GS. For example, a patient with a GS of 8 will not be a candidate for prostatectomy while those with a GS of 7 may benefit from surgery. Therefore, many studies focused on different factors causing this discordance between TRNB GS and RP GS and the ways to overcome these obstacles.

Because of the heterogeneity of prostatic biopsies, some series studied the impact of increasing the number of biopsy cores to decrease the discrepancy of the 2 GS. Kahl et al. found that an extended biopsy scheme with cores numbering more than 12 can help to acquire more accurate GS than a biopsy scheme with cores numbering less than 12 [24]. Moon [25] suggests that at least 13 cores should be taken during TRNB and more aggressive biopsies should be performed at the apex and of hypoechogenic lesions for more precise GS, preoperatively. San Francisco et al. [26] compared 2 groups of patients with a different number of biopsy cores who underwent radical prostatectomy: A group of 340 patients (biopsies with 9 cylinders or less) and a group of 126 patients (biopsies with 10 cylinders or more). They found a concordance with 67 and 76% of cases, respectively. Thus, they concluded that increasing the number of biopsy cylinders better defines the final GS after radical prostatectomy. Divrik et al. [27] also showed that an extended biopsy scheme beyond its superior diagnostic capability also improves the concordance of Gleason scores of needle biopsies and radical prostatectomy specimens. However, Thickman found that there is no interest in increasing the number of carrots to improve the prediction of the GS [15].

Arrabal-Polo et al. [28], comparing 2 groups of patients who underwent radical prostatectomy after sextant prostate biopsy in 98 patients (64% correlation) and 12 cylinder in 30 patients (60% correlation), also didn't find a significant difference in GS correlation.

For the other factors causing the GS discordance, Nayyar et al. reported that upgrading the GS was not associated with a high PSA level [29], whereas Dong et al. reported that a PSA level greater than 5.0 ng/ml is associated with upgrading the GS [30]. Freedland et al. and Tilki et al. also reported that a high PSA level is associated with upgrading the GS [31,32]. In our study, however, we did not determine the PSA level to be a predictive parameter of upgrading.

Another reported factor involved in GS discordance is the prostate volume. Moussa et al. reported that smaller prostate volume is associated with upgrading the GS [33]. Furthermore, Turley et al. reported that patients with a prostate volume $\leq$ 20 cm^3 had more than 5 times the risk of upgrading compared with patients with a prostate volume $\geq$ 60 cm^3 [34]. In Moon's study [25], patients with a prostate volume $\leq$ 36.5 cm^3 had a higher risk of upgrading after radical prostatectomy. Different results have been found by different studies, and until now the accuracy of GS established on TRNB is still problematic, especially since therapeutic attitude is often based on this GS. The largest discrepancies in GS were found for well-differentiated tumors [14,21,35,36], as in our study. It is worth mentioning that patients with a GS of 7 (78%) show the highest percentage of concordance, patients with a GS of 6 or less show the highest percentage of under-staging, and cases with a GS of 8 to 10 (35%) show the highest percentage of over-staging [6]. Garnett found a concordance of 30% and noted that the prediction of the GS is more accurate when the scores are high [37]. Prost et al. [18] reported the same conclusions; the correlation was 54, 73, and 100%, respectively, for groups of tumors well, moderately, and poorly differentiated. The same conclusions were reported by Köksal and Rodríguez Faba [9,38].

In our study, the concordance between TRNB GS and RP GS was 32.5% for a GS of 6 and 7, and the correlation was around 70%, a similar value to that seen in Algaba's and Bostwick's studies [10,16, 35]. In contrast to the other studies [13,18, 37], in our series, the over-grading was more frequent for a higher GS, estimated at 66.6% for a GS of 8 and 100% for a GS of 9.

The classification of patients into 3 distinct groups (well, moderately, and poorly differentiated tumors) allows better concordance between the TRNB results and RP results. Using this conventional Gleason grading system, the correlation in our series was highly improved with 62.5% of patients remaining in the same group after radical prostatectomy. Similar results were found by Cookson et al. [17] who reported a high correlation of 80% between biopsy and final specimen using this classification. This correlation was of 72.6% in the Prost [18] series. Table 7 resumes the correlation of Gleason scores between prostatic biopsy and radical prostatectomy specimens in the literature. In our series we also studied the correlation between the TRNB results and RP results using the modified Gleason grading system with 5 groups of tumor differentiation. We found that the correlation did not significantly improve (in only 35% of cases) with this new classification.

There are many limitations in our study. First, this is a single institute, retrospective study dealing with a relatively small population. Second, this study did not identify the relation between "no concordance" and clinical and biochemical factors such as the PSA level, the free PSA, and prostate volume. Third, because the biopsy strategy was not consistent and because of the number of urologists, we are not sure that the biopsy specimens were taken at exactly the same location in every patient.

And finally, the biopsies and the radical prostatectomy specimens were examined by only 1 pathologist, which allows a uniform interpretation of the results but depends also on the pathologist's experience. Our result implies that more than half of the patients diagnosed with a GS of 6 by TRNB had more

Table 7. Literature review: Correlation of Gleason scores between prostatic biopsy and radical prostatectomy specimens.

Author	Number of Patients	Concordance (%)	Under-staging (%)	Over-staging (%)
Spires [14]	67	58	4.5	-
Bostwick [16]	316	35	-	-
Thickman [15]	124	28	-	-
Cookson [17]	226	31	54	15
Prost [18]	84	37	-	-
Salomon [13]	180	38.8	43.8	17
Kvale [5]	1116	53	38	9
Noguchi [12]	222	36	46	18
Rajinikanth [6]	1363	69	26	5
Altay [11]	61	45.9	42.26	11.84
Montesino [3]	173	52.6	32.4	15
Rodriguez Faba [9]	129	55.8	37.2	7
Algaba Arrea [10]	215	49.7	38.6	11.6
Our series	40	32.5	-	-

aggressive cancer than they seemed to have. Therefore, even if patients are diagnosed with moderate-risk prostate cancer after TRNB, physicians should always consider parameters that can be predictive of over-grading. This awareness affects treatment policy, particularly the watchful waiting criteria.

CONCLUSIONS

In this study, we have noticed that the accuracy of Gleason scores determined by transrectal needle biopsy in patients with prostate cancer seems to be very low. The greatest correlation percentage is found in tumors showing a moderated degree of cellular differentiation (GS of 5 to 7), whereas the over-grading was more frequent for a higher GS.

The classification of patients into 3 distinct groups (tumors well, moderately, and poorly differentiated) increases the correlation between the biopsy GS and final score. The modified Gleason grading system didn't reflect the definitive GS. In practice, physicians must be aware of the limits of the GS established on biopsy and clinical and biochemical parameters must be used with the biopsy GS to provide better information concerning prognosis, and the most adapted therapeutic option for the patient and his prostatic carcinoma.

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Enterovesical Fistulae in Crohn Disease: A Series of 7 Cases

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ABSTRACT

Background: Crohn disease is a chronic inflammatory disease of the bowel that may affect the urinary system.
Objective: The authors review their experience, evaluating the incidence, and examining the various modalities employed in the diagnosis and treatment of patients with Crohn disease complicated by fistulae.
Methods: Of 541 patients with confirmed Crohn disease treated and followed in the Department of Gastroenterology in La Rabta University-Hospital in Tunisia between 1995 and 2010, 7 patients (1.3%) were found to have enterovesical fistulae.
Results: A fistula was diagnosed preoperatively in 6 patients. Six patients underwent resection of the diseased intestinal segment with bladder repair, and a temporary stoma in 1 case.
Conclusion: Enterovesical fistulae complicating Crohn disease is often clinically suspected preoperatively. Treatment, based on resection of the diseased bowel and extirpation of the fistula, can be accomplished with minimal morbidity and mortality.

INTRODUCTION

Crohn disease (CD) is a chronic inflammatory disease of the digestive tract that may reach any segment of it. Although internal fistulae complicate 20 to 40% of CD [1-3], enterovesical fistulae are rare (less than 5%). They are mostly symptomatic and occur after several years of CD evolution. They are usually poorly tolerated and require surgical treatment [1].

We discuss through our series and literature review the natural history, clinical features, diagnostic tools, and the treatment of enterovesical fistulae secondary to CD.

PATIENTS AND METHODS

We reviewed all patients with a confirmed CD followed in the Department of Gastroenterology in La Rabta Hospital-University from 1995 to 2010. Medical records were abstracted for patient demographics, presenting symptoms, diagnostic tests, and management. We also determined CD behavior and location according to Montreal CD classification [4].

RESULTS

During the study period, 541 cases of CD were reviewed. Seven of them had an enterovesical fistula with an incidence of 1.3%, which were 5 males and 2 females with a median age at diagnosis of 30.5 years (19 to 49 years). The median period between CD diagnosis and fistulae appearance was 36 months (0 to 180). Fistulae were inaugural of CD in 3 cases. None of the patients had previously received immunosuppressive therapy or had a history of previous surgical treatment for CD. The location of CD was ileocolonic in 5 cases and ileal in 2 cases (including 1 extensive ileal disease and 1 localized ileal disease). Extensive ileal involvement was noted in 4 patients. Clinical disease activity was severe in 2 cases. Concomitant ileal stenosis was present in 4 patients.

Of our patients, 6 were symptomatic and presented with pneumaturia (N = 4), fecaluria (N = 2), and recurrent urinary tract infections (N = 2). None of them presented with hematuria. One fistula was identified incidentally during contrast radiology in 1 case and 1 fistula was identified during a laparotomy for CD. Preoperatively, the diagnosis of fistulae was confirmed

KEYWORDS: Enterovesical fistula, Crohn disease, bladder, inflammation

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by barium enema examination in 3 patients, computed tomography (CT) scan in 3 patients, and MRI in 1 patient. The most helpful preoperative diagnostic examination was contrast-enhanced CT, which confirmed free air in the bladder and direct communications between the bowel and the bladder (Figure 1). The opening fistula was on the bladder dome in all cases (Figure 2). Four patients had associated internal fistulae: entero-enteral fistula (N = 3) and entero-colic fistula (N = 3). Three patients had internal perivesical abscess necessitating percutaneous drainage and large spectrum antibiotherapy.

Five patients were treated by resection of the area of macroscopically diseased bowel with primary anastomosis and pinching off the dome of the bladder. The bladder defect was repaired in 2 layers using an absorbable suture material and an indwelling Foley catheter that was left in situ for an average of 2 weeks after operation. None of the patients underwent partial cystectomy. In one patient with a complex fistula from the ileum and the colon to the bladder, a colectomy and ileorectal anastomosis was performed, which was protected by a temporary loop ileostomy. One patient refused any surgical treatment.

There were no bladder leaks and no anastomotic leaks. There were no perioperative deaths. After surgery, patients were then treated with azathioprine. With a mean follow-up of 52 months (2 to 184), there has been no fistula recurrence in all operated cases.

Figure 1. A CT scan of the pelvis showing gas within the bladder, confirming the presence of an enterovesical fistula. An inflammatory mass (arrowhead) deforming the right posterior wall of the bladder.

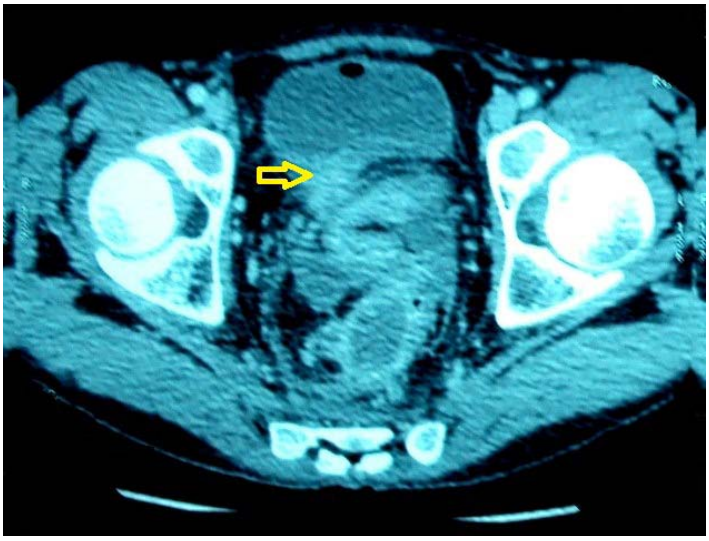
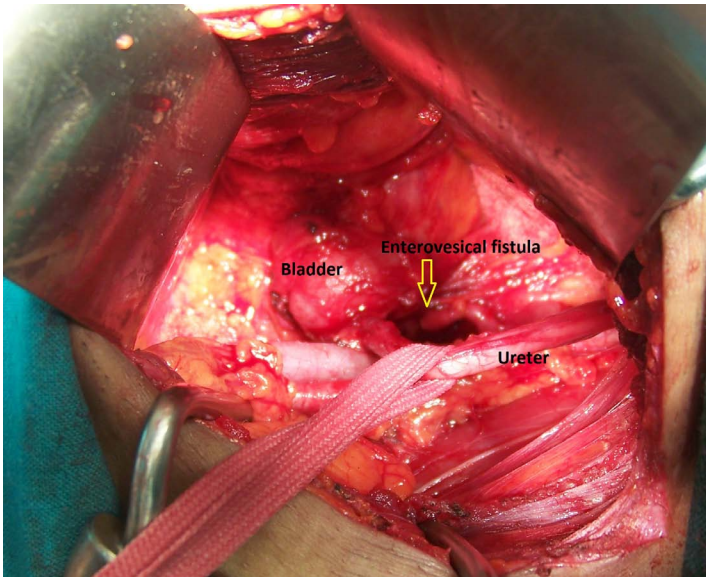


Figure 2. A perioperative view showing an enterovesical fistula between the bladder dome and the ileum (arrowhead).



DISCUSSION

CD is a common cause of fistulae from the gastrointestinal tract to the urinary system [1,5,6]. They occur in up to 8% of patients with CD [7]. These fistulae originate most commonly from the ileum (64%), colon (21%), and rectum (8%)[1,5]. In the series of Saint-Marc, 3% of 589 patients with CD had an enterovesical fistula [1]. It was 6.8% in Pechan's [8] series but only 1.3% in our series. In the series of 78 patients from the Mayo Clinic, the bladder was the primary point of interest (88%) [5]. Most patients in the present series were male.

The pathogenesis of fistulae associated with ileo-colic or sigmoid colon (anatomic proximity to the bladder) included inflammatory processes secondarily extended to the bladder, with or without suppuration and abscess formation that accompanied the establishment of these fistulae [6,10]. They usually affect the bladder dome [1], as in our series. CD can also cause an inflammatory pseudo tumor of the bladder [11,12].

The occurrence of enterovesical fistulae is usually seen in severe and evolving CD (4 in our series), and it is frequently associated with the accentuation of gastrointestinal and infectious symptoms [1,13]. Three of our patients had a deep abscess at diagnosis. Enterovesical fistulae can complicate a known CD or reveal it [12,13] as with 2 of our patients who were not known to have CD. Fistulae may occur after bowel resection for CD as a complication of an anastomotic leakage and abscess [14]. Usually

these fistulae will resolve with conservative management. Very rarely, enterovesical fistulae may be associated with malignancy that complicates CD [15], especially when fistulae involve the base of the bladder.

The diagnosis of enterovesical fistulae is often clinical. Fecaluria and pneumaturia are the most evocative signs (≈70%) but not constant [2,13,16]. Pyuria is very common; chronic pyuria with positive urine cultures in young adults should suggest an enterovesical fistula [6,13,17]. Hematuria is less common [12,18,19]. Thus, any patient with CD having a history of pneumaturia, or males with recurrent urinary tract infections must be assumed to have an enterovesical fistula until proven otherwise. Some authors describe a case of enterovesical fistulae in a patient with CD that presented exclusively as urinary symptoms manifesting as bladder tumors [12] or with Fournier's gangrene [20]. Patients may be totally asymptomatic [6], as with 2 patients in our series.

The fistula may be identified by cystography or intravenous urography [13,16]. The visualization of the fistula at cystography is not always easy to obtain [5]. This emphasizes the importance of locating the fistula in the small bowel and colon by barium or Gastrografin enema examination [3]. Barium or Gastrografin enema and colonic endoscopy allow direct visualization of the fistula. Demonstration of barium in the bladder will also present fistulae, and it will also define the extent of intestinal disease and detect other internal fistulae [1,10,13,14,16].

CT is a sensitive and noninvasive method of evaluating the bladder and can be used to identify patients in the prodromal stage who are at risk of developing enterovesical fistulae [21]. When occurring, CT scan may show 2 aspects: focal bladder-wall thickening adjacent to an extravesical soft tissue mass and/or focal bowel-wall thickening and fistulae formation with intravesical air and associated focal bowel-wall thickening and/or extravesical soft tissue masses [21]. CT scan may also show an intravesical fluid level or an associated abscess [1,13,16]. Magnetic resonance imaging (MRI) is more sensitive than CT in detecting enterovesical fistulae [22].

Cystoscopy is the best method of investigation since it makes the diagnosis in 82.5 to 100% of cases [1,13,16,23]. It shows the ureters and the fistulous orifices but rarely can find lesions of the bullous edema, at the bladder dome [1,13], or a tumoral lesion [18]. In our series, cystoscopy was not indicated to make the diagnosis of enterovesical fistula.

Actually, the most useful exams for diagnosis are cystoscopy (74%) and CT scan (52%) [24]. Enteral administration of indocyanine green solution was indicated to detect enterovesical occult microfistulae in patients with CD before the fistulae had become readily apparent. After oral or rectal administration of the indocyanine green solution, urine was collected and examined using a colorimeter to check for contamination with indocyanine green. The sensitivity of this test is about 92%, higher than other conventional examinations [25].

The management of internal fistulae has changed substantially over the last 2 decades. Resection was previously the only treatment, but now more conservative alternatives, including medical therapy and surgical repair, are available [14]. However, the efficacy of medical therapy for internal fistulae has yet to be shown in randomized, controlled trials. When treating Crohn urodigestive fistulae, practitioners oppose supporters of medical treatment first to those of surgical treatment.
Medical treatment of fistulae with antibiotics and/or immuno-modulators (corticosteroids, azathioprine, mesalamine, and cyclosporine) has been used successfully, but the small sample size did not allow accurate conclusions. However, the potential of infliximab was already mentioned in 2002 [5]. Since then, other authors have proposed the use of infliximab, after formally eliminating tuberculosis, in the initial treatment of CD fistulae, leaving surgery as the secondary treatment of strictures or abscesses [3,26,27].

Medical treatment could be attempted before surgery and can cause lasting relief of urinary symptoms and closure of the fistulae [13,16,28,29], but medical treatment failure is frequent [10]. The discomfort associated with the existence of persistent urinary fistulae (fecaluria), associated complications of CD (intestinal obstruction, abscess, and abdominal mass) [1,13,16,17], or the threat to renal function in chronic infection [1,13,30] often lead to surgery as a primary treatment. The indication for surgery in our patient was the presence of large enterovesical fistulae causing pneumaturia and fecaluria.

Current approaches associate antibiotics, total parenteral nutrition, and various combinations of immuno-modulatory agents. However, only a minority of fistulae subsides under this treatment [26]. Thus, surgery remains the treatment of choice [31]. The principles of surgery are simple: intestinal resection (ileal resection or a subtotal colectomy if the sigmoid colon is involved) and closure of the bladder orifice [1,10,13,16,17,30]. Surgery rarely includes partial cystectomy [32]. The extent of bowel resection should be tailored to actual lesions from CD [13]. Strictureplasty [33] is occasionally appropriate when the ileal segment is short or if a patient has had multiple, previous small bowel resections. An enterostomy may be necessary to prevent the risk of postoperative digestive fistulae because of the importance of local lesions (abscesses), the extension of CD, medical treatment prior to surgery (corticosteroids and immunosuppressants), a patient's very poor general condition, and the large number of associated fistulae complicating the surgical procedure [1,2,16]. It is almost a 2- to 3-month temporary enterostomy [1]. In our case, treatment consisted of an ileal resection with or without ileostomy and bladder fistulae closure.

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The bladder defect must be properly closed after limited excision of inflamed tissues [1,10,13,16]. The bladder defect must be closed primarily in 2 layers using absorbable sutures with omental patches, as reported by Gruner [34]. The bladder drainage by a urethral catheter is essential for a variable duration according to the authors, but more than 7 days [1] and until a postoperative cystogram has shown that the bladder defect has healed satisfactorily [10]. No serious postoperative complication was reported [8].

Postoperative enterovesical fistulae may occasionally occur due to an anastomotic leak [1,2,10,16]. This is usually associated with an abscess, which communicates with the bladder. Most of these fistulae close spontaneously with bladder drainage but if the fistula persists the anastomosis should be resected and the defect in the bladder closed over an indwelling catheter. There is very little evidence to justify the use of parenteral nutrition in enterovesical fistulae [10].

The risk of recurrence is very low [6]. Maintenance therapy may be required in some cases with severe relapse and complicated and extensive involvement to prevent fistulae recurrence after surgery. The question of the appropriate drug is still debated: thiopurine, anti-TNF, or infliximab [8,23].

CONCLUSION

The incidence of enterovesical fistulae in CD is low. The pneumaturia and fecaluria are the most significant symptoms for their presence. A CT scan is a very useful preoperative diagnostic tool for identifying gas within the bladder. Barium or Fastrografin studies are useful also. Treatment, based on a resection of the diseased bowel and extirpation of the fistula, can be accomplished with minimal morbidity and mortality.

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Percutaneous Dilatation of Non-malignant Ureteroenteric Anastomotic Strictures in Patients with Urinary Diversion After Cystectomy for Bladder Cancer: 7 Patients

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ABSTRACT

Background: The management of ureterointestinal stricture in patients who have undergone urinary diversion can be challenging. Endourological techniques have been increasingly used in recent years for such strictures.
Objectives: We report our experience and evaluate our results on balloon antegrade dilatations for benign ureteroenteric anastomotic strictures after total cystectomy and urinary diversion by ileal conduit.
Patients and Methods: Between December 1990 and May 2009, 8 balloon dilatations were performed on 7 patients with a mean age of 56.6 years (range: 50 to 72) to treat ureterointestinal strictures. Strictures were dilated percutaneously via the antegrade approach under fluoroscopic control. A ureteral multi-hole catheter was left for 6 to 8 weeks. Success was defined as radiological resolution of obstruction and the ability to recover normal activity in the absence of flank pain, infection, or the need for ureteral stents or nephrostomy tubes.
Results: The development of strictures occurred a mean of 4.5 months after urinary diversion. Eight renal units were treated (5 left, 3 right), including 1 bilateral procedure. There were 6 complete and 2 partial strictures. The operative time did not exceed 45 minutes. No major complications were encountered during or after these procedures. The overall success rate was 43%. Three patients required open reimplantation. Six of 7 patients showed satisfactory outcomes and 1 patient was lost to follow-up.
Conclusions: Percutaneous balloon dilatation of benign ureteroenteric anastomotic strictures, after radical cystectomy and urinal diversion by ileal conduit, is a minimally invasive and effective treatment option providing durable results. Based on these results, we believe that the procedure should be considered as a first-line treatment, as surgical reimplantation is reserved for failure. The selection of patients with the most favorable prognostic factors leads to excellent results.

INTRODUCTION

The incidence of secondary ureterointestinal anastomosis stricture (UAS) after urinary diversion ranges from 1 to 14% [1-3]. The highest rate of this stenosis was reported with ureterosigmoidostomy (22%) [4]. These strictures are predisposed to numerous complications, including recurrent urinary infection, sepsis, stone formation, and renal failure that is often clinically silent [5,6]. The management of these UAS presents a particular challenge for urologists.

The reference standard and most effective treatment of these strictures is open surgical repair (open ureteral reimplantation), with a success rate greater than 80% [7,8]. However, it is an invasive, difficult procedure with considerable morbidity and prolonged hospitalization [7-10]. In recent decades, endoscopic methods have been established as alternative treatments.

Advances in endourological techniques and instrumentation as well as in interventional radiology have led to a minimally

KEYWORDS: Urinary diversion, ileal conduit, ureteroenteric anastomosis, percutaneous dilatation, surgical anastomosis
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invasive approach to UAS, resulting in decreased morbidity, operative time, hospitalization, and cost compared with open reconstruction [5,11]. The long-term success rate after conservative treatment varies markedly, ranging from 30 to 100% with different modalities [10,12-16]. In this paper we evaluate our experience with balloon dilatations by interventional radiology access of 8 benign UAS in 7 patients, with total cystectomy and urinary diversion by ileal conduit.

