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Laparoscopic Partial Cystectomy for Symptomatic Paraganglioma of the Urinary Bladder: A Case Report

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ABSTRACT

Paragangliomas of the bladder are uncommon neuroendocrine neoplasms. Open partial cystectomy is usually performed because all layers of the bladder are involved. In this case, we used laparoscopic partial cystectomy to minimize surgical morbidity of the transabdominal approach. A 43-year-old female presented with symptomatic paraganglioma of the bladder. The patient was pretreated with alpha- and beta-adrenergic blockers before surgery. A 4-port technique was performed with the patient in the Trendelenburg lithotomy position. The bladder mass was excised with a rim of normal mucosa under both cystoscopic and laparoscopic vision. Total operative time was 170 minutes and blood loss was < 100 mL. The patient's intraoperative blood pressure remained stable. The final histology showed a 6 cm paraganglioma with clear resection margins. Laparoscopic partial cystectomy is feasible for excising a symptomatic paraganglioma with adequate preoperative adrenergic blockage to prevent a hypertensive crisis during resection.

KEYWORDS: Paraganglioma; Symptomatic; Laparoscopic partial cystectomy

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Abbreviations and Acronyms
CT, computed tomography
MIBG, metaiodobenzylguanidine scintigraphy

INTRODUCTION

Paragangliomas are uncommon neuroendocrine tumors that arise from neural crest cells. They usually occur in the adrenal medulla, but 10% to 20% of these tumors are extraadrenal [1]. Paragangliomas of the urinary bladders are rare and account for less than 1% of all bladder tumors. Patients may have symptoms associated with catecholamine release if these tumors are hormonally active. The classic symptoms are gross painless hematuria, headache and palpitations upon micturition, and paroxysmal hypertension. The lateral, posterior, and trigonal walls of the bladder are stated as the most prevalent sites for bladder paragangliomas.

Because paragangliomas are rare, optimal surgical treatment and management have not been established. A high index of suspicion is required to diagnose these tumors. Cystoscopy should ideally be performed after alpha-adrenergic blockage to prevent a hypertensive crisis, but this is not always possible because these tumors might be diagnosed only after a biopsy. Surgery should be performed after alpha-adrenergic blockage and volume expansion. Small lesions (< 3 cm) with no deep parietal infiltration can be treated with transurethral resection [2], but some authors advocate against this procedure for fear of precipitating a hypertensive crisis. The general consensus has been to use an open partial cystectomy because there is multilayer involvement of the bladder wall. This approach is believed to ensure complete resection and reduce the risks of intraoperative hypertension.

Unfortunately, the abdominal approach is associated with wound morbidities and long hospital stay (as with any other open laparotomy). To reduce the surgical morbidity of a

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transabdominal approach, we performed a laparoscopic partial cystectomy for a patient with symptomatic paraganglioma.

CASE REPORT

A 43-year-old female presented after routine follow-up with her gynecologist for fibroids because an ultrasound of the pelvis revealed a possible bladder mass. The patient was referred to the urologist for further investigations. She denied any lower urinary tract symptom or gross hematuria. Examination of the abdomen and pelvis were unremarkable. A urine microscopy revealed 1 red blood cell and 2 white blood cells per high-power field.

In view of the ultrasound findings, an examination under anesthesia and biopsy of the intravesical lesion was next performed. On bimanual palpation, a spherical mass was felt over the anterior wall of the bladder. Rigid cystoscopy revealed a large (5 cm) papillary lesion over the right anterolateral wall of the bladder (Figure 1a). The submucosal tumor looked highly vascular and solid. A cold-cup biopsy of the tumor was performed. During the procedure, it was noted that the patient had a hypertensive episode with maximal systolic blood pressure of 180 mmHg. This resolved spontaneously and she recovered uneventfully after the procedure.

The biopsy showed a tumor composed of cells with round to ovoid nuclei and abundant basophilic to amphophilic granular cytoplasm (arranged in sheets), anastomosing trabeculae and nests, with a rich network of blood vessels (Figure 1b). The tumor cells showed diffuse strong immunostaining for synaptophysin, chromogranin, and vimentin with a few sustentacular cells seen on the S-100 protein stain. The tumor cells were negative for cytokeratins (AE1/3). The features were those of a paraganglioma. Pheochromocytoma screen confirmed the diagnosis with raised 24-hour urinary metanephrine (5626 nmol/day), normetanephrine (39768 nmol/day), and vanillylmandelic acid levels (62.4umol/day). Staging computed tomographic (CT) scan (Figure 1c) and iodine-I3I-MIBG (metaiodobenzylguanidine scintigraphy) nuclear scan revealed no local spread or distant metastases (Figure 1d).