PATIENTS AND METHODS

This retrospective study was conducted at the Department of Urology and the Department of Radiology at La Rabta Hospital-University, Tunis, Tunisia between December 1990 and May 2009. We reviewed the clinical and radiological records of all patients who underwent percutaneous antegrade balloon dilatation of UAS. All patients had undergone total cystectomy and urinary diversion by ileal conduit for muscle-invasive bladder transitional cell carcinoma. The ureter was diverted to an isolated segment of terminal ileum. Patients with strictures due to progressive neoplasia and those who underwent pelvic or abdominal radiotherapy were excluded.

The preprocedural evaluation of patients was initiated with a clinical examination, an abdominal ultrasonography, and laboratory analyses (urea, creatinine, electrolytes, and urine cultures). The evaluation of coagulation parameters was also performed. Coagulation tests included prothrombin time, International Normalized Ratio, activated partial thromboplastin time, and platelet count. Abnormal results were corrected when necessary with platelet or fresh frozen plasma transfusion or an IV of vitamin K. We performed a computed tomography (CT) scan and often "Bricker-oscopy" in order to rule out malignancy of the ureteroileal anastomosis.

A percutaneous nephrostomy was performed in all patients under local anesthesia and sonographic/CT scan guidance to relieve severe obstruction, evaluate obstructed kidney function, and allow subsequent endourological procedures. The preoperative assessment was comprised of antegrade opacification via the nephrostomy tube, and helical CT to assess the length and severity of the stricture and to assess the spatial relationship of the stricture to adjacent organs and vascular structures. Once the diagnosis of UAS was confirmed, the nephrostomy tract was maintained. The treatment of ureteroenteric anastomotic strictures consists of dilatation with placement of a temporary catheter through the UAS.

TECHNICAL ASPECTS OF INTERVENTIONAL PROCEDURES

All operations were performed on patients with sterile urine. They received antibiotic prophylaxis—usually a third generation cephalosporin with gentamycin—1 hour prior to the procedure and for 48 hours after the procedure. Under sedation with intravenous analgesics and minor tranquilizers, the patient was placed in an oblique supine position to expose percutaneous nephrostomy. The technique included the following steps, which were all fluoroscopically monitored in ambulance conditions:

- After removing some urine, contrast media was injected in order to perform antegrade urography and localize the stricture.
- A hydrophilic guide wire was then introduced as a guide wire, passed through the stenosis, and it was looped in the ileal conduit (Figure 1).
- A multipurpose catheter was advanced over the guide wire up to the stoma of the ileal conduit and was extended outside.
- The hydrophilic guide wire was then replaced with a stiff guide wire, which was extended from the site of

Figure 1. Guide wire extended from the site of the kidney incision outside of the ileal stoma.

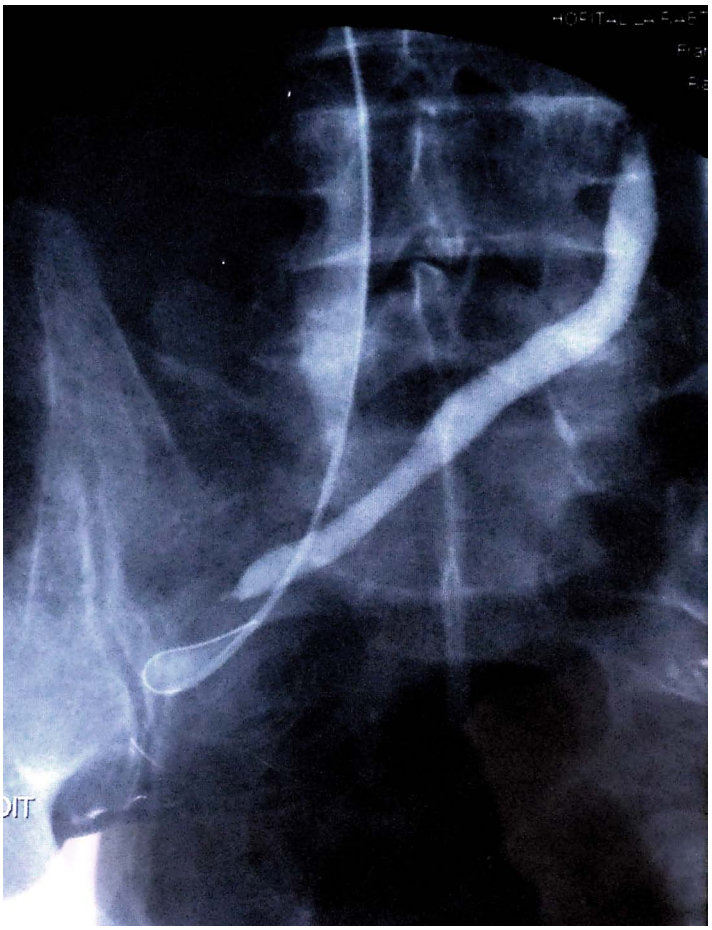


Figure 2. Post-percutaneous dilatation nephrotomography.

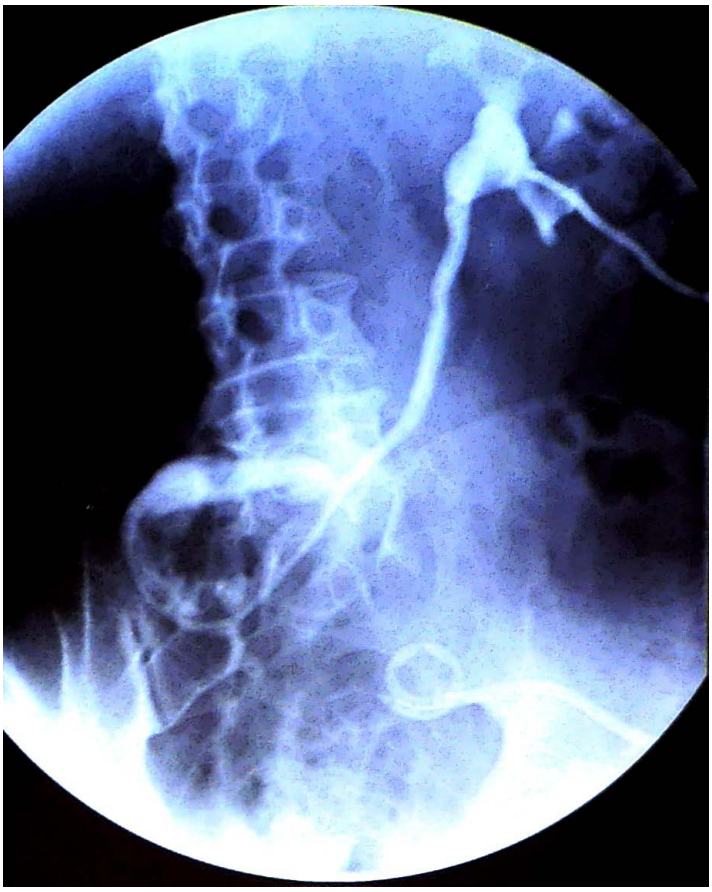
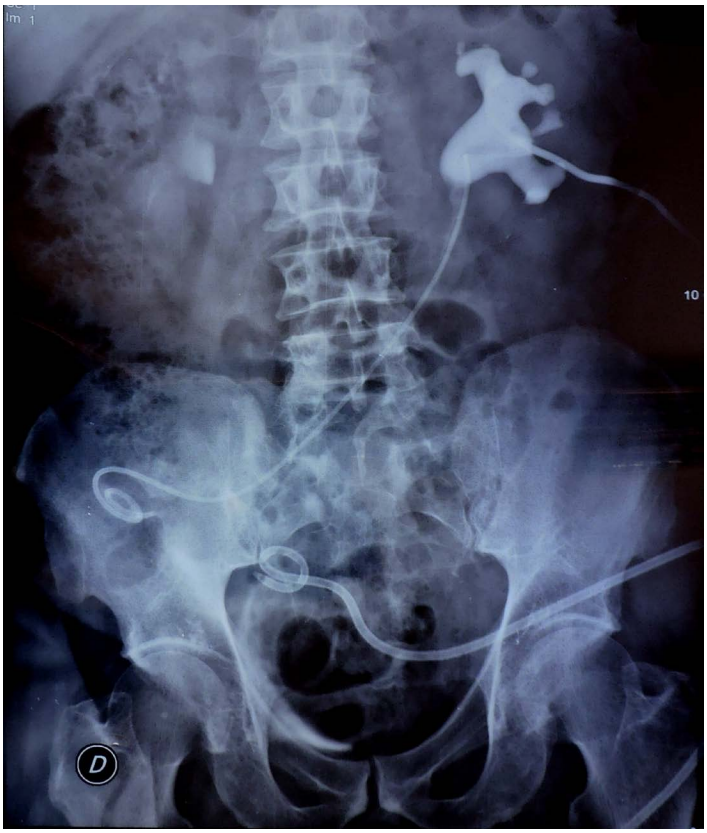


Figure 3. Placement of a double-J catheter in antegrade fashion, through the UAS.

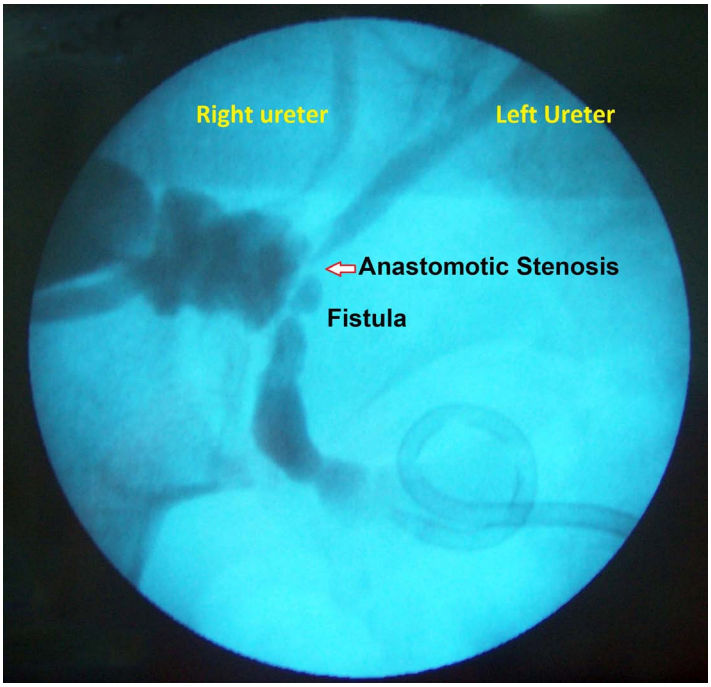


nephrostomy to the ileal stoma. Afterwards, the balloon catheter was advanced over the guide wire in a retrograde fashion—through the stoma of the ileal conduit—up to the site of the stenosis.

- After adequate positioning, the distending balloon was inflated with diluted contrast solution, pending complete expansion, using a manometer syringe. A plane contour distended balloon, less than 10 to 20 atm, was deposed in situ for 3 to 5 minutes.
- If the stricture had remained as a notch on the inflated balloon, dilatation would be repeated several times until the notch had disappeared.
- We applied the contrast through the catheter immediately after recanalization to inspect the anastomoses' permeability (nephrotomography) (Figure 2).
- The balloon was then removed and a 20 Fr or 22 Fr multihole double-J catheter is inserted in a retrograde fashion through the stricture and left in the ureter as a stent (Figure 3).
- The double-J catheter was maintained in place for a 6- to 8-week period.
- Nephrostomy tubes were left in the kidney 7 days after the procedure for eventual repeated recanalization.
- If a smooth urine flow had been confirmed, the nephrostomy catheter would be clamped and removed if the patient passed a further 48 hours without fever or pain.

Total operative time was less than 45 minutes in all cases and patients were generally discharged on the third to fourth day. Six to eight weeks after this procedure, the stent is removed. In the following course, patients were controlled monthly in the first 3 months and twice yearly thereafter. The examination included a standard history and physical examination, kidney ultrasonography (US) or IVU and/or computed tomography, and biochemistry parameters for serum urea and creatinine. The treatment was considered successful if there was no further evidence of obstruction on radiological studies; kidney function parameters remained in/returned to normal levels; and the ability to return to full activity in the absence of flank pain, infection, or the need for ureteral stents or nephrostomy tubes. Possible prognostic factors predicting outcomes were evaluated using the chi-square test for categorical variables and the

Figure 4. Percutaneous opacification: Left UAS with anastomotic fistula (arrow).



Student *t* test for continuous data. A $P \leq 0.05$ was considered statistically significant.

RESULTS

During the period of study, 155 ileal conduit (Bricker) urinary diversions were performed in our department; thus, the incidence of this complication is 4.5%. All of these patients were men, ranging in age from 50 to 72, with a median age of 56.6 years. The mean interval between surgery and the treatment of stenosis was 4.5 months (range: 3 to 10 months). The circumstances of discovery varied. The most frequent presenting complaint was low back pain (N = 2), followed by urinary tract infections (N = 1). Renal failure was detected in 2 patients (1 patient had a solitary functioning kidney and the other had bilateral anastomotic strictures). Three patients had no complaints and were diagnosed at routine radiographic follow-up. In all patients, some degree of hydronephrosis was present. There were 6 complete and 2 partial strictures. Patient characteristics and their outcome are summarized in Table I. Strictures involved the left ureter in 4 cases, the right ureter in 2 cases, and both in 1 case. One patient presented an anastomotic fistula (Figure 4). Mean stricture length was 1.2 cm (range: 0.5 to 2).

Table 1. Patients with ureteroileal (UI) strictures.

Sex/Age	Side	Time to Onset	Length (cm)	Results	Follow-up (mo)	Treatment	Outcome/End of Study
M/56	left	3	2	failure	11	ORA	died with normal kidney function parameters
M/75	right	9	0.5	success	17	PAD	asymptomatic with poorly functioning renal unit
M/78	right	4	1	success	6	PAD	died with normal kidney function parameters
M/62	left	7	0.5	failure	-	ORA	-
M/76	left	3	2	failure	5	NFI	died with multiple metastasis and renal failure
M/61	left	4	0.7	success	20	PAD	still alive
M/50	bilat	10	1-2	failure	23	ORA	still alive, with bone metastasis

ORA: Open revision of anastomosis (repeat Briker)
NFI: No further interventions
PAD: Percutaneous antegrade dilatation

Under direct fluoroscopic control, the guide wire could be passed through the stricture in only 3 patients. Three balloon dilatations of ureteroenteric strictures, with the placement of a temporary catheter, were performed in 3 out of 7 patients. Improvement in the drainage of contrast medium through the ureteroileal anastomosis was recognized after performing balloon dilatation. In these 3 patients, we had success in recanalization of UAS. Primary success rates of the procedure were only 43%. All failures involved left-sided ureterointestinal strictures.

Perioperatively, minimal extravasation was documented in 1 case. However, no urinoma was diagnosed postoperatively by sonographic control. No significant complications from the ureteral balloon dilatations and/or anterograde insertion of a nephrostomy catheter were observed intraoperatively or postoperatively. No specific medication was administered except antibiotics when necessary. The average postoperative hospital stay was 3.7 days with no major complications. In one case, a ureteroenteric fistula healed with external drainage and prolonged stenting. After the removal of the ureteral stent, additional dilatation was not necessary in any patient.

Failure was managed by open surgical revision in 3 cases and abstention because of poor general health conditions in 1 patient. Follow-up data after stent removal were available for all stenoses but 1 [5-23]. No stenoses recurred. For 1 patient (1 stricture) there was lack of follow-up information after the last control and removal of the catheter. Kidney function parameters remained postoperatively within normal limits. Excretory urography (IVP) showed prompt functioning. Furosemide renography showed no evidence of obstruction. The patient, who underwent a bilateral endoureterotomy procedure, had a non-obstructed right kidney but a poorly functioning, obstructed left kidney at the last follow-up visit. However, he was asymptomatic, and he elected not to pursue further treatment. Two patients died of unrelated causes, including myocardial infarction and pneumonia at 6 and 11 months, respectively, after successful management. One patient died of metastatic disease. Only 2 patients are still alive. Patient age and gender, side and length of the stricture, and interval between urinary diversion and UAS were not analyzed as possible prognostic factors because of the little number of patients.

DISCUSSION

UAS are the most frequent causes of gradual deterioration of renal function after urinary diversion [5,6] due to complete obstruction of the interior lumen and consecutive progressive hydronephrosis [17]. The apposition of 2 different types of mucosa (intestinal and ureteral) and technical defects that cause ureteral ischemia are considered the 2 main causes of such strictures [5]. Moreover, the tissue incompatibility causes transitory epithelial metaplasia, which implicates ureteral cicatrization [17]. Other predisposing factors have been identified, such as urinary extravasation and infections [5]. Important factors for avoiding UAS include meticulous surgical technique involving mobilization of the sigmoid mesentery cephalad to the origin of the inferior mesenteric artery to avoid obstruction of the left ureter, and preservation of the ureteral adventitia to optimize blood supply and the use of soft stents postoperatively [18,19].

In most cases, strictures developed within 1 to 3 years of the urinary diversion [20]. In our series, the strictures developed early (mean: 4.5 months) after ileal conduit urinary diversion. Symptomatic ureteral dilatation requires prompt investigation [21]. Occasionally, patients remain asymptomatic, and long-term imaging demonstrates auto-nephrectomy. Therefore, careful postoperative follow-up is essential, particularly in ureteral units that demonstrate some degree of dilatation on the immediate postoperative IVP [21]. These strictures may be associated with tumor recurrence [5]; thus, repeat evaluation with CT, urinary cytology, and possibly endoscopic visualization would help to identify any recurrent malignancy [11].

The major goal of treatment of a UAS is to restore adequate urine drainage from the kidney without using indwelling devices such as ureteral stents or nephrostomy catheters [20]. Open revision of the anastomosis remains the standard in treating UAS [22-24] with a reported success rate of 89% [7]. However, open surgical revision can be difficult to perform, with significant intraoperative and postoperative morbidity, due to dense adhesions caused by previous surgery or fibrosis arising from radiotherapy [22].

Recent advances in cutting devices and stent material have given the urologist less-invasive therapeutic options that have shown positive success with stricture management. Particularly, interventional radiology methods in the treatment of UAS offered minimal invasive approaches in ambulance conditions with the possibility of repeated procedures and radicalization [17]. Currently, conservative techniques are preferred as initial therapeutic options because of decreased associated morbidity, operative time, hospitalization, and cost [12]. First-line endoscopic treatment is often indicated, particularly in obese patients with a poor general state and patients who have already had several surgical procedures [25]. Subsequent open revision does not seem to be compromised by initial endourological procedures [11]. These results demonstrate that there are measurable differences between hydrophilic guide wires based on guide wire characteristics and operator preference

Various endourological techniques have been described for AUS, including implantation of a double-J catheter or self-expandable metallic stent, cold knife or electrosurgical endoureterotomy,

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Table 2. The results of endourological management of ureterointestinal strictures.

References	Population	Treatment	Success (%)	Follow-up (mo)
Touiti [5]	6 strictures	Acucise	50	16
Kramolowsky [7]	7 strictures 9 strictures	endoscopic incision open revision	71 89	14
Bierkens [9]	15 strictures	cold-knife incision	53	32
Meretyk [10]	14 strictures 21 strictures	electrocautery electrocautery cold knife balloon dilatation	57 39 68 26	28.6 36 12 36
Watterson [11]	24 strictures	Holmium:YAG laser	70.8	22.5
Cornud [12]	33 strictures	electroincision	71	> 12
Lin [14]	10 strictures	Acucise endoureterotomy	30	24
Shapiro [16]	37 strictures	balloon dilatation	16	12-72
Preminger [28]	6 strictures	Acucise endoureterotomy	50	7.8
Poulakis [29]	43 strictures	cold-knife incision	60.5	> 36
Wolf [30]	30 strictures	various methods	50	23
Lovaco [31]	25 strictures	intraluminal invagination incision	80	51
Laven [32]	19 strictures	Holmium:YAG laser	57	20.5
Lovaco Castellano [33]	5 strictures	endoscopic incision	100	16.6

balloon catheter dilatation, Acucise endoureterotomy (cutting the balloon), Holmium:YAG laser endoureterotomy, and endoureterotomy with direct endoscopic vision [11,26]. The procedure adopted by our team was a combination of balloon dilatation of the stricture and anastomosis stenting in order to improve the effectiveness of dilatation for ureteral strictures [7, 9,10,12,27]. We believe that balloon dilatation could be the first line of treatment for UAS, except for some patients with a long stenosis or a previous history of intrapelvic radiation.

The success rate at various follow-up intervals is 33 to 80% for the treatment of UAS using conservative modalities [5,7,9-12,14,16,28-33] (Table 2). The results depend on the used tool. The type of hydrophilic wire is a very important factor to consider [34]. The Glidewire and ZIPwire were more likely to have technical and procedural success compared to HiWire ($P < 0.05$) [34].

The success rate of high-pressure balloon dilatation followed by double-J stenting ranged from 30 to 60% [35-37]. It was only 43% in our series. Laser endoureterotomy appears to give better results (75%) than cold knife, electrode, or Acucise endoureterotomy (40 to 60%) [2]. However, there were not significant differences in cutting performance, and there were minimal complications [10,29,30,38].

These endourological approaches to UAS provided satisfactory, long-term results; however, the patency seemed to decrease with follow-up [11,12]. The long-term overall success rates of percutaneous dilatations of ureteral strictures with a balloon catheter vary markedly in the literature, ranging from 5 to 67% [16,39,40]. The success rates of endoureterotomy are 73, 51, and 32% at 1, 2, and 3 years, respectively [12,30].

We stented for 6 to 8 weeks, allowing sufficient time for ureteral regeneration to occur, which is a widely accepted practice in published studies [15,38]. Ravery et al. [41] postulated that the increased duration of ureter stenting may have promoted healing of the ureter, and attributed the high success rate to the very long duration of stenting (4 to 30 months). In contrast, Wolf et al. [30] proved that statistically the stenting duration ($\leq$ 4 weeks versus > 4 weeks) did not influence the short- and long-term success.

Reasons for variation in the results afforded by the different methods are the diversity of the etiologies, the lack of standardized protocols, the small number of cases involved, short follow-up, and the various definitions of success in each

series. Moreover, no large-scale, prospective, randomized trials with controlled variables of endourological methods have been published [5,31].

The main advantages of these methods are their simplicity, safety, the short operating time with extremely low morbidity, decreased blood loss, diminished patient discomfort, and the decreased length of hospital stay [5,7]. They are especially indicated in obese patients, patients with a poor general state, or patients who have already undergone several surgical operations [5]. The main advantage of electrocautery incision is that the incision width and length can be fully controlled, and, if bleeding occurs, coagulation can be performed immediately [11,31,32]. The main limitation of the Holmium:YAG laser and Acucise are their overall cost [5,11]. With balloon dilatation, the procedure took place on an outpatient basis, so cost was low and hospitalization time is not more that a few hours.

Although endoureterotomy has been reported to be more successful than balloon dilatation in managing ureterointestinal strictures, no particular type of incisional procedure has yet proved itself superior to others [32]. Moreover, no consensus has been reached concerning postoperative time to continue stent diversion, stent size, or whether an antegrade or a retrograde approach should be used. Although shorter strictures respond more favorably to endoureterotomy, no definitive cutoff for stricture length has been reached. Numerous studies have suggested that endoureterotomy is most successful in strictures less than 2 cm and of non-ischemic origin [13, 42]. However, regardless of the type of endoscopic procedure, there is always a risk of injury to the vital surrounding structures, such as the nearby blood vessels or intestine [10]. Wolf et al. [30] described 6 major complications (including a lacerated common iliac artery requiring open repair) in a series of endoureterotomies using electrocautery and Acucise modalities for the incisions. Preminger et al. [28] described major vascular injuries to the common iliac artery in 2 patients, with potentially fatal consequences [12]. In our study, we didn't have any periprocedural or late complications, including bleeding, extensive urinoma, or urosepsis.

To prevent such complications, careful preoperative, anatomic evaluations are required to avoid injuring the surrounding structures. CT scans (3-D CT) are essential to assess the anatomical relations of the stricture with adjacent organs (gastrointestinal tract or vessels) [5]. Direct endoscopic observation of the ureter may be of value in preventing arterial injuries because it enables operators to inspect arterial pulsations, as reported by Meretyk et al. [10].

Risk factors for the failure of conservative management are complete UAS longer than 2 cm; a premature appearance of the anastomotic stricture, as in our series (due to a severe surgical/technical mistake with extensive ischemic damage of the ureteroenteric area); kidney function (less than 25% of total renal function) [14,30]; hydronephrosis grade; the presence of urinary infection at presentation; a history of radiotherapy; and the total number of endoscopic strictures involving the distal ureter [5,29,31]. Moreover, a trend toward a lower success rate was noted in procedures involving left-sided anastomotic strictures. It was reported that the additional mobilization of the left ureter as it is brought through the sigmoid mesentery compromises its vascular supply and may render it more resistant to endoureterotomy [8,43]. Ischemic strictures have been shown to have a lower success rate with all endourologic interventions [13]. Thus, ureteral strictures with a compromised vascular supply should be managed by endoureterotomy rather than balloon dilatation [44]. The selection of patients with the most favorable prognostic factors is crucial to obtain excellent results.

In all cases, long-term follow-up is crucial to detect early recurrence and to re-treat or re-stent the structured area to maintain renal function.

Some investigators recommended a second endourologic treatment with balloon dilatation, with comparable long-term results compared to those in the first treatment [39]. A combination of different methods (balloon dilatation and incision) has been suggested [40] as a possible alternative method [9,10,30]. The balloon dilatation is ineffective in patients with a long stenosis of the ureter or a previous history of radiation therapy for uterine cancer [20].

It is important to recognize that the number of strictures in this series was not large enough to allow conclusive statements regarding which factors predict which outcomes.

CONCLUSIONS

We reported our experience for non-malignant UAS after radical cystectomy. Based on our results, we believe that percutaneous antegrade balloon dilatation is a simple, effective, minimally invasive with extremely low morbidity treatment option in patients with UAS after urinary diversion. The success rate obtained is high and it persists after long-term follow-up. It should be proposed as a first-line treatment for strictures with a good prognosis before open surgical correction.

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Percutaneous Nephrolithotomy in Solitary Kidneys with or without Renal Failure: Does Nadir Serum Creatinine Predict Long-Term Renal Function?

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ABSTRACT

Aim: To present our experience of performing percutaneous nephrolithotomy (PNL) in solitary kidneys with or without renal failure, and assessing the postoperative complications and importance of nadir serum creatinine as marker of long-term renal function.

Material and Methods: In a retrospective study, the records of 28 patients with solitary functioning kidney (N = 12) or congenital solitary kidney (N = 16) underwent PNL between January 2004 to July 2012 were analyzed. Mild renal failure (creatinine: 1.6 to 3.0 mg %) was present in 4 patients and moderate renal failure (creatinine: 3.1 to 6.0 mg %) was present in 8 patients. Internal ureteral stenting was performed in renal failure cases, except in 4 patients who required percutaneous nephrostomy and had moderate renal failure with infected hydronephrosis. Diabetes mellitus and/or hypertension were present in 9 patients. Complete stone clearance was achieved in all except 2 cases, which had clinically significant residue (CSR) of 8 mm. Both these required shock-wave lithotripsy (SWL) and they were stone free at 4 weeks. The patients were followed up with serum creatinine and a renal ultrasound.

Results: Gross hematuria requiring blood transfusion was observed in 4 patients. All these patients initially presented with moderate renal failure, infected hydronephrosis, diabetes mellitus, and hypertension. The median follow-up was 42.5 months. The nadir serum creatinine followed internal stenting or nephrostomy if it remained above the baseline; it failed to touch the normal level following PNL.

Conclusion: PNL in solitary functioning or congenitally solitary kidneys is a safe and effective procedure. The bleeding is the commonest complication, and it can be managed conservatively. The nadir serum creatinine remains the most important predictor of long-term renal function.

INTRODUCTION

Percutaneous nephrolithotomy (PNL) is the procedure of choice for kidney stones more than 3 cm, staghorn stones, complex renal stones, stones with renal failure, recurrent renal stones, and in failed cases of extracorporeal shock-wave lithotripsy [1,2]. Stones in solitary kidneys could be life threatening to patients if they progress to renal failure or are complicated by infection [3-5]. The associated comorbidities such as diabetes mellitus and hypertension further compromise renal function [6-8]. Bleeding is a major concern in PNL, with the average hemoglobin drop ranging from 2.1 gm/dl to 3.3 gm/dl [6,9,10]. As a result, 1 to 11% of patients overall and 2 to 53% of those who underwent PNL for staghorn stones require blood transfusions [9-12]. Most of the bleeding can be managed conservatively but it may require super-selective angioembolization in 0.8% of patients. Rarely nephrectomy can be required to save lives [5,10,13]. The presence of either anatomical or functioning solitary kidney with stones requires great caution and planning to avoid major bleeding. Solitary kidneys with compensatory

KEYWORDS: Percutaneous nephrolithotomy, solitary kidney, predictor of renal function

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hypertrophy predispose to major bleeding [2,5,9,13]. Recently, new techniques such as staged minimally invasive PNL with flexible retrograde ureteroscopy have emerged as management therapy for renal stones in solitary kidneys, even in renal failure patients, but it requires great expertise and experience, and the procedures are expensive [14].

In the present study, we retrospectively reviewed the record and assessed the outcome of PNL in solitary kidneys with respect to stone clearance, bleeding requiring transfusion, and renal functions in long-term follow-up.

MATERIALS AND METHODS

In a retrospective study from January 2004 to July 2012, records of 28 patients with solitary kidneys with stones managed by PNL were analyzed. The commonest clinical presentation of the patients was recurrent flank pain followed by hematuria, fever, and dysuria. A tender renal lump was present in 4 cases presenting with infected hydronephrosis. The complete hemogram; renal function test; liver function test; blood sugar test; renal and bladder ultrasound; plain X-ray of the kidney, ureter, and bladder (KUB) and coagulation profile; urinalysis; and a urine culture and sensitivity were done in all cases. An intravenous urogram (IVU) was obtained in cases with normal renal function. In cases with raised serum creatinine, a plain CT scan of the abdomen or an MR urogram was done. The patients with raised serum creatinine with hydronephrosis were subjected to cystoscopy and internal ureteral stenting to relieve the obstruction and preserve renal function. In cases of infected hydronephrosis, a percutaneous nephrostomy tube was inserted. A chest X-ray, electrocardiogram, and pulmonary function tests were done to determine whether patients were fit for anesthesia. Written and informed consent was taken prior to procedures. All patients were subjected to PNL after 2 weeks of either internal ureteral stents or percutaneous nephrostomy.

Under general anesthesia, cystoscopy and ureteric catheterization were performed with a Foley balloon catheter inserted in the bladder. The patient was placed in the prone position with bolsters under the chest. The pelvicalyceal system was opacified with diluted contrast and air injected to locate the most appropriate posterior or superior calyx to puncture. An 18-gauge puncture needle was used for punctures, and the subsequent dilatation of the tract was performed with Alken metallic dilators to 28 Fr. A 26 Fr (Richard Wolf) nephroscope was used for the procedure. A pneumatic lithoclast (Swiss LithoClast) was used to fragment the stone and fragments were retrieved. For complete clearance or maximal clearance, another puncture was made to irrigate the calyx (intracaliceal puncture and irrigation). The puncture tract was dilated to retrieve the stones in 4 cases. A 6 Fr/26 cm ureteral stent and a 16 Fr nephrostomy catheter were inserted at the end of the procedure. Patients had 2 punctures and dilatations, and 2 nephrostomy catheters were inserted. Postoperatively, a chest X-ray was obtained in cases with supracostal punctures. A hemogram was obtained in the postoperative period in cases with significant hematuria with or without hemodynamic instability. If the hemoglobin level was less than 8 g/dl, a packed red cell was transfused to achieve the hemoglobin level of > 10 g/dl.

On the first or second postoperative day, a plain X-ray KUB and renal ultrasound were obtained to see the residual stones and position of the stent. Renal ultrasound was also used to see the status of perinephric collection and hematoma. Nephrostomy tubes were removed once there was complete cessation of hematuria. Postoperative serum creatinine and urine cultures were obtained in all cases. Patients were discharged and advised to remove stents after 2 weeks. The clinically significant residual stones (N = 2) more than 8 mm were taken for SWL (Dornier Compact Alpha). Stents were removed 2 to 4 weeks following SWL depending upon clearance of the fragments. Patients followed-up 3 to 6 times, monthly, with serum creatinine and renal ultrasounds. A 24-hour urine examination was done for total protein, albumin, creatinine, serum calcium, and uric acid estimation. Hypertensive patients had their blood pressure controlled by single or multiple antihypertensives containing angiotensin converting enzyme inhibitors. Diabetes control was maintained with endocrinologist consultations with a combination of plain and mixed insulin. The nephrologist was also consulted for raised serum creatinine, and applicable patients were put on standard treatments for chronic renal failure.

RESULTS

The mean patient age was 38 years (range: 24 to 52) with a male-to-female ratio of 16:12. The mean stone size was 3.4 cm (Table 1). Renal failure was present in 12 patients. Mild renal failure (creatinine: 1.5 to 3.0 mg %) was present in 4 patients, and moderate renal failure (creatinine: 3.1 to 6.0 mg %) was present in 8 patients (Table 1). Internal ureteral stenting was performed in 8 patients and percutaneous nephrostomy in 4 patients. In patients with serum creatinine below 3.0 mg %, the renal function became normal 2 weeks following stenting, but in those with serum creatinine > 3.1 mg %, creatinine showed a downward trend but failed to touch the baseline after 2 weeks of stenting/PCN (Table 3). In 4 patients, PCN was done for the infected hydronephrosis, and the pus culture showed *E. coli*. All 4 patients were hypertensive and diabetic.

The mean operating time was 90 minutes (70 to 120 minutes). The superior caliceal supracostal puncture was done in 14 patients, middle caliceal supracostal puncture in 10 patients (including 4 PCN tract dilatations), and inferior caliceal infracostal puncture in 4 patients. Superior caliceal punctures and dilatation were additionally required in 4 patients in

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Table 1. The demographic characteristics of the patients.

Parameters	Value/No of Patients and Range
total number of patients	23
mean age in years	38 (range: 24-52)
sex ratio (male:female)	18:10
mean stone size (in cm)	3.4 (range: 2.5-6.5)
number of patients with normal serum creatinine (up to 1.5 mg %)	16
mild renal failure (serum creatinine: 1.6-3 mg %)	4
moderate renal failure (serum creatinine: 3.1-6)	8
mean serum calcium in mg %	9.2 (range: 8.8-10.2)
mean serum uric acid in mg %	5 (range: 4.8-7)
congenitally solitary kidney	16
functioning solitary kidney	12
unilateral nonfunctioning kidney with stone	6
unilateral small atrophic kidney	6
simple stone	18
complex stone	10
infected hydronephrosis	4
diabetes mellitus	4
hypertension	9

Table 2. The intraoperative and postoperative parameters.

Parameters	Value	Range/Remarks
superior calyceal supracostal puncture and dilation	14	in 4 initial PCN patients, another superior caliceal puncture and dilation was done for stone removal
middle calyceal supracostal puncture and dilation	10	including 4 PCN patients, which were dilated
inferior calyceal infracostal puncture and dilation	4	
mean operating time	90 minutes	(70-120 minutes)
mean fluroscopic time	5 minutes	(3-7 minutes)
mean irrigation volume (glycine: 1.5 %/normal saline /water in liters)	10 liters	(8-12)
mean hemoglobin drop (in gm %)	2.8 $\pm$ 1.1 gm %	1.8-3.4 gm %
no of patients who underwent SWL for CSR (8 mm)	2	complete clearance at 4 weeks

which initial PCN was done for infected hydronephrosis (Table 2). Single-stage PNL was performed in all cases. The mean fluoroscopic time was 5 minutes (range: 3 to 7 minutes), and the mean irrigation (1.5% glycine/Normal saline/water) volume used was 10 liters (8 to 12 liters). The mean fall in hemoglobin following PNL was 2.8 ± 1.1 gm % (range: 1.8 to 3.4 gm %). Complete stone clearance was achieved in all except 2 cases (CSR: 8 mm) for which SWL was done (Table 2). Finally, all patients were stone free at 4 weeks. The median follow-up was 42.5 months. In 4 patients, gross hematuria started intraoperatively and continued postoperatively for 24 hours, with initial hemodynamic instability. Hemoglobin was less than 8 gm % just following the procedure and required blood transfusion. The mean transfusion of packed red cells was 2.2 units (range: 2 to 3 units). Postoperatively, febrile urinary tract infections (N = 3) were treated with broad-spectrum antibiotics. None of the patients had hydrothorax, pneumothorax, or hemothorax following the procedure. The 24-hour urinary estimation for protein showed micro/macro albuminuria in patients that had persistently raised serum creatinine following PNL. The natural course and progress of the patients initially presenting with renal failure are shown in Table 3. Stone recurrence was seen in 2 patients who were managed with conservative treatment.

DISCUSSION

The stones in solitary kidneys can cause obstruction, which is a risk for renal damage, particularly if associated with infection [1-3]. Chronic kidney disease due to associated hypertension and diabetes mellitus also threatens renal function [4-7]. Renal function remains the most important concern in long-term follow-up, particularly in patients with solitary kidneys. The PNL in a solitary kidney can produce serious consequences that can complicate the procedure. Bleeding is the most significant complication of PNL and this becomes extremely important if the procedure is performed on solitary kidneys.

Table 3. The natural course and progression of renal failure in patients initially presenting with renal failure.

	Stone Character	DM	HTN	Inf HDN	BL Cret	Nadir Creat 2 Wks	Cret 3 M	Cret 6 M	Cret 12 M	Cret 24 M	Cret 36 M	Cret Last FU	Last FU M
1	pelvic	-	-	-	2.8	1.2	1.3	1.2	1.1	1.3	1.2	1.2	90
2	partial stag	-	+	-	2.4	1.1	1.2	1.1	1.2	1.2	1.3	1.3	55
3	pelvic with middle calyceal	-	-	-	2.2	1.1	1.3	1.3	1.4	1.4	1.4	1.5	50
4	pelvic with inferior calyceal	-	-	-	3	1.3	1.3	1.4	1.3	1.4	1.3	1.4	20
5	staghorn	+	+	+	6	3.1	2.5	3.4	3.2	3.8	3.9	4	75
6	staghorn	+	+	+	5.5	3.3	2	2.3	2.4	2.5	2.8	2.9	60
7	partial stag	-	+	-	3.7	2	2.1	2.2	2.8	2.9	3	3	59
8	pelvic with sup calyceal	+	+	+	4.3	3	3.2	3.4	4	3.8	3.9	4	52
9	pelvic	-	+	-	5	2.5	2.1	2.8	3.2	3.3	3.5	3.5	40
10	staghorn	+	+	+	4.8	2	1.9	2.2	2.3	2.2	2.3	2.4	38
11	partial stag	-	+	-	4.9	2.3	2.2	2.3	2.3	3	3.5	3.7	37
12	staghorn	-	+	-	4.5	2.8	3	4.2	4.6	5.2	6.3	6.5	12

DM: diabetes mellitus; HTN: hypertension; Inf HDN: infected hydronephrosis; BL Cret: baseline cretanine; Nadir Cret 2 Wks: nadir creatinine at 2 weeks; Cret 3 M: creatinine at 3 months; Cret 6 M: creatinine at 6 months; Cret 12 M: creatinine at 12 months; Cret 24 M: creatinine at 24 months; Cret 36 M: creatinine at 36 months; Cret Last FU: creatinine at last follow-up; Last FU M: last follow-up, in months

The life-threatening hemorrhage requires super-selective angioembolization and even nephrectomy may be required in settings where interventional radiology is not available [2-6]. Bleeding requiring transfusion rates have been reported between 0.8 and 45% in PNL series [1,2,4,6,7,]. Most of the bleeding can be managed with conservative measures, except in < 1% of cases requiring angioembolization [8-10]. The presence of diabetes mellitus, hypertension, intraoperative complications such as trauma to the urothelium and infundibular tear, multiple tracts, and prolonged operative time are the other risk factors [7,8,11-13]. Renal failure and infections might have a role in the excessive bleeding in PNL [6,7,13-17].

In a retrospective analysis of 3 878 PNL patients, El-Nihas et al. reported risk factors for extensive post-PNL bleeding. These are superior caliceal puncture, staghorn stones, multiple punctures, comparatively inexperienced surgeons, and the presence of a solitary kidney [19]. In our present study, the bleeding requiring transfusion was seen in 4 patients (18.2%) but none required angioembolization. All these 4 patients had staghorn stones, initial PCN for infected hydronephrosis, superior caliceal puncture and dilatation, diabetes mellitus, hypertension, and multiple (2) tracts for stone clearance. The tract size was 28 Fr in all patients. Making comparatively smaller tract sizes could have decreased the bleeding but again the operative time would have been longer, leading to more complications. The larger tract sizes allow for rapid removal of larger stone fragments and thus minimize operative time and intracalyceal irrigation and manipulations, which might contribute to bleeding, infection, and electrolyte imbalances [3,9,13,16,18].

Renal function remains a definite short-term or long-term outcome concern of PNL in anatomical or functional solitary kidneys. Resorlu et al. showed that patients who underwent PNL for a solitary kidney had a significant decrease in serum creatinine and an increase in estimated glomerular filtration rates (eGFR) after a period of 1 month, postoperatively [2]. Canes et al. retrospectively reviewed the effect of PNL on

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renal function in 81 patients that had solitary kidneys. They estimated the eGFR preoperatively and postoperatively, and they showed a mean increase in eGFR from 44.9 ml to 51.5 ml/min/1.73 m^2 1 year following PNL, which was statistically significant. The other important observation of this study was that the eGFR could worsen following PNL, which was seen in 6.8% of patients [20]. Witherow and Wickham reported that mean creatinine clearances increased significantly after nephrolithotomy in patients with severely decreased renal function because of stone disease [21]. The CROES PCNL Global Study Group reported the largest series of PNL in 189 patients having solitary kidneys and has compared the procedure in patients with bilateral kidneys. It was interesting that the level of renal impairment was significantly higher, and stone-free rates were significantly lower following PNL with solitary kidneys in comparison to bilateral kidneys. Bleeding was equal in both groups but solitary kidney patients required significantly more transfusions [22]. Kuzgunbay et al., in an interesting paper, reported the PNL in patients with impaired renal function. With a mean follow-up of 51 months, they concluded that most of the patients presenting with renal stones with renal failure experience improvement or stabilization of renal function following PNL. Despite the relief of obstruction, if the patients have solitary kidneys, diabetes mellitus, or atherosclerosis there is a greater risk of renal function deterioration [23].

The potential effect of multiple tracts on renal function in solitary kidneys remains another concern. Handa et al. reported that a single PNL procedure in humans and animals produces a small but permanent parenchymal scar at the site of the nephrostomy tract after several weeks [24]. Associated interstitial inflammation and the local parenchymal injury by tract dilatation usually resolve but can progress to fibrosis and scarring involving large distances from the tract. It is also not clear whether punctured papilla can regain its normal function over time [20,25]. Multiple-tract PNL may magnify the loss of parenchymal tissue with resultant, diminished, global renal function, but the renal function has not been tested by well-planned, single-tract PNL versus multitract PNL [9,17,18,24,26]. Akman et al. have shown that renal function in the early and late postoperative periods was not significantly or clinically affected by the creation of multiple tracts. In their series, only 1 patient (1 out of 12) had multiple tract procedures that showed delayed deterioration in renal function [9].

The presence of chronic kidney disease due to diabetes mellitus and hypertension increases blood loss in PNL. The associated renal failure further complicates the problem [1,6,7,13,19,21]. The mechanism is associated with arteriosclerosis and thickened basement membranes, making such patients more prone to bleeding after initial trauma of tract formation. El-Nahas et al. reported that staghorn stones were a significant independent risk factor because during PNL for such complex stones multiple tracts and excessive manipulation were needed. They also identified that a solitary kidney was a significant risk factor for bleeding because compensatory hypertrophy is a normal physiological response as thickened renal parenchyma increases with increased kidney size [19]. It is speculated that punctures and dilatation through thick renal parenchyma may increase the possibility of damage to more renal tissue and its vascular supply, which could be the major cause of excessive bleeding [26-28].

In the present study, gross hematuria with initial hemodynamic instability requiring a blood transfusion was observed in 4 patients. All of these patients had large stone bulk with infected hydronephrosis for which they initially required percutaneous nephrostomy. They had diabetes, hypertension, and renal failure. The serum creatinine showed a downward trend following PCN but failed to reach the normal level. These patients required 2 punctures and dilatations for complete stone removal. The serum creatinine in long-term follow-up did not touch the baseline but remained consistently raised, and the patients were labeled as having established chronic renal failure. Renal failure was investigated and found to have associated diabetic nephropathy with albuminuria. Hypertension as an associated comorbidity was present in 5 patients, who also presented with renal failure. Of this, 1 patient had serum creatinine below 3 mg %, which reversed to normal levels following internal stenting. In the other 4 patients, renal failure was moderate (creatinine > 3.1 mg %), which on internal stenting showed a downward trend (raised nadir serum creatinine at 2 weeks) but the serum creatinine remained raised in follow-up consultations. Renal failure in such patients was labeled as hypertensive nephrosclerosis with albuminuria.

Stone clearance and recurrence are 2 very important aspects of PNL with solitary kidneys. Stone clearance in the present study was assessed by 3 methods. These were the intraoperative evaluation with a fluoroscope following Amplatz sheath removal, and both postoperative X-ray KUB and renal ultrasound. The ultrasound was done by a highly experienced sonologist dedicated to urology; therefore, the chances of overestimation or underestimation of stones was unlikely. While computed tomography (CT) is used at many centers worldwide to assess stone clearance, it is associated with radiation exposure, and it is expensive compared to ultrasounds [29,30]. Stone recurrence was seen in 2 patients. Stone size ranged from 5 to 6 mm, which was managed conservatively using alkali therapy, and subsequent, follow-up ultrasounds did not show stones although there was no definite history of lithiuria.

CONCLUSION

PNL in solitary functioning or in congenital solitary kidneys is a safe and effective procedure. The presence of infection and associated comorbidities predispose patients to significant

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bleeding, requiring blood transfusions. Renal failure is multifactorial, which is due to obstruction, infection, and associated comorbidities. Nadir serum creatinine remains the most important predictor of long-term renal function.

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The Technique of Precise Injection of Floseal Along the Nephrostomy Tract to Facilitate Tubeless Percutaneous Nephrolithotomy

Pradeep Durai, Fiona Wu Mei Wen, David Terrence Consigliere, Ho Yee Tiong

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LETTER TO THE EDITOR

Dear Editor,

After percutaneous nephrolithotomy (PCNL), a nephrostomy tube has been routinely placed to ensure hemostasis, provide drainage, and maintain access to the collecting system. This causes pain after surgery and persistent urine leaks after its removal. Recently, efforts have been expended to either reduce the size of the nephrostomy tube or eliminate it altogether. Hence, tubeless percutaneous nephrolithotomy is now increasingly advocated for the treatment of uncomplicated, large kidney stones [1-3]. After surgery, closure of the skin without sealing the nephrostomy tract postoperatively risks bleeding and urinary extravasation [4]. Hemostatic agents have therefore been advocated to seal the PCNL tract. Herein we describe a method to facilitate the accurate application of a Floseal Matrix from the renal parenchyma to skin, and we report the outcomes of tubeless PCNL.

TECHNIQUE

The selection criteria for tubeless percutaneous nephrolithotomy (PCNL) include a single-access tract, no significant residual stones, minimal bleeding, and no requirement for a secondary percutaneous procedure.

Routine PCNL is performed. After stone clearance, an intraoperative nephrostogram and flexible nephroscopy were performed to ensure total calculus clearance and no ureteric obstruction. The access sheath is then withdrawn to the junction of renal parenchyma and collecting system under direct nephroscopic vision and fluoroscopic guidance. The nephroscope is then removed and exchanged for the Floseal laparoscopic applicator; its tip is carefully aligned with the access sheath tip under fluoroscopic guidance (Figure 1). A rubber band is then placed around the applicator to fix its position within the access sheath (Figure 2). Five mls of Floseal was injected down the sheath, which was slowly withdrawn simultaneously with the applicator held in position with the sheath by the rubber band. The tract is re-examined at the skin level for bleeding, and another 5 mls of Floseal was given, if necessary. The skin can then be closed with DERMABOND.

Clinical data of our initial patient series were collected prospectively. No DJ stents were placed on our patient postoperatively, but a ureteric catheter connected to the Foley catheter is left in situ until postoperative day 1.

RESULTS AND DISCUSSION

In our series of 5 patients, the median age was 47 (range: 29 to 61) years; the average stone load was 23.4 (range: 16.7 to 30) mm. The average duration of surgery, on average, was 174 (range: 155 to 194) min, and 100% stone clearance was achieved in all patients. The median length of stay of tubeless PCNL patients was 2 days. There were no complications reported, including bleeding or urine leaks. In particular, there were no

KEYWORDS: Tubeless percutaneous nephrolithotomy, PCNL, Floseal, Floseal Matrix

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Figure 1. An image of the flouroscopy..