On retrospective questioning, this patient had a long history of headache and palpitations on micturition. She was previously referred to the cardiologist for palpitations and an electrocardiography (ECG) showed sinus tachycardia. All other cardiac investigations were unremarkable.

Following diagnosis, her blood pressure was controlled with titrated alpha-adrenagic blockers (phenonybenzamine, 10 mg daily) and subsequently beta-blockers (atenolol 50 mg daily) with advice from an endocrinologist before an elective laparoscopic partial cystectomy was performed. Different surgical options were discussed with the patient and she was informed of our surgical experience with this rare tumor [1]. In view of the location and size of the tumor, she was offered a laparoscopic approach 4 weeks after alpha-adrenergic blockade was started.

Figure 1a. Flexible Cystoscopic View of the Tumor on the Right Lateral Wall.

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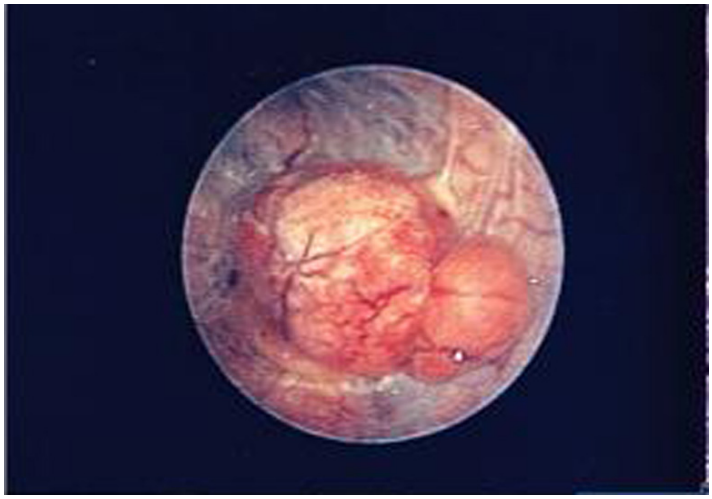

Figure 1b. Photomicrograph Showing Tumor Cells With Abundant Basophilic to Amphophilic Granular Cytoplasm, With Interspersed Small Blood Vessels (Hematoxylin and Eosin, x 200).

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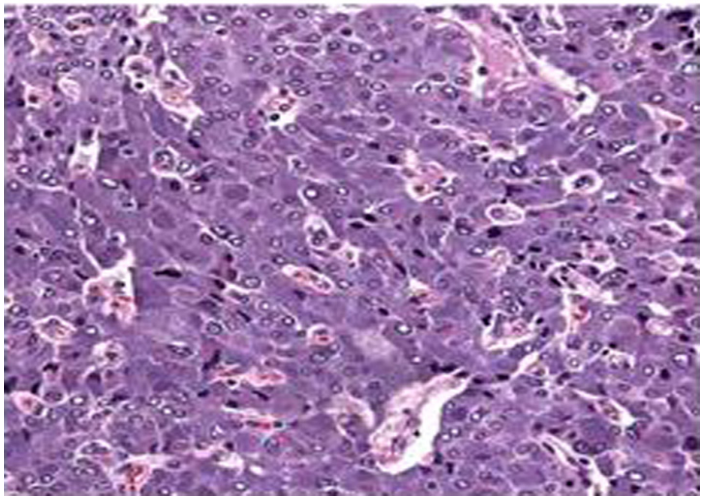