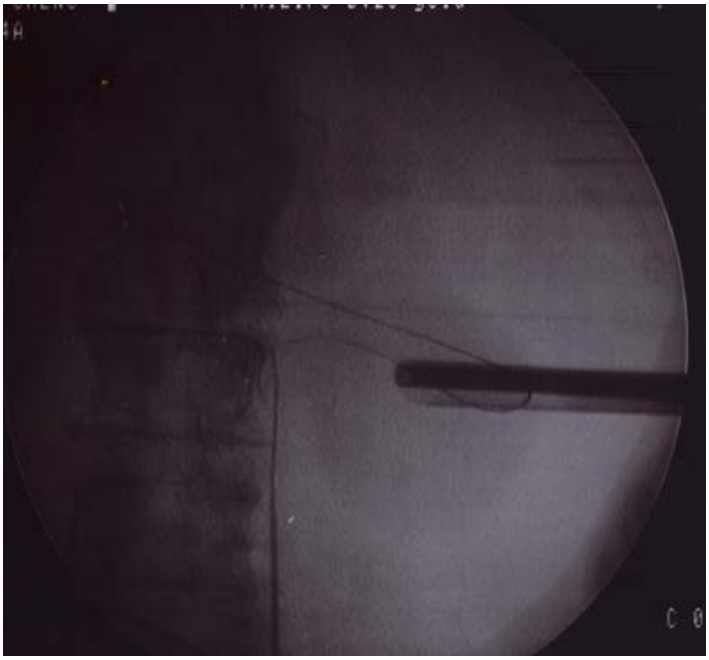
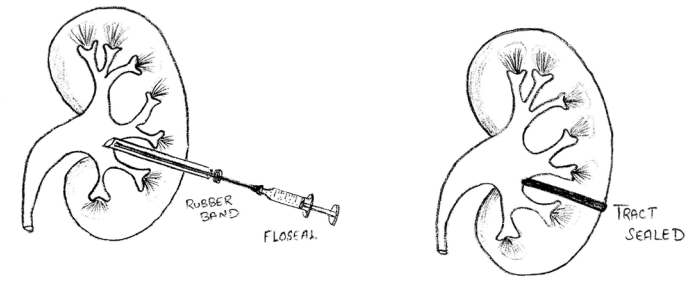


Figure 2. Tubeless PCNL.



wound complications. This was compared to our earlier series whereby only the skin was closed and no Floseal applied; the wound complication was 20%.

CONCLUSION

For patients who have been rendered completely stone free during uncomplicated PCNL, the administration of Floseal Matrix to the nephrostomy tract, precisely with the above novel technique, may achieve immediate hemostasis and eliminate the need for the placement of a nephrostomy tube. This novel technique can potentially facilitate safer tubeless PCNL than just skin closure alone.

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An Unusual Cause of Bladder Stones In a Female: A Migrant Intrauterine Contraceptive Device

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ABSTRACT

Intrauterine contraceptive devices (IUCD) have been widely accepted contraceptive methods among women for many years due to their efficacy, longevity, reversibility, and safety. There is a possibility of uterine perforation and migration, but an intravesical perforation is extremely rare. Only a few case reports depicting incrustation of such foreign bodies in the bladder, mostly incomplete and fixed to the perforated wall, are available in the literature. We are here reporting a T-shaped floating stone in the bladder in a female due to complete incrustation of a migrated IUCD in the bladder, which she had received seven years before presentation.

INTRODUCTION

Intrauterine contraceptive devices (IUCD) are some of the most frequently used contraceptive methods. Although they are generally safe modalities for long-term contraception, still, on occasion, an IUCD can give rise to complications. Uterine perforation and migration are rare complications. A perforated IUCD may migrate to any adjacent pelvic organ. An IUCD in the urinary bladder may present with features of UTI, hematuria, incontinence due to vesicoutrine fistulae, and obstruction due to the formation of secondary stones over the migrated device.

CASE REPORT

A 31-year-old woman presented with complaints of intermittent dysuria associated with fever and suprapubic pain for two years. She had 1 recent episode of hematuria 10 days prior to presentation, which resolved on some medication. She had 2 children and the younger one was 4 years old. Her menstrual cycle was regular, and there was no history of vaginal discharge. Upon abdominal examination, there was tenderness in the suprapubic region, and her vaginal examination was normal. Her investigations revealed red blood cells and pus cells in her urine, and *E. coli* on her culture. Her X-ray for the kidney, ureter, and bladder (KUB) showed a T-shaped radio-opaque shadow around the arms of a suspected Copper-T device in the pelvic region. The patient was questioned about this and she gave the history of an IUCD insertion 7 years prior to presentation. According to her, contraception failed and she became pregnant after 3 years. Assuming the IUCD may have dropped, no attempt was made by her caregiver to locate the device.

Her ultrasound (US) and intravenous urogram (IVU) were suggestive of a solitary bladder stone with normal upper tracts and insignificant post-void residual urine. Cystoscopy was done, which confirmed a large, T-shaped, dark brown, floating stone with a rough, irregular surface in the bladder. The stone had features of cystitis and was without a scar. Cystolithotomy was done to remove the stone and to avoid any residual fragment of the Copper-T device. The stone was 4 cm x 4 cm in dimension, and its core was made of coiled copper wire. The postoperative period was uneventful, and the catheter was removed on the tenth day. The patient remained symptom-free on follow-up.

DISCUSSION

Intrauterine contraceptive devices (IUCD) are some of the most popular methods of reversible contraception. They are generally safe modalities for long-term contraception [1]. However, they

KEYWORDS: Intrauterine, contraceptive, bladder, stone, incrustation

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Figure 1. The X-ray KUB.

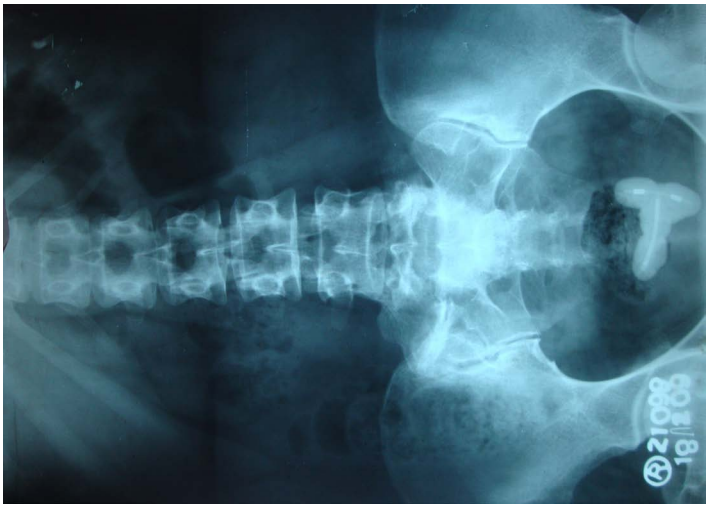
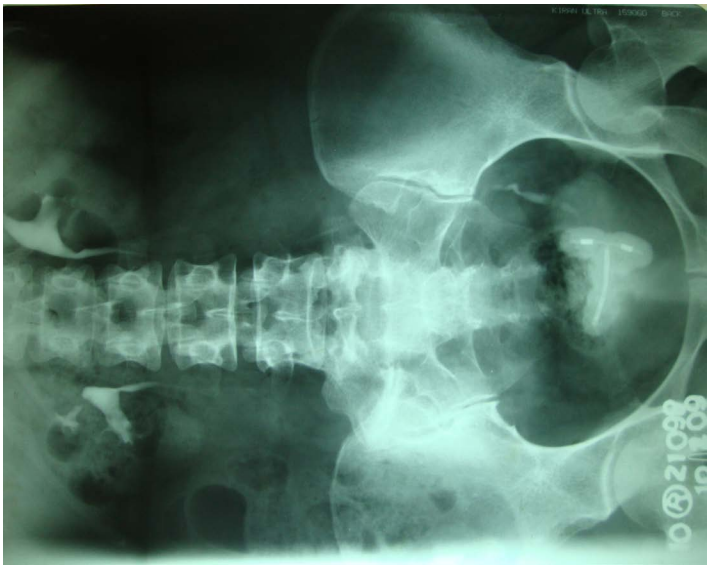


Figure 2. The intravenous pyelogram (IVP).



have some complications such as hemorrhage, hypermenorrhea, dysmenorrhea, pain, septic abortion, ectopic pregnancy, and pelvic inflammatory disease [2,3]. Uterine perforation is a rare event (1 to 3 perforations per 1 000 insertions) [3], and they occur primarily during insertion. These perforations depend on the time and technique of insertion, the type of IUCD, the skill of the physician, and the anatomy of the cervix and uterus [2]. Undetected, extreme posterior uterine position is the most common reason for perforation at the time of insertion. This risk increases during the puerperium period, after a recent abortion or medical termination of pregnancy (MTP), after cesarean section, in sepsis, and in multiparous births [4].

A perforated IUCD may migrate to the nearby structures such as the peritoneum, the omentum, the adnexa, the colon, the bladder, and the appendix [1]. In a review of 165 cases of migrated IUCD, Kassab and Audra reported the bladder as the destination in only 23 cases (14%) [5].

Erosion and secondary perforation can also occur at any time after insertion, by slow migration across the muscular wall of the uterus and bladder, which can be augmented by spontaneous uterine contractions [6,1].

A direct transurethral introduction of IUCD into the bladder is a highly unlikely possibility provided the device is inserted by paramedics with adequate levels of skill and anatomic knowledge, but it can't be ignored [7].

The migrated IUCD may remain silent for a long period [8], or it may present with abdominal or pelvic pain and lower urinary tract symptoms [2]. Such IUCD in bladder works as a nidus for stone incrustation, and it is often associated with stone formation and subsequent obstructive symptoms [9]. There is also a chance to develop vesicouterine fistulae and subsequent incontinence, either during the migration or the removal of a partially migrated IUCD [1].

In the present case, patient became pregnant after 3 years with IUCD and had symptoms for the last 2 years only, suggesting it may be a case of gradual progression and migration.

Primary vesicle calculi are very unusual in women, and the presence of intravesical stones should raise suspicion of the presence of a foreign body [10]. Conversely, any patient with a missing IUCD must be carefully searched for the lost device, and any symptoms of recurrent urinary tract infection, incontinence, or obstruction in such patients should be suspected as an indication of IUCD migration into the bladder [1]. Such migrated devices can easily be detected with abdominal radiography or ultrasonography (USG) [6].

Any displaced IUCD should be removed due to its potential complications. It can be removed from the bladder by cystoscopy or by suprapubic cystotomy [2] but the motive should always be for the complete removal of the device with the least trauma to the bladder and urethra, as any residual fragment may lead to a recurrence of symptoms.

A trained professional should always do an IUCD insertion after a proper case selection and physical examination, and it should be avoided in early puerperium or following a recent abortion or MTP [2]. Women should be informed of the potential

Figure 3. The stone with a copper coil core.

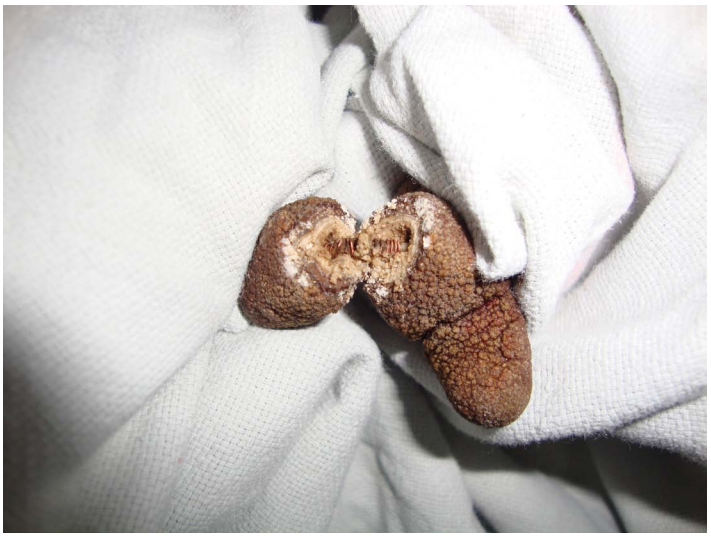
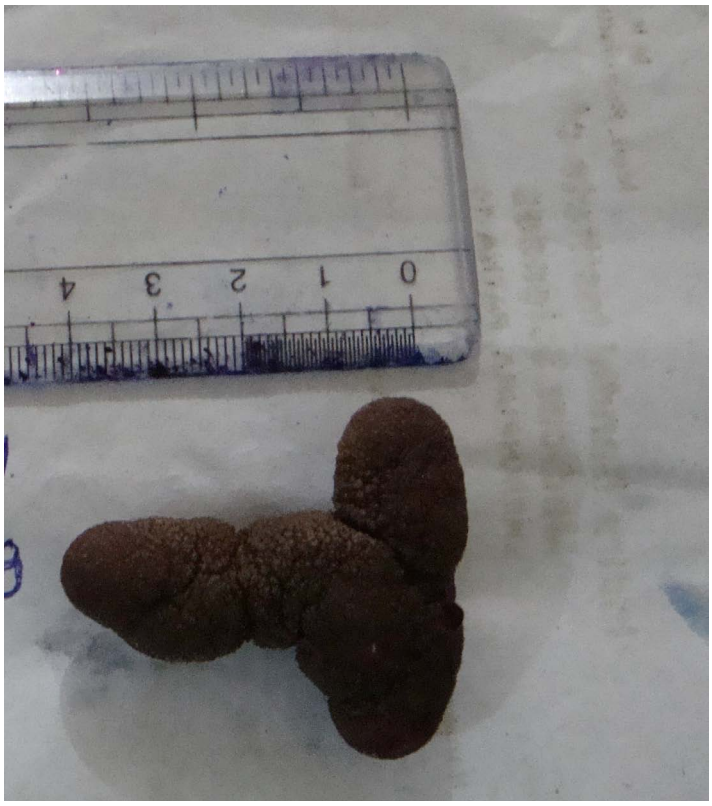


Figure 4. The length of the stone.



complications and should check the device string regularly [1,6]. If the string is not found, abdominal radiography should be done, even in asymptomatic patients. If uterine rupture is suspected, US should be performed to determine the probable location of the rupture [1,2].

CONCLUSION

Intravesical migration and stone formation is a rare complication of IUCD insertion and it should be suspected in women with an IUCD who have recurrent or persistent urinary tract infections, persistent LUTS, or vesicle stones, especially if the IUCD is missing or failed. Diagnosis can be made easily with abdominal radiography and US. Any such device should be removed in totality. Such conditions can be avoided with proper case selection, an informed patient, a trained staff, and careful follow-up.

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Congenital Seminal Vesicle Cyst Associated with Ipsilateral Renal Agenesis and Cryptorchidism Causing Bladder Outlet Obstruction: A Case Report and Review of the Literature

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ABSTRACT

Seminal vesicle cysts combined with ipsilateral renal agenesis are a rare urological anomaly. We present a 24-year-old single man who suffered from difficulty urinating and irritative voiding symptoms for 4 years. The symptoms worsened in the last 6 months. A physical examination revealed right cryptorchidism with a pelvic mass. Digital rectal examination revealed a palpable large soft mass behind the prostate.

Diagnostic imaging (ultrasound, IV urography, computed tomography scan, and magnetic resonance imaging) showed a right seminal vesicle cyst. The ipsilateral kidney and ureter were absent. Open surgery cystectomy was performed, improving urinary symptoms.

INTRODUCTION

Seminal vesicle cyst (SVC) is an extremely rare disease, occurring in 0.005% of the population [1]. It is often associated with other anomalies. Zinner [2] reported the first case of SVC in combination with ipsilateral renal agenesis in 1914, and then associated anomalies have been reported in the literature [3-5]. Treatment of SVC depends on symptom existence.

Here we present a giant SVC with agenesis of the right kidney and ipsilateral cryptorchidism presented with lower urinary tract symptoms. A brief review concerning the symptoms, diagnostic procedures, and treatment options in literature are discussed.

CASE REPORT

A 24-year-old single man presented to our department with a 4-year history of lower urinary tract symptoms, constipation, and right lumbar pain. He initially paid little attention to these symptoms. However, his urinary discomfort had worsened over the preceding 6 months. His International Prostatic Symptom Score was 13.

He was obese (BMI: 34). On physical examination, his urinary bladder was palpable on the right side of the suprapubic region. External genitalia were normal, but the right testis was not palpable. The digital rectal examination revealed a soft, large, palpable cystic mass arising from the upper border of the prostate. Laboratory data were within normal ranges, especially urinalysis and creatinine. Semen analysis revealed predominantly immotile spermatozoa. Severe bladder outlet obstruction was noted. Preoperative uroflowmetry studies revealed a maximal urinary flow rate of 14 mL/s and a mean urinary flow rate of 7 mL/s. The residual urine volume was 29 mL.

Abdominal and pelvic ultrasonography could not find the right kidney, and it revealed the presence of a retrovesical hypoechoic mass measuring 18 cm. Intravenous urography could not depict the right kidney or right ureter, and it showed a contrast-filling defect of the right posterolateral surface of the bladder (Figure 1). Endorectal ultrasonography revealed a pelvic cystic mass. Computed tomography (CT) of the abdomen and pelvis confirmed right renal agenesis and the presence of a nonenhancing retrovesical cystic mass (Figure 2). Through these data we concluded an obstructive right SVC.

KEYWORDS: Renal agenesis, seminal vesicle cyst, cryptorchidism

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Figure 1. Intravenous urography showing the absence of the right kidney and compensatory enlargement of the left kidney. SVC is visible as a large impression in the bladder (arrow).

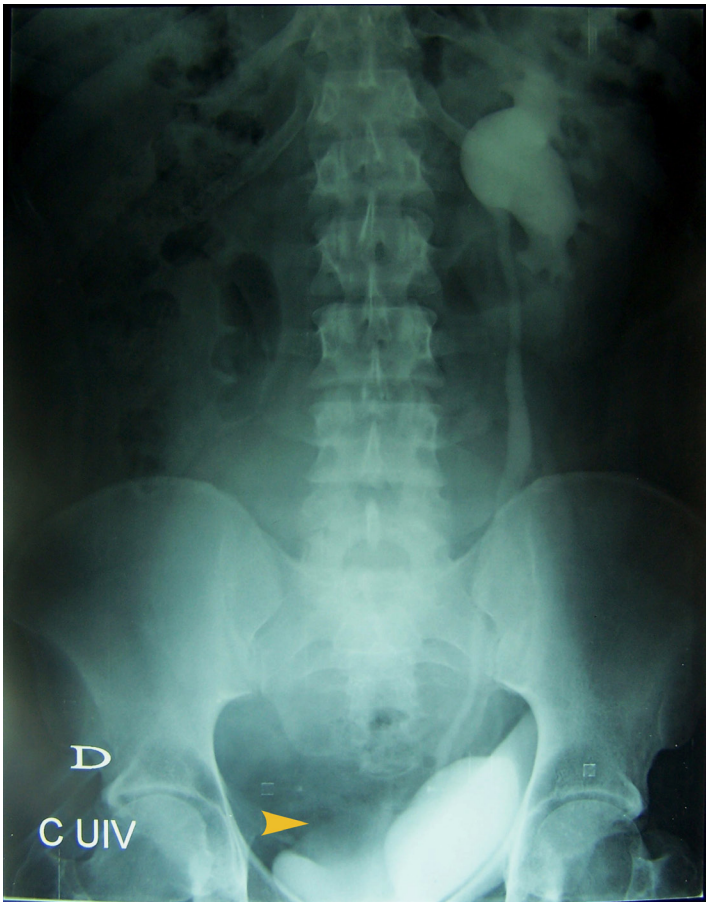
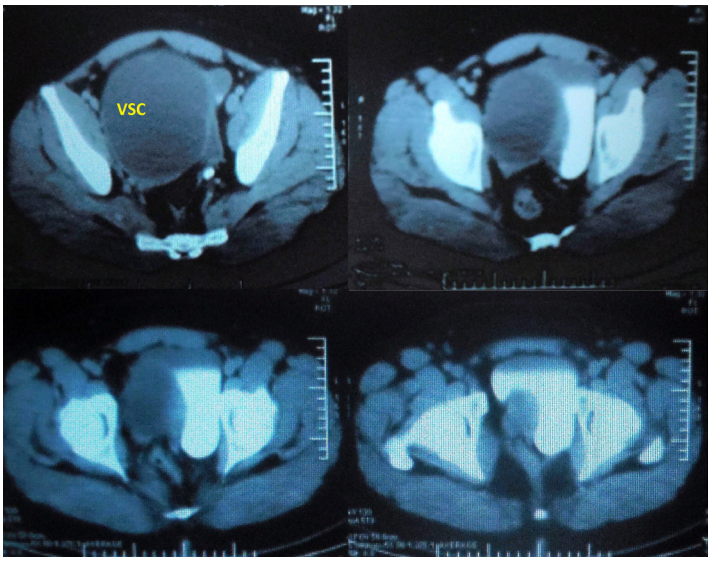


Figure 2. A CT scan of the pelvis with intravenous contrast injection: A 16.5 cm x 12.7 cm nonenhancing retrovesical mass (SVC) with no calcification, occupying mainly the right side of the pelvis, with extrinsic compression on the urinary bladder. Note that the right ureter is absent.



We decided to explore the pelvis and remove the presumed SVC. Through a standard midline suprapubic incision, the bladder was dissected medially to the left and the peritoneum was completely removed. We found a large pelvic cyst that depended on the right vesicle. The right vas deferens was traced into the wall of the mass, which was then freed. The right testis was ectopic and hypotrophic (Figure 3). This cyst contained 1 liter of brown liquid. A total cystectomy and right orchidectomy were performed. There were no operative complications or need for transfusion.

The pathological assessment of the specimens revealed benign SVC. The cystic walls were composed of fibrous connective tissue. Columnar and basal cells lined them with villous projections in hematoxylin and eosin stains (Figure 4). The cystic fluid was full of immotile spermatozoa and was not an infection. No malignancy was found.

The postoperative period was smooth, and the patient has experienced no further genitourinary discomfort. Postoperative uroflowmetry studies showed a maximal urinary flow rate of 27 mL/s and a mean urinary flow rate of 18.6 mL/s. There was no residual urine volume and the outlet obstruction had disappeared. The patient's International Prostatic Symptom Score had reduced to 4. A follow-up ultrasound at 25 months did not show any recurrence of the cyst.

DISCUSSION

Unilateral renal agenesis is present in 0.1% of newborns [6]. Genitourinary anomalies are found in 12% of men with unilateral renal agenesis [7]. SVC is associated with ipsilateral renal agenesis in 68% [7]. Kidneys with this anomaly were dysplastic or absent [8]. In the literature, this association is only reported in case reports; no series exists. Environmental and hereditary factors causing SVC are unknown [5].

SVC is diagnosed in adults during the second to fifth decade of life [5,9-11], as in our case. They are usually found at a time of greatest sexual and reproductive activity [12]. They may be congenital or acquired [12]. Congenital cysts are usually unilateral with no predilection for either side [9]. Acquired cysts are often bilateral and are seen in older patients with a history

Figure 3. A preoperative view of the pelvis.

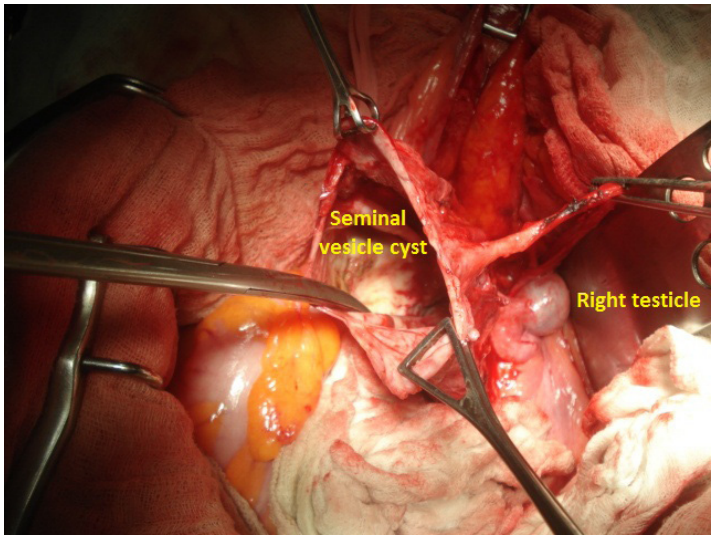
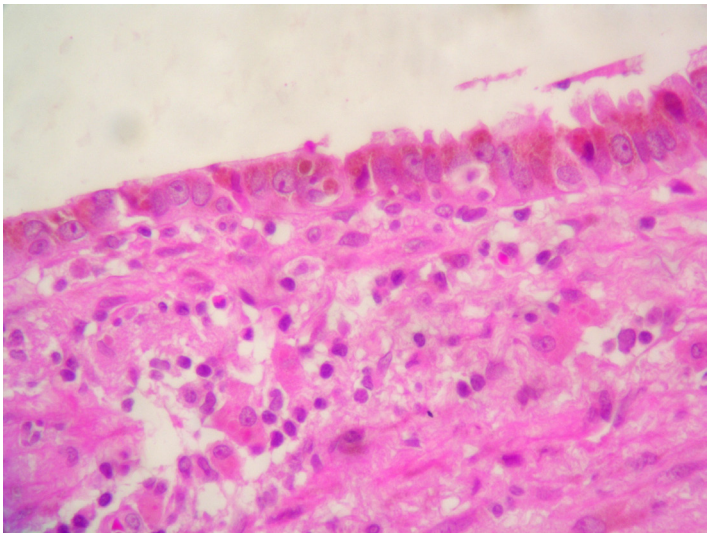


Figure 4. The histopathological view of SVC.



of chronic prostatitis or prostate surgery [11]. In our case, there had been no previous surgical interventions. An association between congenital SVC and ipsilateral renal agenesis is not unusual because both organs originate from the mesonephric (Wolffian) duct during embryogenesis [9]. Isolated failure of the development of the ureteral bud results in renal agenesis, but the remaining genital tract is unaffected. However, maldevelopment of the mesonephric duct in gestational week 12 affects the ipsilateral seminal vesicle and vas deferens, as well as the ureter and kidney [7].

SVC is usually asymptomatic [13]. Those smaller than 5 cm in diameter can remain asymptomatic and are usually discovered incidentally [11,14]. However, the cyst can grow and induce inflammation and stimulate surrounding viscera [13]. Once seminal vesicle cysts exceed 5 cm, the clinical symptoms become obvious [7]. These cysts can present with symptoms related to bladder irritation and obstruction [7,15]. The most commonly reported symptoms include abdominal, perineal, and pelvic pain; constipation; ejaculatory pain; dysuria; increased urinary frequency; hematuria; hematospermia; urinary tract infection; and symptoms of epididymitis and prostatitis [7,9,13-15]. Other reported symptoms include infertility and rarely enuresis [5,15]. In our case, the patient presented with symptoms mimicking bladder outlet obstruction without genitourinary tract infection.

SVC is usually diagnosed as incidental sonographic findings in patients with voiding complaints, or they are totally asymptomatic [16]. Diagnostic procedures include digital rectal examination, abdominal or transrectal ultrasonography (TRUS), abdominopelvic CT, and pelvic MRI [13]. Additional studies include intravenous urography, retrograde cystourethrography, cystoscopic evaluation, and vesiculography [5,10].

Roehrborn et al. [4] advocate the use of transabdominal ultrasonography as the first diagnostic procedure, because it is non-invasive, inexpensive, and brings no radiation exposure. Ultrasound showed cystic masses with heterogenous contents adjacent to the seminal vesicle [13]. Weyman and McClennan [17] and Bon et al. [18] underline the excellent diagnostic properties of ultrasonography and CT scanning, whereas Schwartz et al. [19] prefer CT scanning above ultrasonography because of the reduced chance of missing the diagnosis. Moreover, CT scan provided an excellent demonstration of associated anomalies [20]. In a series of 13 boys explored by MRI, Chen et al. found high signal intensity on T2-weighted images but variable signal intensity on T1-weighted images. They concluded that MRI is a powerful tool for detecting SVC and in delineating associated congenital anomalies of the urogenital tract [13,21]. A cystoscopy helps to confirm a hemitrigone, the absence of a ureteral orifice, and other anomalies in the bladder [14].

Patients without clinical symptoms (without pain or a functional deformity) should not be treated, and they can be monitored by TRUS [12]. They should be treated if a growth or symptoms occur [12,18]. Conventional treatment methods include open exploration with vesiculectomy, transrectal or transperitoneal aspiration of the cyst, or transurethral unroofing of the cyst [5,9,10,22]. Surgical excision of the SVC, as in our case, is the preferred definitive management because simple aspiration is often complicated by a recurrence of the cyst and infection of

the area [23]. However, conventional surgery is very invasive because of the deep location and dissection difficulty of the seminal vesicles in the retrovesical space [13].

Recently, the laparoscopic approach has been advocated as an optimal minimally invasive technique for the surgical treatment of seminal vesicle pathology. It provides excellent intraoperative access, a direct approach, magnification, good visualization with an easy approach, and minimal postoperative morbidity. Also, without damage to the bladder and rectum, the seminal vesicle can be dissected from the peritoneum that is covering the bladder and prostate. It is likely to become the treatment of choice for this rare developmental anomaly [13,24]. Seo et al. [13] have reported 4 cases of SVC with ipsilateral renal agenesis, which were successfully treated by laparoscopy (transperitoneal approach). A malignancy cannot be excluded, and histological examination of the cyst is necessary. Adenocarcinoma of the seminal vesicles has been reported [25]. Ultrasonography is used for follow-up in a patient with an asymptomatic SVC. The investigation is non-invasive, cheap, and can be performed by the urologist [5].

CONCLUSION

Congenital SVC associated with renal agenesis is a rare association and can cause lower urinary tract symptoms and infertility.

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Ectopic Scrotum: A Rare Clinical Entity

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ABSTRACT

Congenital scrotal disorders, including penoscrotal transposition, bifid scrotum, ectopic scrotum, and accessory scrotum are unusual anomalies. We present a case of ectopic scrotum with renal agenesis.

INTRODUCTION

Congenital scrotal disorders, including penoscrotal transposition, bifid scrotum, ectopic scrotum, and accessory scrotum are unusual anomalies [1,2]. We present a case of ectopic scrotum with renal agenesis.

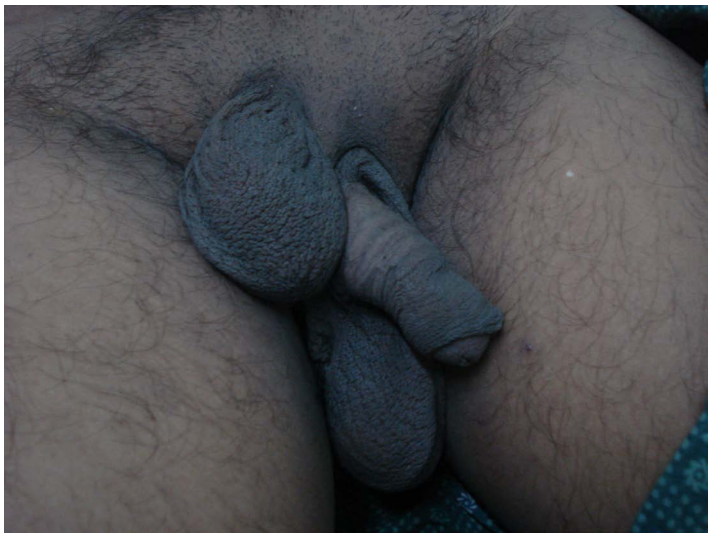
CASE REPORT

A 35-year-old male presented with swelling of the right side of the abdomen. There was no family history of any congenital anomalies. His physical examination showed an ectopic scrotum in the right inguinal area. The left hemiscrotum was in a normal location, and the left testis was contained in the left hemiscrotum. Scrotal raphe did not develop. The right hemiscrotum was located in the right inguinal area, and the right testis was contained in the hemiscrotum. The phallus was normal. His hematological and biochemical tests were normal. His abdominal sonography and renal isotope scan showed agenesis of the right kidney. The patient underwent right scrotoplasty and orchidopexy. The right testis showed normal characteristics. The patient proved asymptomatic during six weeks of follow-up.

DISCUSSION

Congenital scrotal disorders include four groups of anomalies: penoscrotal transposition, bifid scrotum, ectopic scrotum, and accessory scrotum [1,2]. Ectopic scrotum occurs in a variety of locations ranging from perineum and inguinal canal to the medial thigh, but it is mainly found in inguinal, suprainguinal, infrainguinal, or perineal areas [3,12]. Scrotal development starts with the appearance of paired labioscrotal swellings lateral to the cloacal membrane at the 4-week gestation period [3,17]. The genital tubercle elongates to form the penis and is flanked by these labioscrotal swellings. After 12 weeks, these swelling migrate inferomedially, or, by a different assumption,

Figure 1. Ectopic scrotum with renal agenesis.



KEYWORDS: Ectopic, scrotum, suprainguinal

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Table 1. Comparison of literature findings by author.

Authors	Area	Renal Anomalies	Other Anomalies	Testis Location
Adair and Lewis [5]	right inguinal	right renal agenesis	diphallia, chorde, hypospadias, ventral hernia	right ectopic scrotum
Flanagran et al. [6]	left inguinal	left renal agenesis	left talipas, duplicated equinovarus, left popliteal pterygium, absent left thumb, right collecting system	left ectopic scrotum
Milroy [7]	left inguinal	none	atrophic testes, hydrocele, left inguinal hernia	left ectopic scrotum
Han et al. [8]	right inguinal	right renal agenesis	imperforante anus, persistent urachus	right ectopic scrotum
Okuyama et al. [9]	left inguinal	none	left inguinal hernia	left ectopic scrotum
Ueyama et al. [10]	right inguinal	none	skeletal	right ectopic scrotum
Jaeschock and Drewes [11]	right inguinal	none	none	right ectopic scrotum
Lamm and Kaplan [12]	right inguinal	right renal agenesis	right inguinal hernia	right ectopic scrotum
Guha [13]	left inguinal	none	none	cryptic
Elder and Jeffs [14]	left inguinal	left dysplastic kidney	bilateral inguinal hernia	left ectopic scrotum
Edler and Jeffs	left inguinal	left hydronephrosis	none	left ectopic scrotum
Elder and Jeffs	left inguinal	left renal agenesis	multiple skeletal defects	left ectopic scrotum
Jehannin et al. [15]	left inguinal	left renal agenesis	none	nearby
Kolandaivalu [16]	right inguinal	none	none	nearby
Spears et al. [17]	left inguinal	none	none	cryptic
Kim et al. [18]	right inguinal	none	none	right ectopic scrotum
Gunayadin et al. [19]	right inguinal	none	imperforate anus	right ectopic scrotum
Hoar et al. [20]	right inguinal	dysplastic right kidney	penile torsion, chordee, imperforate anus, cardiac aryth, right vesicoureteral reflux	right ectopic scrotum
Lee et al. [21]	left inguinal	left renal agenesis	none	left ectopic scrotum
Lee et al. [22]	left inguinal	none	none	left ectopic scrotum
Kumar et al. [23]	right inguinal	right renal agenesis	covered exstrophy	right ectopic scrotum
our study	right inguinal	right renal agenesis	none	right ectopic scrotum

they grow toward each other to form the scrotum. The median scrotal raphe is the result of this fusion [17].

On the other hand, a condensation mesenchymatous tissue appears during the fifth week, and then it extends from the mesonephros to the abdominal wall. These tissues develop into the gubernaculum, and the inferior gubernaculum inserts into the labioscrotal swellings to descend into the testis [17].

Because gubernaculum and scrotal embryogenesis are related both anatomically and chronologically, it is advocated that a defect in distal gubernacular formation could prevent the migration of labioscrotal swelling and would result in a unilateral ectopic scrotum [3,14].

Lockwood described 4 different locations of the distal

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gubernacular attachment: the pubic area, saphenous area, superficial inguinal area, and perineal area. Therefore, the testis with the predominant portion of gubernaculums is misdirected to one of these other sides [4].

In most cases of unilateral scrotum, the testis is in the abnormally positioned scrotum. This also supports the statement that gubernaculum, which is present before the labioscrotal swellings, have begun their migration, and it directs testicular descent to the scrotum in this case of superficial inguinal locus [12].

A case with suprapubic inguinal scrotum was reported to be associated with ipsilateral upper tract anomalies, where there is not any renal anomaly with infrainguinal ectopic scrotum [14,15]. Unilateral penoscrotal transposition has been reported previously, 23 times only, in worldwide literature. All of these cases, including our own, have had associations with genitourinary anomalies.

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UroToday International Journal®

The Guide Wire: When Too Much of a Good Thing Is No Good at All

Guan Hee Tan, Hemanth Kumar Ramasamy, Kah Ann Git

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ABSTRACT

The guide wire is a very useful medical device that helps make the cannulation of blood vessels or hollow structures safer. However, guide wires themselves can be a source of complication, such as with perforation and bleeding. Kinking of the guide wire is another complication that is less described. We postulate the sequence of events that precede kinking and discuss the ways to avoid them.

A 60-year-old man underwent optical urethrotomy for a bulbar urethral stricture. A guide wire was passed into an existing suprapubic catheter (SPC) track to facilitate the passage of a flexible cystoscope. This was performed to examine the proximal extent of the urethral stricture. At the end of the procedure, there was unexpected resistance when withdrawing the guide wire from the bladder. Cystoscopic examination via the SPC track eased the guide wire out eventually. It was found that a kink in the guide wire had prevented its smooth retrieval. The cause of this complication was likely due to looping of the guide wire within the bladder. The loop then resulted in the guide wire getting kinked. In order to prevent kinking, one must avoid looping. Looping occurs when an excessive length of guide wire is forced into a confined space. Therefore, it is important to stop advancing the guide wire when resistance is felt. Another method to avert this problem is to first estimate the length of guide wire that would pass into the space without it curling back. Then pass the guide wire only up to the point where it is deemed adequate. By practicing such precautions, the chances of running into a complication, such as guide wire kinking, can be reduced significantly.

INTRODUCTION

Guide wires are widely used in the field of surgery and medicine. They are commonly used in procedures that involve the cannulation of blood vessels or hollow structures. Their application has been expanded with the advent of the Seldinger technique [1]. However, guide wires are associated with complications such as perforation, bleeding, and knotting [1-4]. Kinking of the guide wire is another complication that is described very little. Our case illustrates the possibility of this problem. We postulate how kinking might arise and describe the steps to prevent this from happening.

CASE REPORT

A 60-year-old man underwent optical urethrotomy for a short bulbar urethral stricture. He developed this stricture following trauma from transurethral catheterization when he had coronary artery bypass graft surgery (CABG) 6 months prior to presentation. His urine had been drained through a suprapubic catheter (SPC) since the surgery. At the beginning of this surgery, a rigid cystoscope was passed into the urethra until the distal part of the stricture was seen. There appeared to be a pinhole-sized communication with the proximal urethra. However, there was difficulty in advancing a guide wire retrogradely into the bladder. The SPC was removed and a guide wire was passed into the track. The guide wire was used

KEYWORDS: guide wire, complications, endourology

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Figure 1. The appearance of the guide wire upon withdrawal from the bladder. The inset illustrates a magnified view of the kink..

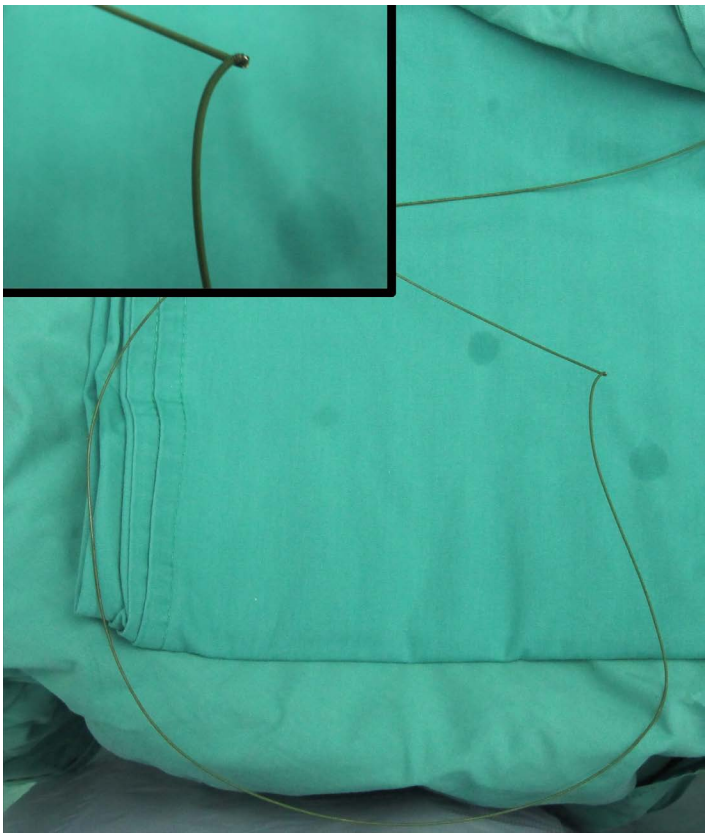
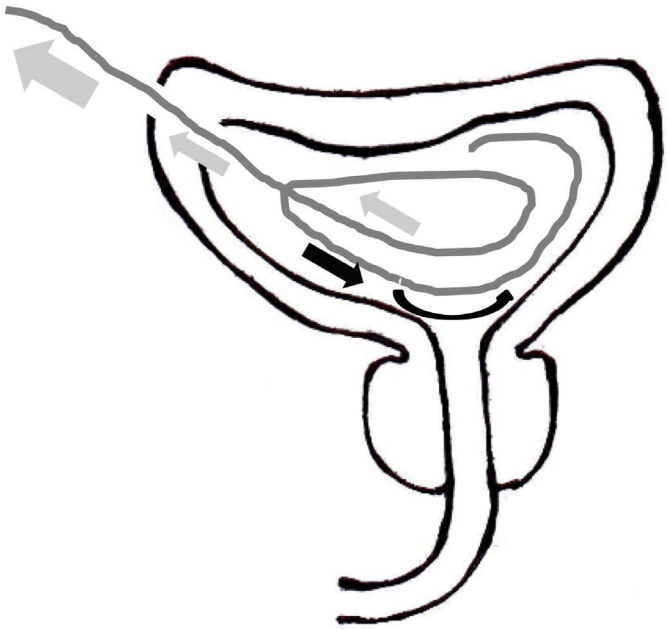


Figure 2. When an excessive length of guide wire forms a loop within the bladder, it produces a force in the opposite direction (black arrows) when it is being withdrawn (grey arrows).



to keep the track obvious while facilitating the introduction of a flexible cystoscope through it. The flexible cystoscope was guided to the point proximal to the stricture. A second surgeon then passed an optical urethrotome retrogradely and cut the stricture using the light from the proximal side as the guide. This rendezvous method successfully recanalized the urethra. A urinary catheter was passed into the bladder via the urethra.

The surgeon unexpectedly faced resistance when the guide wire was being withdrawn from the bladder via the SPC track. It was suspected that the guide wire had formed a knot within the bladder. After several unsuccessful attempts at extracting it, the flexible cystoscope was reintroduced through the SPC track to examine the cause of this complication. There was no knot seen in the wire but the passage of the flexible cystoscope within the track helped ease the guide wire out. It was then noted that the guide wire had kinked severely (Figure 1). The patient recovered uneventfully from the surgery.

DISCUSSION

Guide wires have become an integral part of many procedures in surgery and medicine. Its use spans over many specialties, and it is particularly useful in areas where the cannulation of a blood vessel or a hollow structure is involved. The popularity of guide wires probably stemmed from a very simple yet effective technique first described by Sven-Ivar Seldinger [1]. In the technique that now bears his name, a guide wire is passed through a needle that is first punctured into a particular vessel or hollow structure. Upon removal of the needle, the guide wire is used to facilitate the passage of a cannula into the structure by sliding the device over the guide wire. This technique makes cannulation much safer than “blind” insertion.

In urology, the guide wire is commonly used to help steer urological devices or endoscopes within confined spaces. Typical procedures where a guide wire is used in urology are ureteric stenting and ureterorenoscopy. Occasionally, a guide wire is used to maintain the patency of a SPC track in order to facilitate endoscopy via this route. This technique was employed in the management of our patient and it allowed an easy passage of the flexible cystoscope through the SPC track. However, the use of guide wires is not without complications.

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Figure 3. The loop tightens within the bladder when the outward force (grey arrows) is countered by the inward force (black arrows).

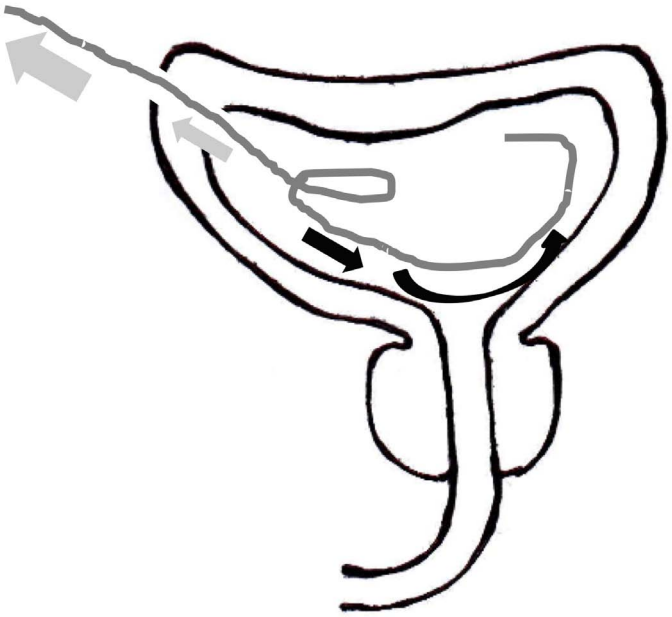
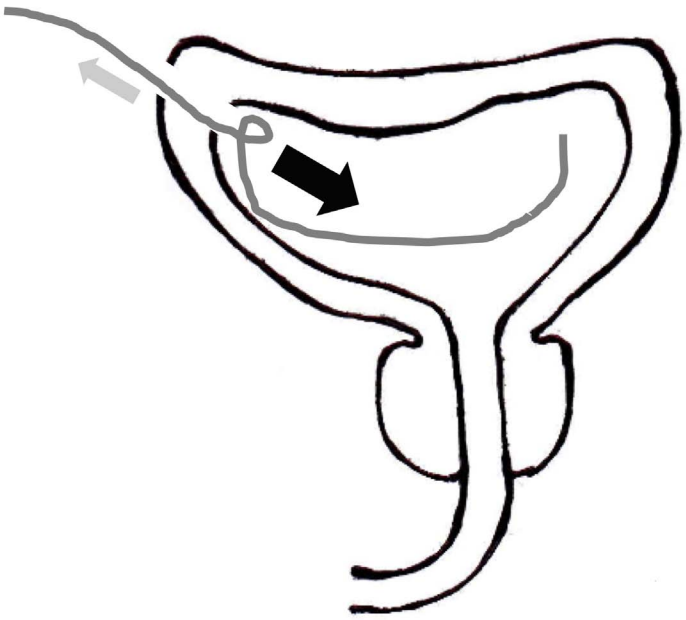


Figure 4. The loop eventually forms a kink within the bladder and prevents the guide wire from being withdrawn.

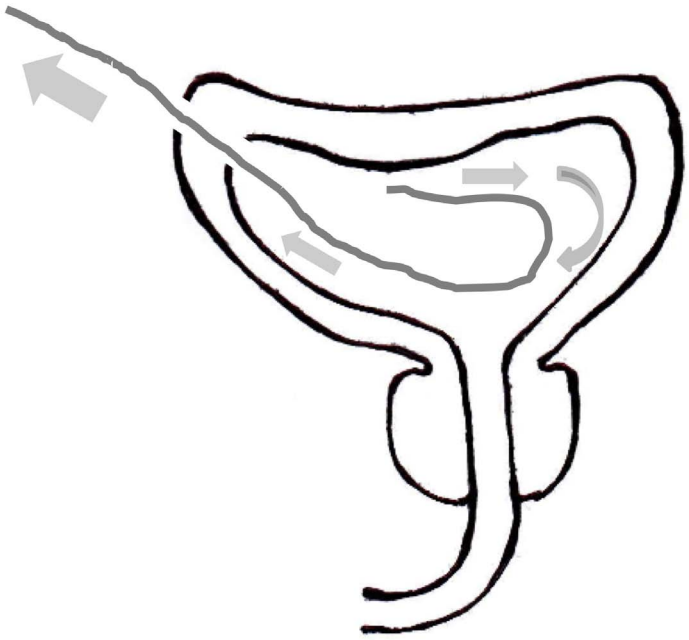


Perforation and bleeding are among the complications that can occur [1]. This is especially so if a stiff guide wire is used in a thin-walled structure such as a vein. Knotting, infection, fistulization, and retained guide wires have also been described [1-4]. Although kinking is not widely reported, it is certainly possible as illustrated by this case.