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Figure 1c. Computed Tomograph Scan Showing the Bladder Mass.
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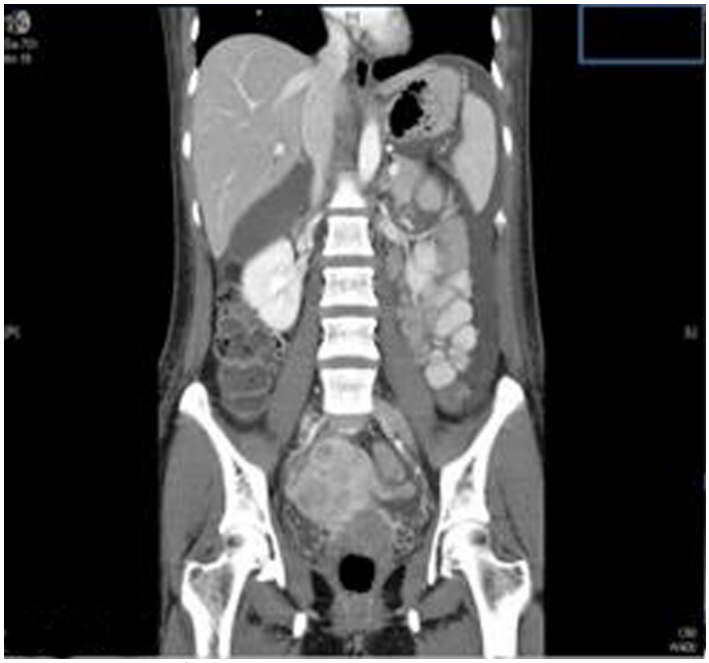

The mass arises from the right lateral wall and does not appear to be invading surrounding structures

Figure 1d. MIBG Nuclear Scan Showing no Local Invasion or Distant Metastases From the Bladder Paraganglioma.
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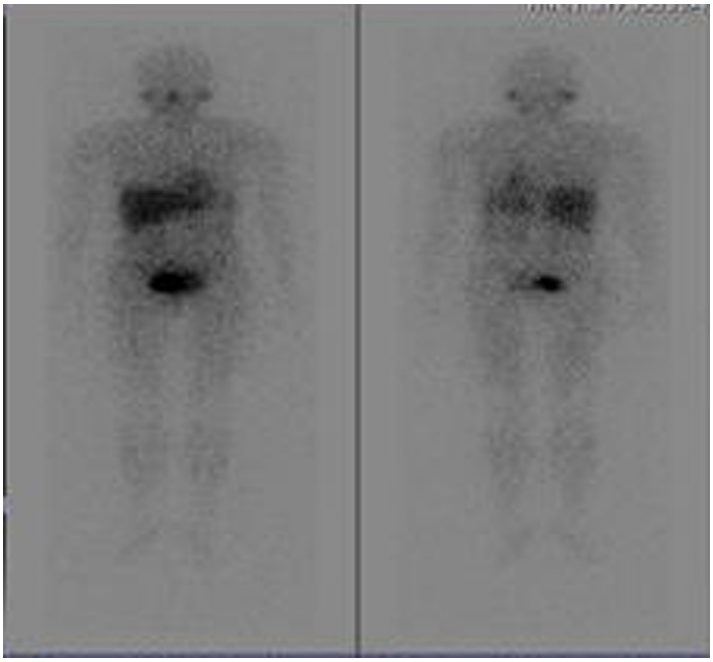

The final histology of the specimen (Figure 2) was 6.0 cm paraganglioma of the bladder with tumor invasion into the bladder wall (detrusor muscle). The resection margins were free of tumor and there was no invasion of the perivesical fat.

Surgical Technique

Under general anesthesia, the patient was placed in the lithotomy Trendelenberg position. She received preoperative intravenous antibiotic.

A 15 mmHg carbon dioxide pneumoperitoneum was induced via a subumbilical incision using Veress needle entry. A 12 mm port was placed at the subumbilical incision after the pneumoperitoneum was created. A 30° viewing laparoscope was then inserted through the primary camera port. After a thorough inspection of the abdomen and pelvis, 2 more 12 mm ports were placed under direct vision at the McBurney's point over the right iliac fossa and its mirror image at the left iliac fossa (Figure 3).

Under direct vision, the anterior aspect of the bladder was mobilized by taking down the urachus and the lateral attachments using endoscopic scissors with diathermy. The space of Retzius was entered and a plane was developed laparoscopically with both blunt and sharp dissection to further mobilize the bladder until it was completely freed anteriorly. Care was taken not to directly manipulate the tumor. Gentle traction of the urethral catheter balloon facilitated the dissection of the bladder.

Figure 2. Cut Surfaces of the Partial Cystectomy Specimen Showing a Tumor Invading the Bladder Wall.
doi: 10.3834/uij.1944-5784.2011.02.03f2

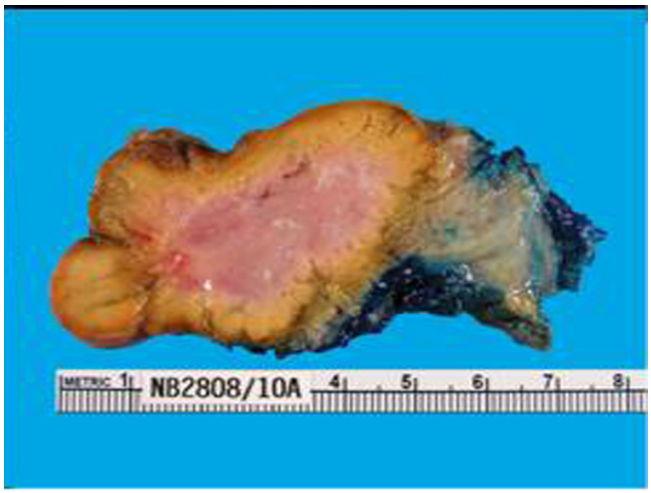

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Figure 3. Diagrammatic Illustration of Port Sites.
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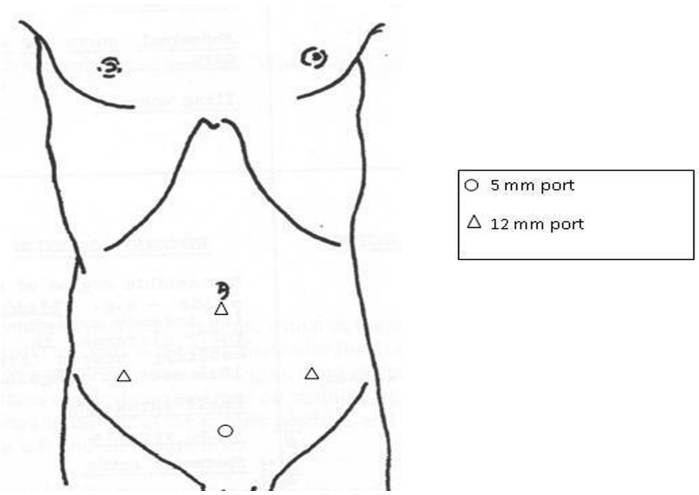

Figure 4b. Resection of the Bladder Tumor.
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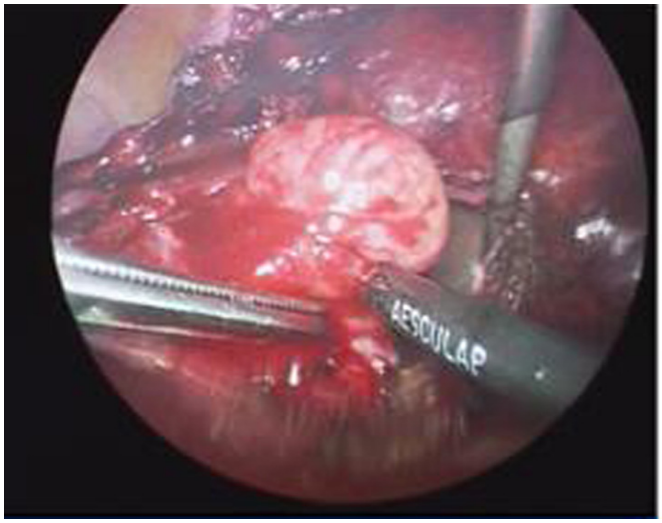

A rigid cystoscope was then inserted after removal of the Foley's catheter and the bladder was partially filled with normal saline. A 5 mm port was created over the suprapubic region for the insertion of an endoscopic soft bowel clamp. The clamp was placed to facilitate anterior retraction of the bladder (Figure 4a). Using simultaneous laparoscopic and cystoscopic guidance, the tumor was isolated and partial cystectomy was performed with a generous rim of normal bladder mucosal tissue using monopolar endoscopic scissors (Figure 4b). An Endocatch bag (Covidien Surgical; Dublin, Ireland) was used to contain the tumor after it was completely resected.