It is thought that looping must precede knotting [5]. We postulate that kinking has a similar origin because looping can also lead to kinking. Looping occurs when an excessive length of guide wire is forced into a confined space such as the bladder (Figure 2). The extra length of guide wire then forms a coil or loop within that space. When the guide wire is withdrawn, the weight and memory of the guide wire loop allows it to produce a force in the opposite direction (Figure 3). As the operator applies more force outwards, the loop tightens within and eventually forms a kink (Figure 4). In a situation where there is no looping, the guide wire can easily slide out of the space because the distal end of the wire does not produce any opposing force (Figure 5).

Kinking is an avoidable complication. In order to prevent kinking, one must avoid looping. Extra care has to be taken to ensure that no excessive length of the guide wire is inserted. Often, slight resistance can be felt once the excess guide

Figure 5. When there is no looping, the guide wire slides out easily because there is no opposing force that would cause it to kink.



wire starts to form a loop within. The surgeon should avoid advancing the guide wire any further at this point. However, sometimes the guide wire can coil without much resistance until it has formed several loops. One way to circumvent this problem is to first estimate the length of guide wire that should safely enter the space without looping. If an adequate length is deemed to have passed, it is wise to stop advancing the guide wire further. This is one situation where too much of a good thing may not be good at all.

The guide wire has become an indispensable tool in the arsenal of devices used in modern surgery and medicine. It has made interventional procedures such as cannulation, stenting, and endoscopy much safer. Nevertheless, the design of the guide wire continues to evolve to improve its performance. Research is aimed at making it more resistant to structural failure and therefore less prone to complications [6,7]. Despite our quest for the perfect guide wire, we should still bear in mind that it is the manner in which we use it that really matters. Good knowledge of the guide wire's property and behavior is the key to minimizing complications. When it is handled with great care and skill, the guide wire is one of the most useful medical devices of our time.

CONCLUSION

When using the guide wire, it is crucial to be aware of the possible complications that might arise. Kinking of the guide wire is one such complication. It is, however, an avoidable complication because looping is postulated to precede kinking. In order to prevent looping, the operator must not forcefully advance the guide wire once resistance is felt. It is also good practice to estimate the length of guide wire that can enter the space without forming a loop. These steps can help avert looping and thus reduce the possibility of kinking.

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UroToday International Journal®

Malignancy of a Horseshoe Kidney: A Case Series with a Rare Presentation

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ABSTRACT

Horseshoe kidney is the most common fusion anomaly. Patients with horseshoe kidney typically present with symptoms related to infection, stone formation, and hydronephrosis. Rarely, patients may present with malignancy of horseshoe kidney, and most of them arise from isthmus. We are presenting a case series of 2 cases of renal cell carcinoma arising from horseshoe kidney.

INTRODUCTION

Horseshoe kidney (HSK) is the most common fusion anomaly, with an incidence rate of 1 in 400 of the general population [1]. While most of the reported cases are incidental findings, sometimes a patient may present with pictures of hydronephrosis, infection, and calculus formation [2]. Rarely, a patient presents with malignancy of the renal unit. Hildebrand, in 1895, is credited with reporting the first case of malignancy of HSK [3]. Most of these malignancies were arising from isthmus of HSK [4], and the majority of these were of the clear-cell variety. We are reporting here 2 cases of renal cell carcinoma (RCC), including a very rare case of the papillary-cell variety arising from the upper pole.

CASE REPORT

Case Number 1

A 50-year-old female patient presented to our outpatient department with a chief complaint of a single episode of painless, total gross hematuria not associated with the passage of clots 2 months before presentation. There was no history of flank pain, dysuria, fever, graveluria, weight loss, or anorexia. On physical examination, an ill-defined lump 7 cm x 5 cm was palpable in the upper right quadrant involving the right lumbar and umbilical regions. The baseline blood investigations were within the normal limit. His urine examination revealed 30-35 RBC/HPF. An ultrasonography of the abdomen indicated the presence of HSK with a mass approximately 7 cm x 6 cm arising from the upper pole of the right renal moiety.

The multidetecting computer tomography (CT) scan confirmed the presence of an HSK with fusion at the lower pole, an enhanced lesion of 7.3 cm x 7 cm arising from the upper pole of the right renal moiety, and areas of calcification and necrosis suggestive of RCC (Figure 1). The metastatic work-up, which included a chest X-ray and liver function test, was normal. On exploration, HSK with a well-formed isthmus connecting the lower pole of both kidneys with a mass arising from the upper pole of the right renal moiety was seen. No significant lymphadenopathy was noticed (Figure 2). The patient underwent right radical nephrectomy with isthmectomy by the right subcostal transperitoneal approach. Intraoperatively, the finding of a HSK with a mass arising from the right upper pole was confirmed. A well-formed isthmus was found connecting to the lower pole. The stump of the isthmus was run under with an absorbable running suture, and then it was covered with an omental patch to prevent hemorrhage and urinary fistula

KEYWORDS: Clear-cell carcinoma, fusion anomaly, horseshoe kidney, papillary-cell carcinoma, renal cell carcinoma

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ABBREVIATIONS AND ACRONYMS

HSK: Horseshoe kidney
LFT: Liver function test
OPD: Outpatient department
RCC: Renal cell carcinoma

Figure 1. A CT scan showing a mass arising from the right renal moiety of a horseshoe kidney. .

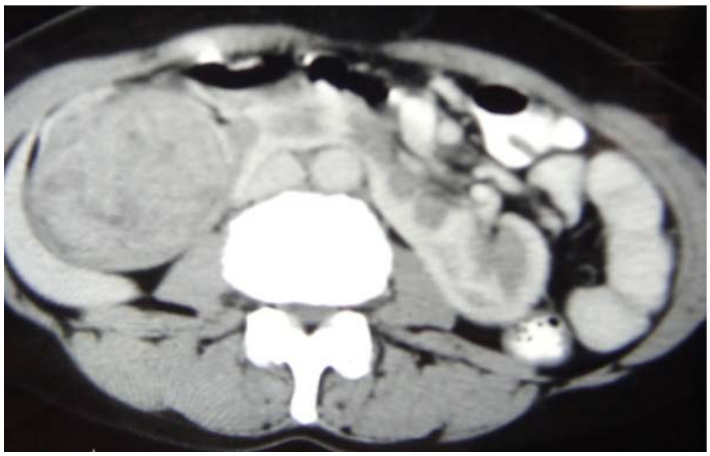


Figure 2. An intraoperative picture of the right renal moiety with the isthmus.

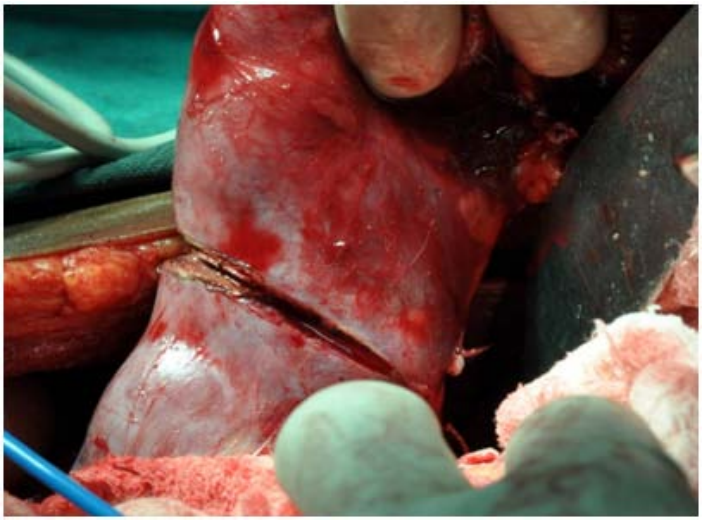
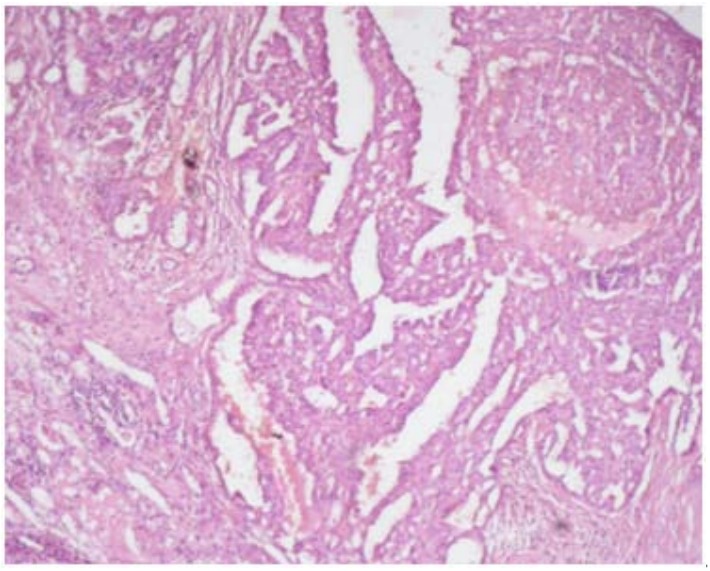


Figure 3. The microscopic appearance of type II papillary RCC demonstrating eosinophilic cells.



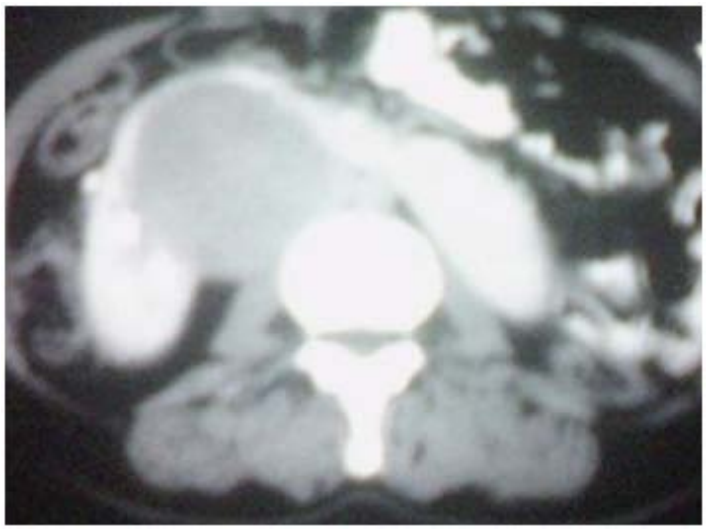
formation. Postoperative recovery was uneventful and the patient was discharged on the fourth postoperative day. The microscopic diagnosis was papillary carcinoma type II with no invasion of the capsule and negative surgical margins (Figure 3). The patient is under regular postoperative surveillance without any local recurrence or metastatic activity after 10 months postoperation.

Case Number 2

A 40-year-old female patient presented to our OPD with a chief complaint of right flank pain with a few episodes of painless, total gross hematuria with the passage of clots. There was no history of dysuria, fever, graveluria, weight loss, or anorexia. On physical examination, an 8 cm x 7 cm lump was palpable in the right lumbar region. Her baseline blood investigations were within the normal limit. An ultrasonography of the abdomen revealed HSK with a mass approximately 10 cm x 8 cm arising from the lower pole of the right renal moiety. A multidetecting CT confirmed HSK fused at the lower pole with an enhanced 10 cm x 8 cm lesion arising from the lower pole of the right renal moiety and adjacent isthmus, along with areas of calcification and necrosis suggestive of RCC (Figure 4). Metastatic work-up, including a chest X-ray and liver function test, was normal. On exploration, HSK with a mass arising from the lower pole and part of the isthmus was seen. The patient underwent transperitoneal right radical nephrectomy with isthmectomy. Intraoperative findings of a HSK with a mass arising from the right lower pole involving part of the isthmus were confirmed. No significant lymphadenopathy was noticed. The stump of isthmus was run under with absorbable running sutures, and then it was covered with an omental patch to prevent hemorrhage and urinary fistula formation. Postoperative recovery was uneventful. A microscopic diagnosis revealed the clear-cell variety of RCC with no invasion of the capsule and negative surgical margins.

DISCUSSION

Figure 4. A CT scan showing the mass arising from the lower pole of the right renal moiety and isthmus of a horseshoe kidney.



Horseshoe kidney is the most common fusion anomaly, with an incidence of 0.25% in the general population [1]. Jacopo Berengario da Carpi first described it in 1522 during an autopsy, but Botallo, in 1564, presented the first extensive description and illustration of a horseshoe kidney [5]. It is found to be more frequent in men, with a 2:1 male/female ratio. This anomaly consists of 2 distinct renal masses lying vertically on either side of the midline and connected at their respective lower poles by a parenchymatous or fibrous isthmus that crosses the midplane of the body. Embryologically, the abnormality occurs between the fourth and sixth week of gestation after the ureteric bud has entered the renal blastema. There are several variations in the basic shape of the horseshoe kidney. In 95% of cases, the kidneys join at the lower pole, which occurs before the kidneys have rotated on their long axes. In a small subset, an isthmus connects both upper poles [6].

Because of the increased use of ultrasound screening, most of the time it is diagnosed incidentally, and sometimes patients present with pictures of hydronephrosis, infection, and calculus formation. However, it is rare that a patient presents with malignancy of the renal unit. About 150 patients with horseshoe kidney presenting with malignancy of the renal unit have been reported [7]. Two cases of bilateral tumors have been reported [8]. Of all the reported cases, renal cell carcinoma accounts for about half of the cases [4] while renal pelvic tumors and Wilms tumor account for the remaining 50% (with equal incidence). Rarely, sarcoma and carcinoids have been reported. The incidence of RCC in HSK is no greater than that in the general population, but renal pelvic tumor and Wilms tumor are greater. Except for renal pelvic tumors, most of the renal malignancy in HSK arises from the isthmus [4,9]. The first case report in our case series is very rare because of the origin of RCC from the superior pole of the right renal moiety of a female patient. Moreover, the histological finding of papillary type II RCC is also unusual as most of the individual case reports in literature for RCC in HSK is of the clear-cell variety. Papillary renal cell carcinoma is typically composed of cells with abundant, clear to faintly eosinophilic, cytoplasm arranged in nests and papillary structures, as seen in Figure 3 of our case [10]. Papillary RCC is the second most frequent RCC subtype after clear-cell carcinoma accounting for approximately 13 to 15% of all known diagnoses of RCC in a normal kidney. Type II papillary RCC is less common than type I. Preoperative information about neoplastic localization, including a local extension to the surrounding structure and vasculature, is an indispensible part of the diagnostic approach to horseshoe kidney tumors, so that complete resection of the tumor can be carried out without unnecessarily removing functional tissue. When planning the operation, the possibility of growth of the tumor through the parenchymatous isthmus from one side of the kidney into the other side should be taken into account. If the tumor is present on both sides of the isthmus, surgery for both renal units is necessary. If the tumor is small and confined to the isthmus, isthmectomy is feasible [9]. Regardless of whether the procedure is radical or organ-sparing, the division of the isthmus is essential, not only to achieve complete access to the lymph nodes, but also to normalize the course of the ureter and to prevent the potential development of Rovsing syndrome [11]. Survival from these tumors is related to the pathology and the stage of the tumor at diagnosis, and not to the renal anomaly [12]. In our case series, survival seems to be good since the tumor was localized and didn't involve perinephric fat or any adjacent structure. The objective of postoperative kidney tumor surveillance is the early identification of local recurrence and metastatic activity.

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Metanephric Adenoma of the Kidney: Can We Take a Step Forward in a Presurgery Diagnosis?

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ABSTRACT

The widespread use of imaging diagnostic tools has led to the detection of a greatly increased number of incidental renal tumors. Many of these tumors are benign and can be treated with nephron sparing surgery or radical nephrectomy. However, the clinical and even imagiological aspects of these histopathologically benign tumors are too scarce and nonpathognomonic, making their diagnosis rather difficult. Metanephric adenoma (MA) of the kidney, a rare and benign neoplasm, is an example of an entity usually difficult to distinguish from malignant neoplasms. We report one clinical case and review of this clinical entity emphasizing the need for better and more accurate diagnostic means for benign renal masses.

INTRODUCTION

Benign lesions of the kidney represent a challenging clinical diagnosis. Despite the sensitivity of current imaging techniques, a definitive diagnosis is made histologically. The metanephric adenoma of the kidney is a rare, slow-growing tumor with a good prognosis (although there are descriptions of metastatic disease) [1,2]. It can present itself (through ultrasound and computed tomography (CT) scans) as a well-circumscribed, solid lesion, sometimes with calcifications, and hypovascular on angiography [3]. Usually it is asymptomatic, with a 10% association with polycythemia [4]. It occurs mostly in young and middle-aged people, usually in females [4]. Histologically, metanephric adenoma (MA) is composed of epithelial cells whose origin is related to the development of the fetal kidney proximal tubule. Differential diagnoses with malignant lesions such as nephroblastoma or papillary renal cell carcinoma (PRCC) may make this condition regularly over treated [1]. Clinical and radiological aspects of this tumor are not enough for a correct diagnosis before histological evaluation. Cytological diagnosis using fine-needle aspiration can be difficult [5]. At these times, genetics can acquire a significant role in the diagnosis and follow-up of renal benign lesions such as metanephric adenoma [6]. We present, in this paper, 1 rare case report of MA of the kidney that illustrates how difficult an accurate diagnosis for this pathology can be, emphasizing the requirement of new, improved, and tailored diagnoses.

MATERIALS AND METHODS

This paper results from a structured and comprehensive literature review. Searches were done with PubMed. Initial search terms were "metanephric adenoma" and "kidney" (in articles published between 2000 and 2012). Based on the results of these initial searches, additional separate searches were performed using terms such as "renal benign tumor," "radiological diagnosis," and "treatment in combination with metanephric adenoma." The references section in published articles was also examined and compared with electronic search results to maximize the review and inclusion of pertinent data. Medical records of 1 patient submitted to renal surgery for renal masses with a pathology diagnosis of metanephric adenoma of the kidney were reviewed. Images were obtained from the patient's clinical file.

Disease Case Analysis

MCF, a 37-year-old woman, was sent by a general practitioner

KEYWORDS: *Echinococcus*, cystic hydatid disease, retroperitoneum, secondary hypertension

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Figure 1. The abdominal CT, renal view: A solid nodule in the external cortex of the middle third of the left kidney measured 20 mm. It was well circumscribed and exophytic but organ limited. It was hypovascular after intravenous contrast..

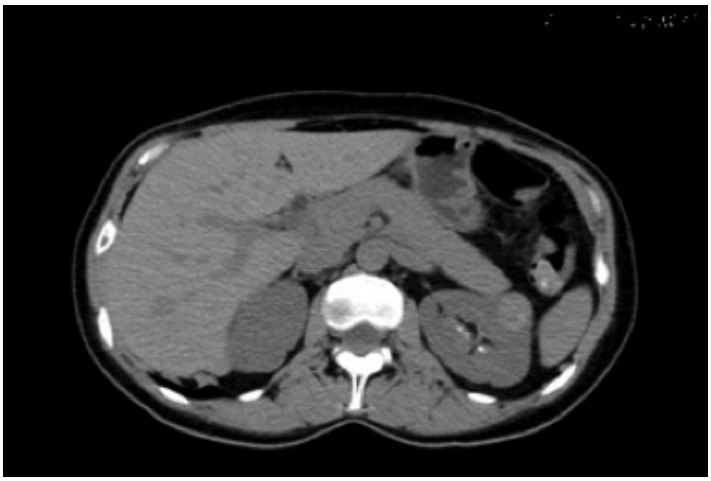
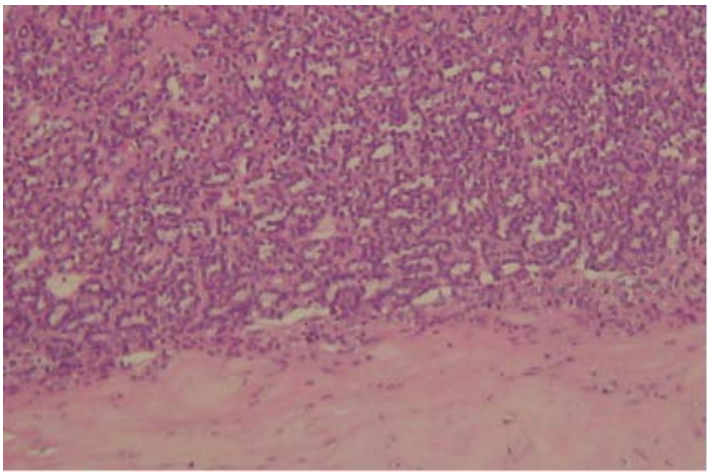
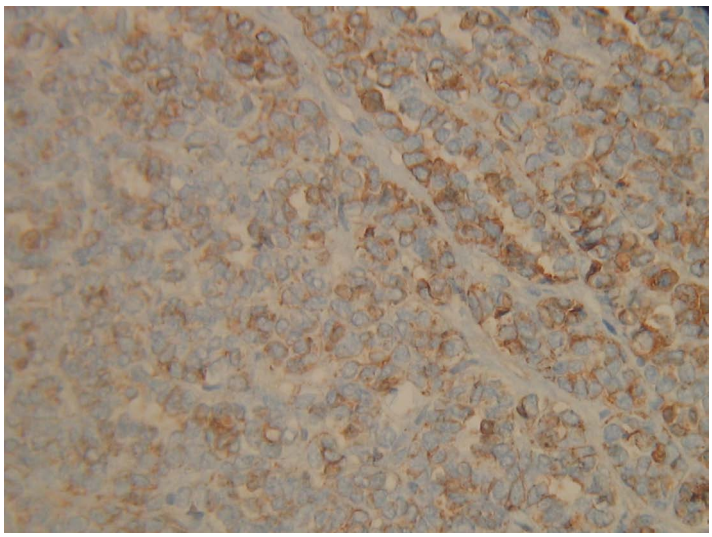


Figure 2. The microscopic appearance of MA (H&E, magnified 100 x). It is noncapsulated and densely cellular (occasional papillary and tubular morphology) with specific glomeruli. There are small uniform epithelial cells and round nuclei without prominent nucleoli or mitoses. Little stromal hyalinization was also observed.



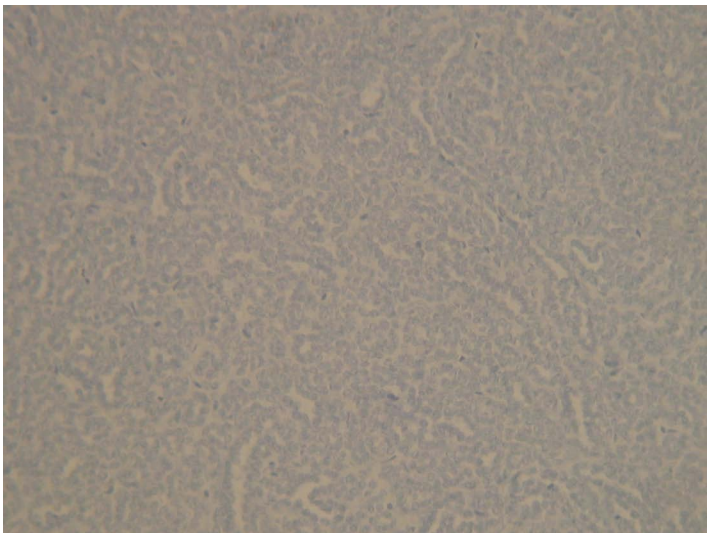
(GP) to urology consultation because of a history of recurrent urinary tract infections (UTIs) over a period of 2 years. She exhibited UTIs with dysuria and fever (maximum of 38° C) but no hematuria. She had no history of other medical diseases or surgery. She took no prolonged medication, and she denied any sexually transmitted diseases. A renal ultrasound revealed a solid and limited right renal mass of 2 cm, suggestive of a cyst without liquid content and bilateral, millimetric renal sinus lithiasis. Her abdominal CT scan (Figure 1) revealed a solid nodule in the external cortex of the middle third (left kidney) measuring 22 mm. The nodule remained hypovascular after intravenous contrast suggesting a complicated cyst or a poorly vascularized solid mass. The liver, spleen, and pancreas were unremarkable, and the right kidney showed no evidence of mass or hydronephrosis. The CT did not show any lymph node involvement. Her urine cytology did not show any malignant cells. Her complete blood count (CBC) showed no alterations. Her biochemical assessment presented normal renal function and normal hepatic function, and both urinalysis and urine cultures were negative. She had normal coagulation tests. Given the size, localization, and the patient's age, a laparoscopic partial nephrectomy was performed.

Figure 3. Immunostaining: Immunopositivity for CD57 in most tumor cells, and focal positivity for AE1/AE3.



Pathology results revealed a noncapsulated renal neoplasia, with 2.5 cm x 2.2 cm x 1.5 cm densely cellular cells with tubular morphology, occasionally papillary, with aspects specific to glomerulus. Hematoxylin and eosin stains revealed neoplastic epithelial small cells, uniform with round nuclei without mitoses (Figure 2). Diffuse-positive staining for CD57 (Figure 3) in almost all cells, focal or the absence of positivity for AE1/AE3, and EMA and cytokeratin 7 are characteristics that allow the diagnosis of metanephric adenoma of the kidney. Immunostaining for racemase (P504) was not performed; neither were cytogenetic studies to evaluate trisomy for chromosomes 7 and 17 (for the

Figure 4. Immunostainning: No immune stain for CK7.



diagnosis of PRCC). The predominance of epithelial cells also excludes the diagnosis of Wilms tumor. After 2 years of follow-up, the patient remains disease free with normal renal function.

DISCUSSION

Metanephric adenoma is a rare and benign (only 1 case of metastatic disease neoplasm of the kidney reported) renal disease [7]. Generally, the patients are asymptomatic, although symptoms can include abdominal pain, abdominal mass, hematuria, dysuria, fever, and hypertension [1]. Polycythemia has been described [4,8,9], probably related to the production of erythropoietin and cytokines by MA cells [10]. This lesion generally appears in middle-aged adults and more frequently in women (> 2:1) [11].

Similar to other small renal masses (SRMs), this tumor is normally revealed incidentally during radiologic studies for other clinical problems and constitutes a serious diagnostic challenge. Several diseases can resemble MA, including Wilms tumor, PRCC, and metastatic papillary thyroid carcinoma [1]. Radiologic findings are not pathognomonic. The ultrasound (US) shows a lesion hypo-, iso-, or hyperechoic compared with the adjacent renal cortex. MA is considered hypovascular or weakly vascularized, with no vascular flow on the color Doppler US [3]. It is a well-circumscribed, solid, and homogeneous neoplasm showing higher attenuation than adjacent renal parenchyma on CT [3]. However, in some cases, areas of hemorrhage, necrosis, and cystic degeneration have been reported [3,4,12] and generally form well-demarcated masses without fibrous capsules in their majority [4,12].

Protrusion above the renal capsule is common [4], but not extrarenal invasion [13]. Cytology and immunohistochemistry assays can unveil the diagnosis, although the differential diagnosis from epithelial carcinoma, predominantly Wilms tumor, and solid variants of papillary carcinoma can be problematic. Wilms tumors generally appear at a younger age, are grossly tan-gray with hemorrhage or cysts, triphasic. WT1+, CD57+, and vimentin appear on the immunohistochemistry stain. PCCR is red-brown with thick capsules, and cells have more cytoplasm, nuclear grooves, and prominent nucleoli. Immunostaining shows strong cytokeratin 7 (CK7), strong AE1, strong alpha-methylacyl-CoA racemase (AMACR), epithelial membrane antigen (EMA+), CD57-, and WT1-.

Metanephric adenomas are composed of tight, short papillae and loose sheets of cells with scant cytoplasm, round nuclei, fine chromatin, and rare small nuclei. MA shows reactivity for CD57, vimentin, S-100 protein, and lysozymes [14]. Diffuse-positive immunostaining for CD57 and WT1 are often observed; CD57 staining argues against Wilms tumor. Weak or negative staining for CK7 and EMA argue against PRCC. Chromosomal analysis may also be helpful. Wilms tumors show alterations at chromosome 11p, and PRCC is characterized by the loss of chromosome 3, trisomy of chromosomes 7 and 17, and the loss of chromosome Y [15,12].

The need for accurate diagnoses has led some surgeons to perform diagnostic biopsies preoperatively. Nevertheless, even some reports support that percutaneous fine-needle aspiration biopsy can be sufficient to establish the diagnosis [5] while others defend that immunocytochemical analysis is essential [16] for differentiation between MA and Wilms tumor. However, recent studies showed excellent results in the genetic identification of MA of the kidney. DNA studies (from samples harvested by biopsy) performed by Choueiri et al. revealed that BRAF V600E mutations are present in approximately 90% of all MA cases studied. This new discovery has potential value in the differential diagnosis of SRMs undergoing a percutaneous biopsy and consequent clinical management and follow-up [6]. Genetic studies have been limited because of the rarity of such tumors, but recent findings are a step closer in the diagnosis of benign small renal masses that can be amenable just by surveillance. More studies are needed to have better accuracy in the diagnosis of renal masses, reducing the need for surgical approaches in most patients and the resulting morbidities.

CONCLUSION

The author's intent is to highlight a rare disease that may simulate other malignant renal tumors. In our department, this is the second MA of the kidney operated on since 2007, confirming the increased and widespread use of radiologic tools and the consequent diagnosis of small renal masses, the

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majority of them asymptomatic and benign. MA is a rare renal tumor, which remains a diagnostic challenge since it is similar to 2 aggressive renal tumors: Wilms tumor and PRCC. Most of the time, diagnoses are made postoperatively with cytogenetic and immunohistochemistry assays.

MA showing typical features can be safely regarded as a benign tumor, and treatment should consist of local resection or active surveillance. However, there is scarce knowledge about the genetic and histologic behavior of renal masses in order to permit the conscientious management of these lesions and appropriate surveillance.

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Primary Retroperitoneal Granulosa Cell Tumor

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ABSTRACT

Granulosa cell tumors (GCT) of the ovary are rare tumors that represent 2% of all ovarian tumors. However, cases involving the retroperitoneum are exceedingly rare. We describe a case of primary retroperitoneal granulosa cell tumor, which, to our knowledge, has been previously reported in few cases.

A 64-year-old female presented with large intra-abdominal mass and vague abdominal pain. She had a history of hysterectomy and bilateral salpingo-oopherectomy 22 years ago for a large uterine leiomyoma. She underwent exploratory laparotomy that revealed a retroperitoneal mass measuring 11 cm x 13 cm in size, with multiple cyst formation and areas of necrosis and hemorrhage. The gross, histologic, and inhibin-positive immunostaining findings of the retroperitoneal mass were characteristic of adult-type GCT. Excluding any previous history of primary ovarian GCT with this patient, a de-novo retroperitoneal diagnosis was carried out.

INTRODUCTION

The name "granulosa cell tumor of the ovary" (GCT) was proposed by von Werdt in 1914 and has been widely adopted [1]. GCTs account for approximately 2% of all ovarian tumors belonging to the sex cord-stromal category and include tumors composed of granulosa cells, theca cells, and fibroblasts in varying degrees and combinations [2]. What's peculiar for this type of tumor is that it can recur or metastasize long after initial treatment [3]. However, to have primarily originated retroperitoneal GCT is extremely rare [4,7].

CASE REPORT

A 64-year-old postmenopausal female presented with intermittent, vague abdominal pain of a 1-year duration. She has known cases of hypertension, diabetes mellitus, left ectopic pelvic kidney, and hysterectomy with bilateral salpingo-oophorectomy that were performed 22 years prior to presentation, with a provisional diagnosis of uterine leiomyoma and normal ovaries which was confirmed by histopathology. Her physical examination revealed a large, left-sided, firm, irregular, 10 cm x 8 cm abdominal mass with ill-defined margins. On investigation, her hemoglobin, kidney function, and liver function tests were within normal limits, and she had negative urine cytology for malignancy. Tumor markers, including CEA, CA-125, AFP, B-HCG, and LDH, were normal. Her computerized tomography (CT) revealed a large, lobulated, heterogenous, faintly enhanced left retroperitoneal mass measuring 8 cm x 13 cm with cystic components, displacing the pancreas and the duodenojejunal flexure anteriorly, and it shifted great vessels slightly without significant mass effect (Figure 1 and Figure 2).

Ultrasound-guided Tru-Cut biopsy revealed a tumor characterized by proliferating small to medium sized cells with low mitotic rates and eosinophilic cytoplasm, arranged in trabecular pattern with rosette formations. The differential diagnosis was broad and included renal metanephric adenoma, primary renal malignant tumor, lymphoma, and others (Figure 3).

The patient underwent exploratory laparotomy, and the excision of a retroperitoneal mass was accomplished. It extended from the level of renal vessels to the level of bifurcation of great vessels. Grossly, the mass was encapsulated, grayish-yellow, and measured 13 cm x 11 cm x 7 cm. The cut section showed a white-to-yellow whorly cut surface with multiple foci of hemorrhages and necrosis.

Microscopically, the tumor was composed of islands of

KEYWORDS: Granulosa cell tumors, retroperitoneum, inhibin

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Figure 1. Axial CT section showing the retroperitoneal mass displacing great vessels, pancreas, and the duodenojejunal flexure (arrow).

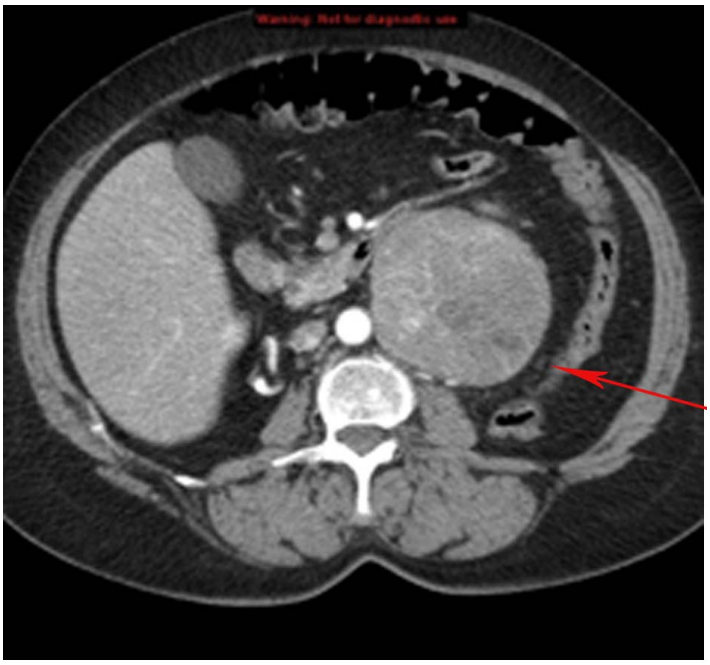
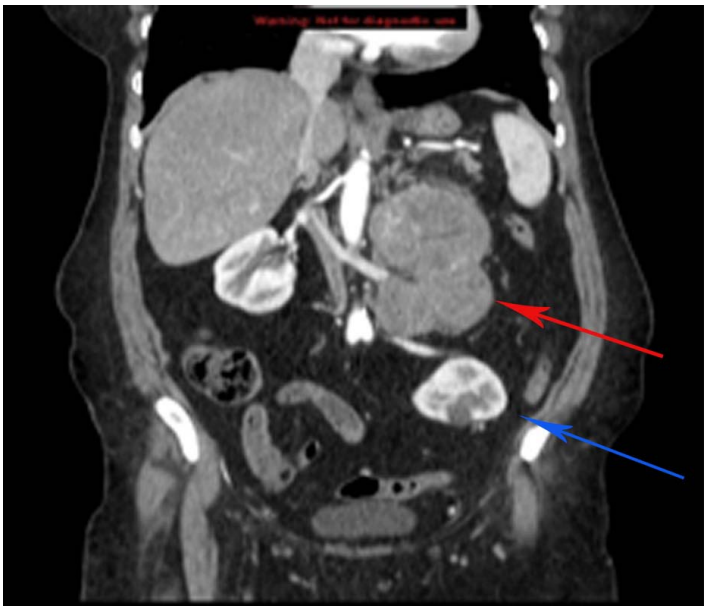


Figure 2. Coronal CT section showing the retroperitoneal mass displacing great vessels and taking direct blood supply from them (red arrow). See also the congenital, malrotated, left ectopic pelvic kidney (blue arrow).



proliferating uniform cells with hyperchromatic nuclei, and ill-defined cell borders with ill-defined and abundant eosinophilic cytoplasm. Longitudinal nuclear grooves were present. Mitotic activity was low; microfollicular patterns with Call-Exner bodies were also evident (Figure 4).

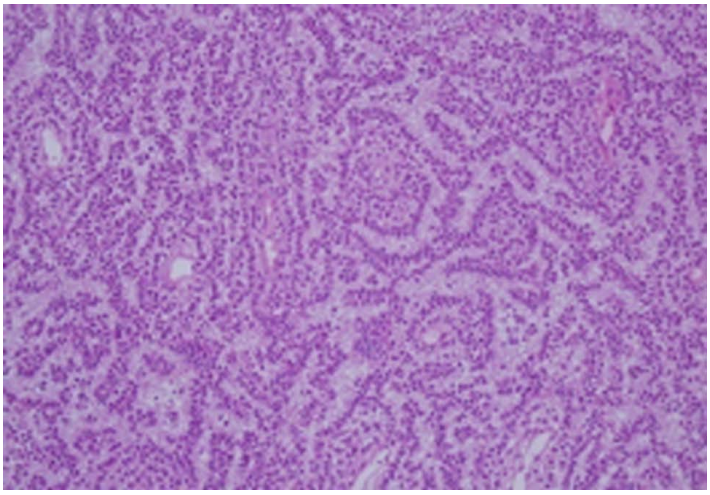
The morphology showed granulosa cell tumors, which were confirmed by strong, diffuse, cytoplasmic positive reactions of the tumor cells for alpha-inhibin antibodies upon immunohistochemical (IHC) staining, and then a diagnosis of primary retroperitoneal granulose cell tumor was rendered (Figure 5).

After surgery, the patient recovered well; no adjuvant chemotherapy or radiotherapy was given, and the patient was sent home for regular follow-up with history, clinical examination, imaging, and tumor markers.

DISCUSSION

GCTs are uncommon ovarian tumors that compromise 2% of all ovarian cancers. There are 2 subtypes: adult and juvenile, based on different clinical and histological features [3]. Adult granulosa cell tumors of the ovary are oftentimes hormonally active stromal cell neoplasms that are distinguished by their ability to express aromatase and secrete sex steroids such as estrogen [5].

Figure 3. Trabecular (gyriform) growth pattern of the tumor presented in the core biopsy.



Granulosa cell tumors can arise in locations other than the ovary and may be derived from the mesenchyme of the genital

ridge. Women who have undergone oophorectomy may have the potential to develop granulose cell tumors [8]. An English literature search to 2009 revealed 16 such primary extraovarian sex-cord stromal tumors: 7 arose in the broad ligament, 4 in the retroperitoneum, 1 in the fallopian tube, 1 in an umbilical hernia sac, 1 in the adrenal gland, 1 in the pelvic side wall, and 1 in the mesentery of the ileum [4,7].

The cytogenetic abnormalities of GCT of the ovary are only partially known. Up to now, mainly numerical chromosomal aberrations have been described; for example, trisomy 12 and 14 are frequent aberrations. However, monosomy 22 is even more prevalent [6].

It has recently been reported that 95 to 97% of adult granulosa cell tumors carry a unique somatic mutation in the FOXL2 gene. This mutation is a potential driver in the pathogenesis and appears to play a major role in the cell-cycle regulation of adult-type GCTs [9]. Patients with GCT require long-term follow-up with history, physical examination, and tumor marker studies because 17% of relapses occur more than 10 years after diagnosis [3]. The most common site of recurrence is in the pelvis [3].

Extraovarian GCT should be differentiated from other metastatic carcinomas of the ovary as it has similar morphology. It also has to be differentiated from other tumors such as small-cell carcinoma, undifferentiated carcinoma, endometrial stromal sarcoma, carcinoids, and lymphoma. Inhibin, calretinin, and epithelial membrane antigen (EMA) immunostains can help in differentiating these tumors. GCT is positive for inhibin and calretinin and negative for EMA. Other tumors do not show positivity for inhibin and calretinin [10].

Figure 4. Microfollicular pattern with Call-Exner bodies. Eosinophilic material and debris are in the center. Longitudinal grooves are seen in the right lower corner.

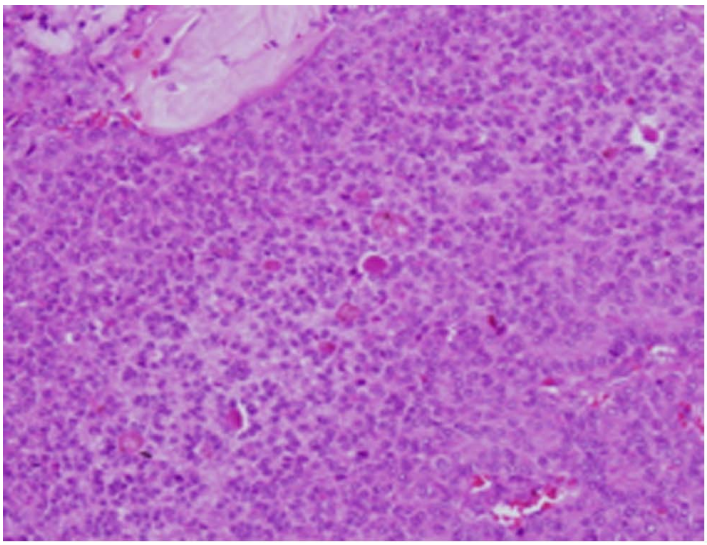
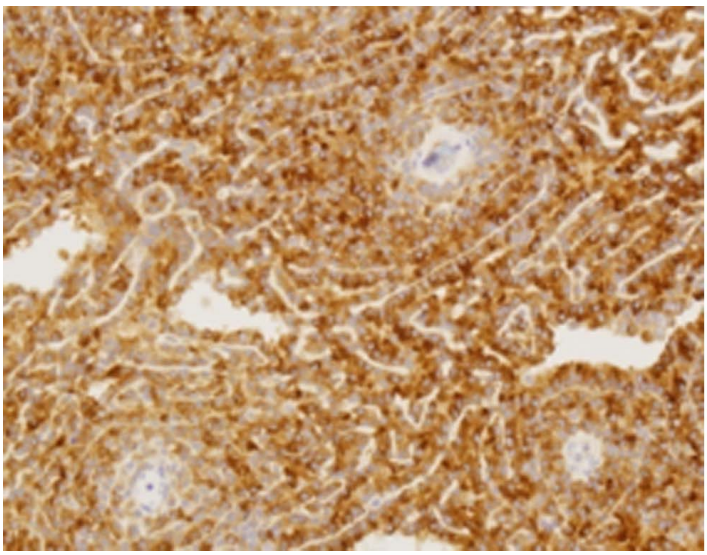


Figure 5. Alpha-inhibin positive cytoplasmic staining.



CONCLUSION

The case of primary retroperitoneal granulosa cell tumor is reported for its rarity after excluding previous ovarian origins. We have noticed during our thorough literature review that all those rare cases, including ours, occurred in patients with a history of previous oophorectomy. Surgery is the primary treatment for these tumors; however, long-term follow-up with history, clinical exams, and tumor markers is crucial for GCTs, since later relapse is a behavior for these unique tumors.

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Primary Retroperitoneal Hydatid Disease Causing Secondary Hypertension: A Case Report and Review of the Literature

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ABSTRACT

Hydatid disease is caused by the parasite *Echinococcus granulosus*. Humans are accidental intermediate hosts, and the parasite commonly affects the liver and the lungs. Primary retroperitoneal hydatid disease is extremely rare. We present a rare case of a primary retroperitoneal hydatid cyst with secondary hypertension treated through surgical means.

INTRODUCTION

Hydatid disease is a zoonosis produced worldwide by *Echinococcus* tapeworm larvae. The most commonly involved organs are the liver (75%) and the lungs (15%), with only 10% of cases occurring in other parts of the body [1]. Retroperitoneal involvement was always thought to be secondary to a rupture of the liver or spillage during liver surgery for hydatid disease [2]. Primary retroperitoneal hydatid disease is extremely rare, accounting for only 0.8% of cases [2,3]. We present a rare case of a primary retroperitoneal hydatid cyst with secondary hypertension that was treated with surgery.

CASE REPORT

A 65-year-old female presented with dull aching pain on the left side of her abdomen for a duration of 6 months. She was recently diagnosed with hypertension 3 months prior to presentation. Urinary symptoms were absent. On examination, her blood pressure was 160/100 mm Hg. There was a cystic, lobulated, non-tender mass measuring 20 cm x 12 cm noted in the left side of her abdomen. Other systemic examinations were unremarkable. Her hematology and biochemical investigations were normal. Her urine examination showed traces of albumen. The patient underwent an ultrasound of the abdomen (USG), which revealed a well-defined complex cyst with internal echoes measuring 20 cm x 14 cm. They were discovered in the left lumbar region, and they extended into the left hypochondrium and left iliac fossa (Figure 1). Computerized tomography (CT) of the abdomen revealed a large cystic lesion measuring 25 cm x 13 cm x 12 cm, with multiple internal radial septations with specks of calcifications noted in the left hemiabdomen. She also exhibited left mild hydronephrosis. The lesion was displacing the left kidney superiorly and laterally, and the left ureter, small bowel, and descending colon were displaced medially, suggestive of a retroperitoneal hydatid cyst (Figure 2). Her chest roentgenogram was normal, and her serological tests were negative. Echocardiography showed normal left ventricular function with an ejection fraction (LVEF) of 70%. The renal arterial Doppler showed turbulent flow in the left renal artery (peak systolic velocity (PSV): 286 cm/s; refractive index (RI): 0.46). The patient started combination therapy (albendazole (ABZ): 15 mg/kg/day; praziquantel (PZQ): 600 mg, single dose) 2 weeks prior to surgery. Three classes of antihypertensive medications were used (amlodipine: 5 mg, twice daily; atenolol: 25 mg, once daily; hydrochlorothiazide: 12.5 mg, twice daily) for adequate control of her blood pressure prior to surgery. She underwent surgery through a left flank approach, and total cystectomy was done before the abdomen was closed with a drainage tube (Figure 3). The postoperative period was uneventful. Her histopathology report revealed a hydatid cyst with no viable protoscoleces. She continued taking albendazole (15 mg/kg/day) for a 28-day cycle followed by 14-day albendazole-free interval for a total of 3 cycles. Post surgery, all antihypertensive

KEYWORDS: *Echinococcus*, cystic hydatid disease, retroperitoneum, secondary hypertension

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Figure 1. An ultrasonogram showing a multiloculated cyst with thick internal septa in the left retroperitoneum..

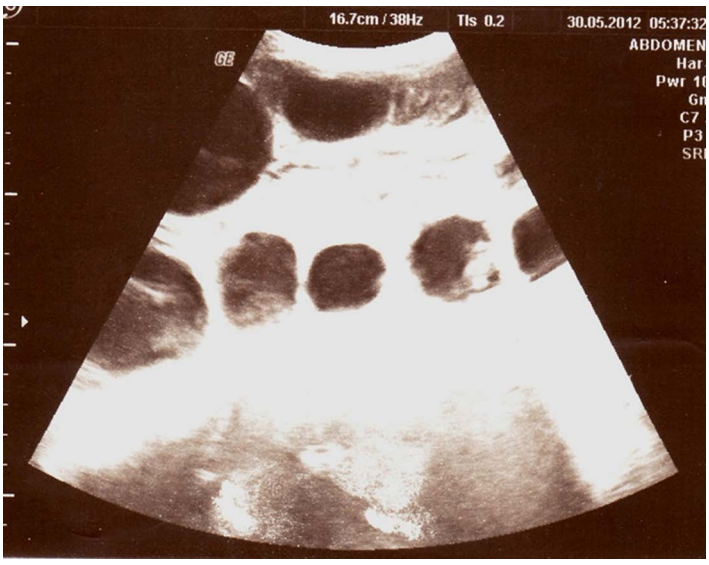
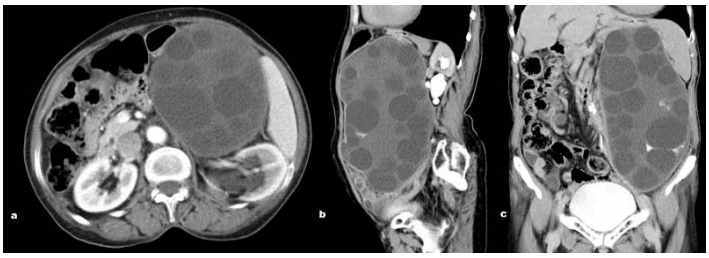


Figure 2. (a) A CT showing the retroperitoneal cyst causing compression; (b) displacement of the left kidney causing mild hydronephrosis; (c) calcifications.

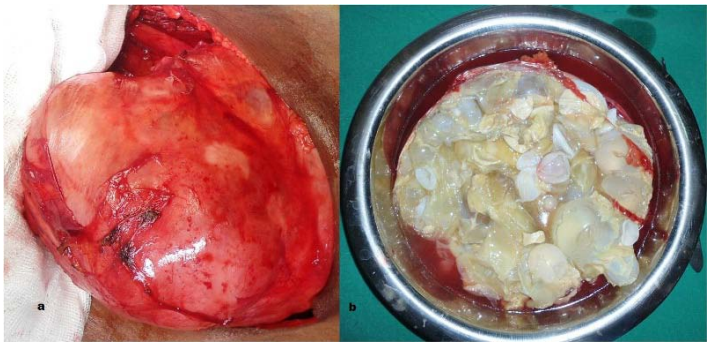


medications were discontinued and a salt-free diet was advised. She was normotensive, and there was no recurrence of hydatid disease at a 1-year follow-up.

DISCUSSION

Humans are accidental hosts for Echinococcus disease by ingesting ova through contaminated water or fomites. Once the ova are ingested, the outer protective coat is digested in the stomach. The larvae penetrate the duodenal mucosa and enter the portal circulation. Most of the larvae are trapped in the liver and the lungs; hence, they commonly noted there. Only 5 to 15% of them escape into systemic circulation [4]. Lockhart and Sapinza first reported a primary retroperitoneal

Figure 3. (a) Intraoperative imaging showing a large cystic mass; (b) the hydatid cyst after complete excision.



hydatid cyst without other organ involvement in 1958 [2]. Since then, approximately 50 cases have been reported in the literature [5,6]. In our case, primary retroperitoneal hydatid disease presented with a palpable lump, causing extrinsic compression on the left renal hilum and ureter (confirmed by radiological imaging). Secondary hypertension treated with surgery is rare and has not been reported in the literature. The cause of secondary hypertension was due to compression and the stretching of the left renal vessels and left ureter by the cystic lesion, resulting in renal hypoperfusion and obstruction, the activation of the renin-angiotensin-aldosterone system, generalized vasoconstriction, and systemic hypertension. The renal artery Doppler showed a high PSV and low renal involvement, suggestive of extrinsic compression and turbulent flow in the left renal artery. The echocardiography showed no evidence of chronic hypertension in the form of left ventricular hypertrophy. As there was extrinsic compression of the renal hilum by the cyst, further evaluation for hypertension in the form of a captopril renogram, or renal vein sampling for renin levels, was not done. Our primary aim was to control the hypertension and surgical excision of the cyst.

Three antihypertensive medications (a calcium channel blocker, a beta-blocker, and a diuretic) were given. ACE inhibitors were not given because of the increased risk of hypotension during surgery. Radiologic imaging is most important because negative serologic tests do not rule out hydatid disease. Plain abdominal X-rays may show calcification of the cyst wall. USG sensitivity ranges from 93 to 98% to detect hepatic and extra hepatic hydatid cysts. Computed tomography (CT) is the imaging technique of choice for determining the number, size, and anatomic location of the cysts, and it is also superior to an ultrasound when detecting extra hepatic cysts, as noted in our case [7]. Chemotherapy for hydatid disease is given in the form of monotherapy (ABZ) or combination therapy (ABZ and PZQ) [8]. Praziquantel is an effective protoscolicidal

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agent with poor cyst-wall penetration. Albendazole is active against both protoscoleces and germinal epithelium. Another proposed mechanism for the enhanced efficacy of PZQ and ABZ in combination is that PZQ causes prolonged bioavailability of ABZ [9]. Combination chemotherapy was given in our case to kill viable protoscoleces and prevent recurrence. Surgery is curative, with cystectomy a desired option. During surgery, if complete cystectomy is not possible, partial cystectomy or marsupialization can be done after irrigating the cavity with scolicidal agents to prevent recurrence. The scolicidal agents used are 10% povidone-iodine, 0.5 % silver nitrate, 5% sodium chloride, 10% formalin, and other hypertonic solutions that prevent secondary hydatidosis. In most of the cases, complete cyst excision may be difficult because of dense adhesions or the involvement of vital organs. It is preferable to evacuate the parasite and excise the redundant portion of the pericyst, leaving the rest of the cavity open, or it can be drained externally with a wide-bore catheter. Adequate precautions should be taken to prevent anaphylaxis during surgery, which can be fatal. Recurrence is due to the rupture of a cyst, incomplete cyst removal, or previously unidentified cysts. Postoperative chemotherapy with ABZ can be given to prevent recurrence [10]. Serial imaging in follow-up care to detect recurrence is required. Although retroperitoneal hydatid disease is rare, differential diagnosis of cystic tumors like chronic abscesses, pseudo-cysts of the pancreas, chylolymphatic cysts, mesenteric cysts, soft-tissue sarcomas, or complex cysts of the kidney should be considered. Radiologists and surgeons should both be aware of this rare disease.

CONCLUSION

Ours is a rare case of primary retroperitoneal hydatid cyst presenting with an abdominal mass and hypertension. Radiological imaging was used to diagnose hydatid disease in the absence of negative serology. Combination chemotherapy was given to kill the viable protoscoleces and prevent recurrence if spillage occurred during surgery. Surgery cured the disease and hypertension.

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Retroperitoneal Ganglioneuroma: A Rare Case Presenting As Right Ureteric Colic

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ABSTRACT

Background: Ganglioneuromas are rare benign tumors arising from the autonomic nervous system, and they are composed of well-differentiated Schwann and ganglion cells.

Case Report: An 11-year-old girl presented with colicky right loin pain that had occurred on and off for the past 1 year. On evaluation, she was found to have a retroperitoneal mass of 6 cm x 4 cm just below the right renal hilum. Her laboratory parameters were normal. The mass was hormonally silent. Surgery was performed and the mass was resected completely. The mass was closely opposed to the inferior vena cava with tributaries to it. Fibrous attachments were also noted on the spine, which were freed. Her histopathology and immunohistochemistry confirmed the mass to be a ganglioneuroma. Her neuron-specific enolase marker was positive. She was symptom free at 3 months post surgery, and her imaging was normal.

Conclusion: Ganglioneuromas have an excellent prognosis. This case is presented for its rarity and unique presentation as right colicky pain.

CASE PRESENTATION

An 11-year-old girl presented with complaints of right loin pain for the past 1 year. The pain was colicky in nature. It was associated with nausea but there was no vomiting. There was no fever. She did not have any bowel or urinary complaints. There was no hematuria. Her general examination was unremarkable. Her blood pressure was normal. She did not have any lymph nodal enlargement. There was no renal angle tenderness on the right side.

On evaluation, an ultrasound displayed a retroperitoneal mass lesion. The ultrasound revealed a 6 cm x 4 cm well-defined hypoechoic lesion medial to the right kidney. There was mild hydroureteronephrosis noted on the right side up to the upper ureter. Her laboratory parameters were normal. The urinary catecholamine levels were normal. The contrast-enhanced computed tomography (CT) scan revealed a 6 cm x 4 cm homodense lesion just below the right renal hilum and medial to the right ureter. There was minimal hydroureteronephrosis noted up to the upper ureter on the right side. It was closely opposed to the inferior vena cava (IVC). There was no calcification or necrosis noted within the mass. No enhancement was noted, even in the delayed films. Magnetic resonance imaging (MRI) was not done due to cost constraints.

She was advised to have an excision biopsy of the retroperitoneal mass lesion. Intraoperatively, under general anesthesia, she was placed in the right flank position and a subcostal incision was made. The retroperitoneal mass was excised in toto through the retroperitoneal approach, taking care not to injure the renal vessels and the ureter. Perioperatively, the kidney was displaced above and laterally by the mass. The mass was lying on the IVC with tributaries to the IVC (Figure 1). The tributaries were isolated, ligated, and cut. The IVC was not injured during the surgery. There were fibrous attachments to the spine, which were freed, and the mass was excised completely (Figure 2). The operation lasted for a little over 3 hours. The postoperative period was uneventful.

KEYWORDS: Ganglioneuroma, retroperitoneal mass, retroperitoneal ganglioneuroma, ureteric colic

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Figure 1. Intraoperative picture showing the mass lying on the IVC.

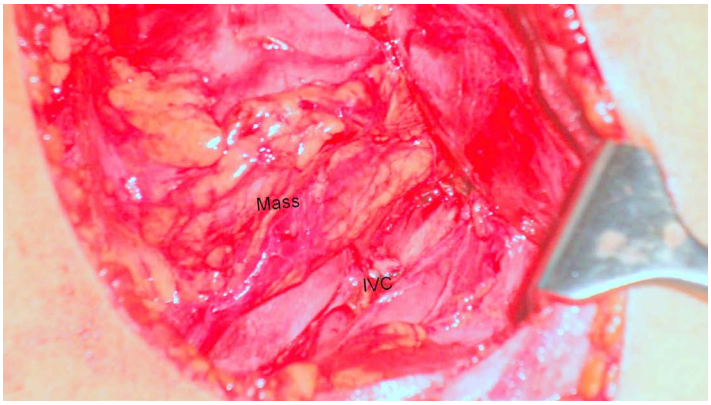
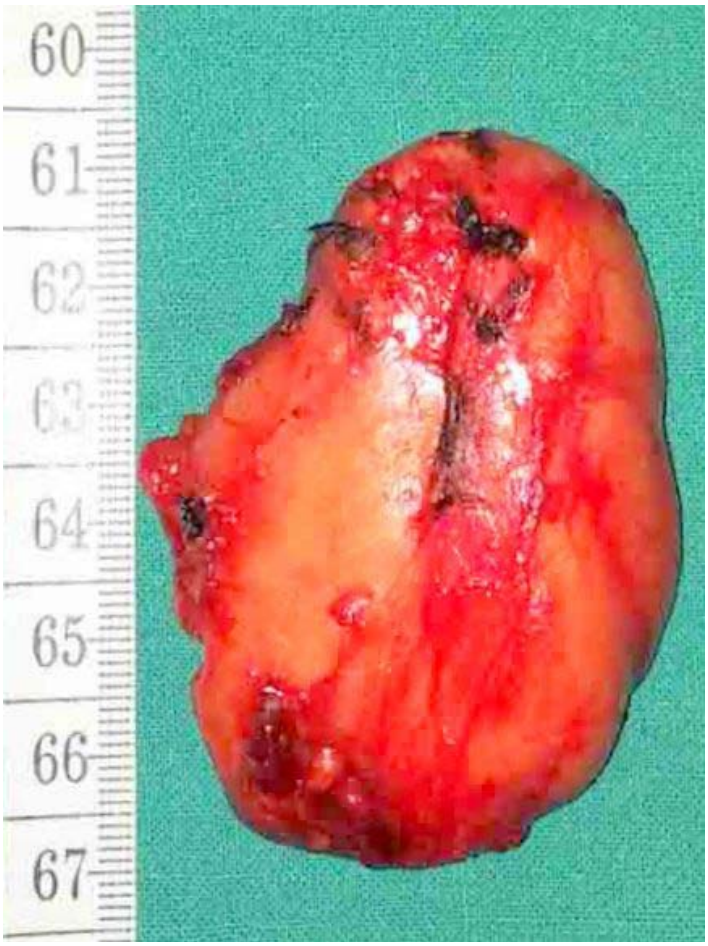


Figure 2. The excised specimen.



Histopathology of the lesion confirmed a ganglioneuroma. There were well-differentiated Schwann cells, with eosinophilic cytoplasm and ganglion cells. Immunohistochemistry was done for neuron-specific enolase, which was positive. The Ki-67 proliferation index was 2 to 3%. The patient recovered well after the procedure and was discharged on the fourth postoperative day. Her symptoms were completely relieved. She remained asymptomatic at her 3-month follow-up, and an ultrasound of the abdomen was normal.

DISCUSSION

Loretz first described ganglioneuroma in 1870. Ganglioneuroma is a rare, benign neuroblastic tumor arising from the immature cells of the sympathetic nervous system. These tumors consist of mature Schwann cells, ganglion cells, and nerve fibers.
It is commonly seen in the second and third decade of life, with a slight preponderance in females. The most common locations, in descending order, are the retroperitoneum, the mediastinum, the adrenal medulla, the cervical region, and the presacral area. Rarely, they can be associated with neurofibromatosis type I. They usually arise in relation to the sympathetic chain or adrenal medulla. It usually grows slowly to a large size before presenting with symptoms, which occur predominantly due to the compression of adjacent structures. Our patient had symptoms due to intermittent compression on the right ureter.

Usually, ganglioneuromas are hormonally silent. Rare cases have been found to be functioning, with the secretion of catecholamines or vasoactive intestinal peptides [5]. An hourglass extension into the spine had also been observed [2]. Very rare associations have been reported with seminoma [4] and pheochromocytoma [6]. Very rarely, malignant transformation has been noted [3]. The CT description is usually of a homodense lesion with well-defined margins and delayed contrast enhancement [1,7]. Discrete or punctate calcification may be noted in up to 20% of cases [7]. The mass can also be heterodense due to necrosis, when a mass outgrows its blood supply. The peculiarity in our case was that there was no enhancement at all, even in delayed films.

MRI usually reveals a homointense lesion with low signal intensity on the T1 weighted images. On the T2 weighted images, they are hyperintense, but the extent depends on the ratio of myxoid stroma to the cellular components [7]. MRI would be better than CT to predict intraspinal involvement. A nuclear bone scan had been suggested, rather than CT, for the detection of bony erosions [8].

The diagnosis of retroperitoneal ganglioneuroma is difficult to clinch preoperatively, and they are usually diagnosed by histopathological examination. Nevertheless, they should be considered in the differential diagnosis of retroperitoneal and

posterior mediastinal masses. Ganglioneuromas are usually cured with surgical excision. Some masses are not amenable for complete excision due to the location adjacent to or circumscribing major vessels. Even with subtotal resection, they usually do not recur. No adjuvant therapy is indicated. The prognosis is excellent. These patients do not require long-term follow-up.

CONCLUSION

This case is presented due to the rarity of the situation. The peculiarities about this case are the mode of presentation, with symptoms due to compression of the right ureter and the total absence of delayed enhancement on the CT scan.

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Spontaneous Transvesical Migration of a Foreign Body

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ABSTRACT

Spontaneous migration of foreign bodies into the bladder is rare. Patients present late with urinary symptoms. Here we report two such cases of delayed tranvesical migration: a large bullet and an intrauterine device (Copper-T), with their successful retrieval by endoscope and a minimally invasive procedure.

KEY MESSAGE

Spontaneous transvesical migration of foreign bodies, though rare, may occur, leading to delayed urinary symptoms, such as in our 2 cases. Successful retrieval is possible in most cases by endoscopic or by minimally invasive techniques.

INTRODUCTION

The literature in medical journals is scattered with articles regarding foreign bodies in the lower urinary tract. In most of these cases, the foreign body was introduced through the external urinary meatus. But here we report 2 cases of spontaneous delayed migration of foreign bodies into the urinary bladder: a bullet from the pelvic cavity after a 10-month-old gunshot injury, and an intrauterine device (IUD) from the uterus after 8 years of its insertion. Silent spontaneous migration of foreign bodies is a rare occurrence, which prompted us to report these cases.

CASE REPORT

Case Number 1

A 35-year-old male patient was admitted with sudden acute urinary retention and a history of mild dysuria for 5 days prior to presentation. He had a gunshot injury 10 months before. On examination, the urinary bladder was distended, with tenderness on the suprapubic region. Catheterization relieved the retention, with mild resistance in the prostatic urethra. An X-ray of the kidney, ureters, and bladder (KUB) region showed rounded opacity in the bladder region (Figure 1A). Ultrasonography (USG) suggested a foreign body within the bladder. An X-ray of the abdomen with contrast in the Foley's bulb showed the bullet close to the bulb (Figure 1B), suggesting the intravesical position of the bullet. Under general anesthesia, cystoscopic removal of the bullet failed due to its large size. The urinary bladder was breached through a small cystostomy incision using a cut-to-the-light approach, and the bullet was extracted under vision. The patient had an uneventful recovery.

The patient had a history of gunshot injury 10 months before. The bullet entered just above the left iliac crest without any clinical signs of bladder or bowel injury. An abdominal X-ray at that time showed the bullet overlying the shadow of the superior pubic ramus of the right pubic bone (Figure 1C) leading to a nondisplaced fracture of the lower margin of the right pubic ramus. A computed tomography (CT) scan of the pelvis and abdomen did not reveal any injury to the pelvic or abdominal organs, with a bullet in the right side of pelvis. The patient was managed conservatively as he was hemodynamically stable without any clinical or radiological signs of any visceral injury. He was discharged on the tenth day with a retained bullet in the pelvis and he was advised to perform a follow-up visit. On the second follow-up visit 2 months later, the bullet migrated medially of its initial position without any urinary symptoms (Figure 1D).

KEYWORDS: Foreign bodies, intravesical, migration, IUD

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Figure 1. a) The X-ray film showing the bullet over the pelvic region. b) The X-ray film showing the intravesical position of the bullet beside the radio-opaque Foley bulb. c) The initial X-ray film showing close proximity to the right pubic ramus. d) The X-ray film 2 months after the incident showing the bullet in the pelvis.

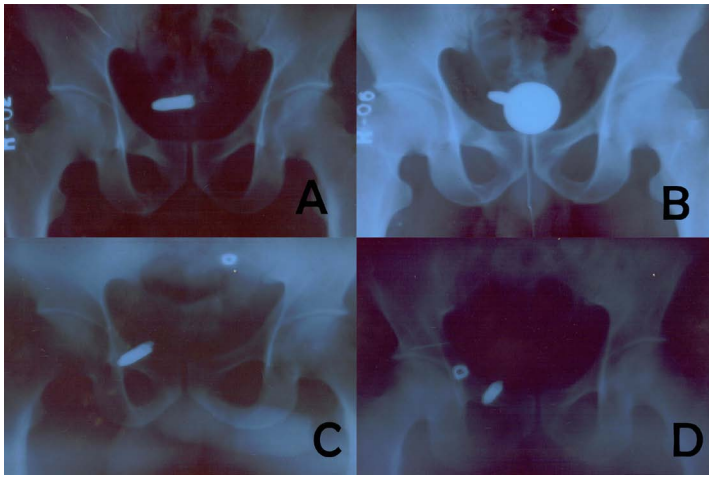


Figure 2. An X-ray of the abdomen showing the Copper-T with stone in the pelvis.

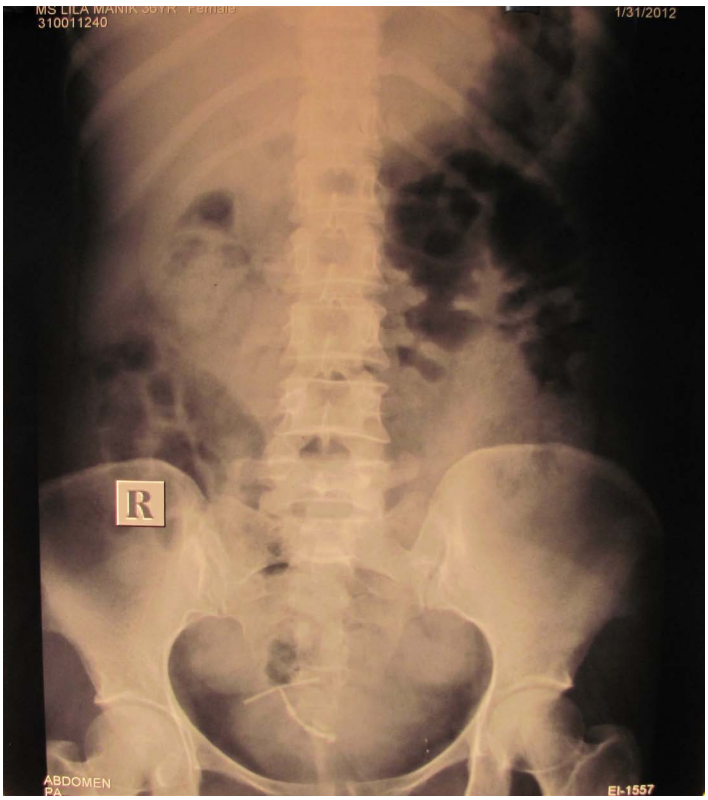
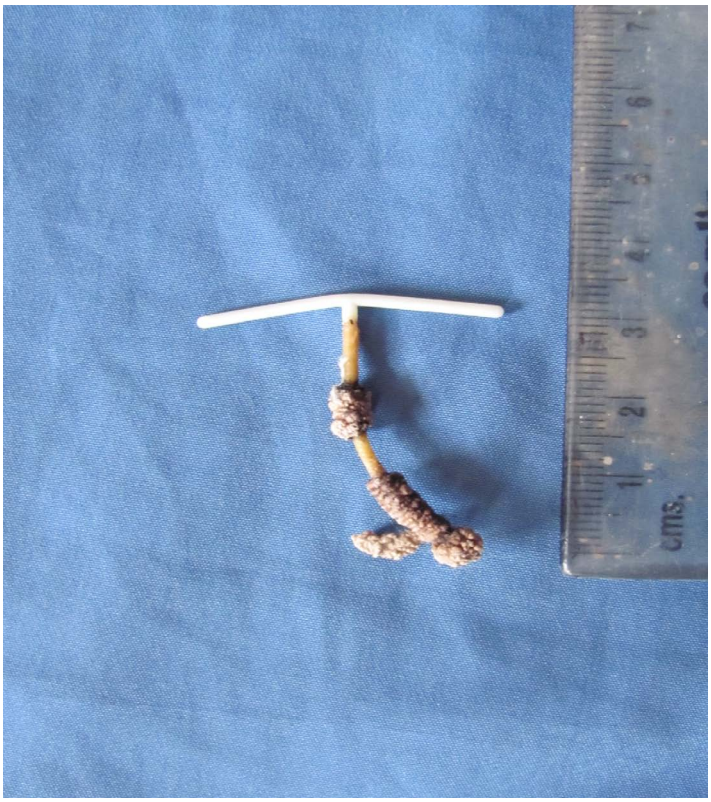


Figure 3. The retrieved specimen of Copper-T with stone on it.



Case Number 2

A 31-year-old female patient presented with recurrent urinary tract infection that has lasted 3 years. She received several courses of antibiotics elsewhere without any long-term improvement. Her urinalysis showed plenty of pus cells with red blood cells 15-20/HPF. Her urine culture showed E. coli growth > 10^5 CFU/ml. An intrauterine device (Copper-T) with stone was found in the pelvic area upon X-ray of the abdomen (Figure 2). Ultrasonography revealed a foreign body in the urinary bladder. On further inquiry, she admitted the insertion of a Copper-T device 8 years back. During the initial period, she used to palpate the thread on the vagina, but later on she forgot its existence. She was treated with antibiotics as per her urine culture sensitivity. The Copper-T and stone (Figure 3) were removed with a cystoscope. The patient had an uneventful recovery.

DISCUSSION

Foreign bodies introduced through the external urethral meatus are not uncommon [1]. These include objects such as a

wooden stick, electrical wire, a chicken bone, a thermometer, intrauterine devices (IUD), pieces of Foley catheter, broken pieces of endoscopic instruments, a lead pencil, a ball-point pen, a hair pin, screws, pellets, metal rods, etc. [1-3]. Most of these cases are associated with psychiatric disorders, senility, intoxication, autoerotic stimulation, or iatrogenics [2,3]. Foreign bodies may sometimes reach the urinary bladder directly via the traumatic route, and these are bullets, pieces of shells, and splinters [2].

Spontaneous migrations of foreign bodies to the urinary tract are extremely rare [2]. Foreign bodies can migrate into the urinary bladder from the gastrointestinal or female genital tract [2]. The spontaneous migration of foreign bodies, such as a surgical sponge, surgical mesh, and even a prosthetic acetabulum, has been reported [4]. Two cases have been reported where a bullet entered the renal parenchyma and subsequently entered the collecting system before advancing through the ureter to the bladder [5,6]. Even delayed spontaneous migration of multiple short gun pellets into the ureter from the retroperitoneum and then to the bladder with spontaneous voiding has been reported [7]. A rare complication of IUD is its migration to adjoining structures or the peritoneal cavity. In a review of 165 migrated IUDs, 23 migrated into the urinary bladder [8].

The penetration of an IUD into the bladder is painless and slow, and the patient presents with recurrent cystitis, hematuria, and pelvic pain [9]. The physical examination is usually unremarkable [2]. We believe that in our first case, the bullet was outside the bladder at the time of injury, as there were no urinary symptoms, and in the second case, the IUD was properly placed in the uterus as the patient palpated the thread in the proper position initially. But later on in both cases, foreign bodies eroded into the bladder lumen by compression of the bladder wall from outside, causing focal ischemia and necrosis, which led to the erosion of the bladder wall.

Ultrasonography or an X-ray of the abdomen almost gives a clue to the diagnosis. Cystoscopy is the confirmatory procedure. Endoscopic retrieval is usually successful, but sometimes, large foreign bodies may be removed with endoscopic and minimally invasive procedures, as described by DeLair et al. [10], as in our first case. Transvesical migration is an important possibility when urinary or pelvic symptoms may be attributed to a forgotten trauma or IUD insertion. A strong index of suspicion helps us to diagnose the erosion of the bladder wall by a foreign body that presented with late urinary symptoms.

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