The bladder was closed intracorporeally with continuous 3/0 Vicryl suture (Ethicon Inc; Somerville, NJ, USA) in a single layer (Figure 4c). It was filled in a retrograde manner with 150 mL normal saline via the Foley's catheter to check for any leakage in the closure.

A redivac drain was placed through the suprapubic 5 mm incision. The specimen was then removed with the Endocatch bag through the right iliac fossa port incision. The wounds were closed in layers with Vicryl and Monocryl (Ethicon) and dressed with Dermabond (Ethicon). The bladder was drained

Figure 4a. Suprapubic Port to Facilitate Anterior Retraction of the Bladder.
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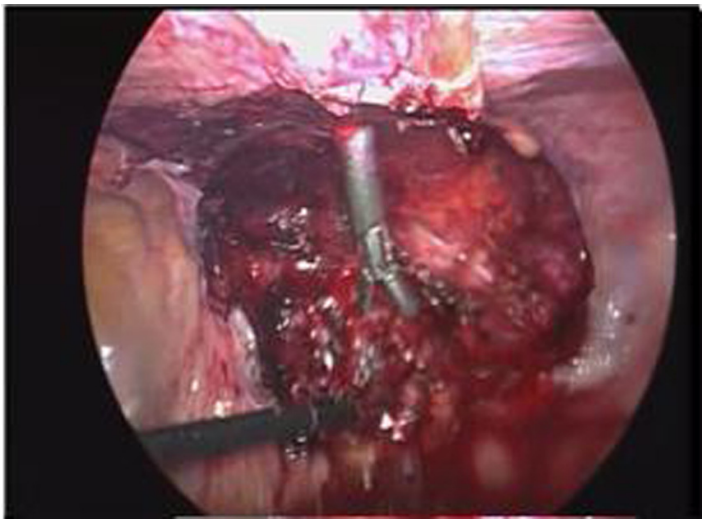

Figure 4c. Intracorporeal Suturing of the Bladder After Resection.
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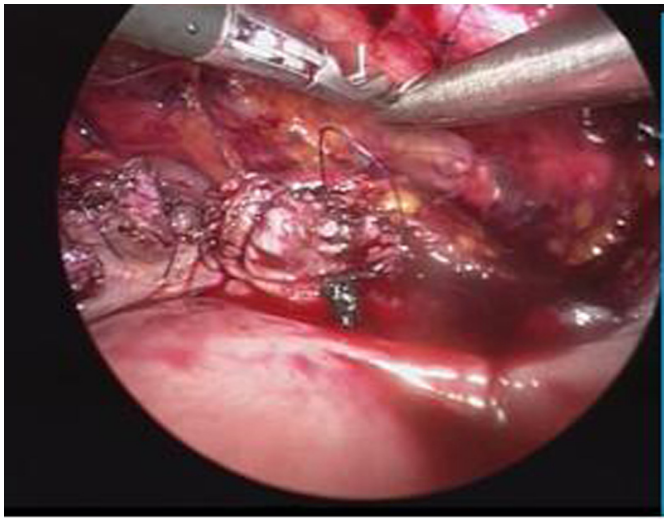

postoperatively with an 18-Fr urethral catheter.

The total operation time was 170 minutes and blood loss was estimated to be < 100 mL. The patient's blood pressure was stable throughout the operation with systolic readings of 130-140 mmHg and the heart rate was between 70-80 beats per minute. The highest systolic blood pressure recorded was 165 mmHg during the creation of the pneumoperitoneum and insertion of the endoscopic ports. Blood pressure stability was achieved with 4 weeks of preoperative alpha and beta-adrenergic blockade. Intraoperative anesthetic management included central venous line, arterial blood pressure monitor, and alpha-blocker drip containing phenoxybenzamine. Surgical excision was performed with minimal manipulation of the tumor.

Postoperative Results

The immediate postoperative pain score was 4 on a pain analogue scale of 0-10. She was able to ambulate and normal diet was resumed 5 days after the operation. The patient's blood pressure was well controlled immediately after the operation and both alpha and beta blockers were stopped without the need for gradual reduction of the doses. She was discharged with an indwelling catheter after the drain was removed. A follow-up micturating cystourethrogram was performed 3 weeks after the operation and there was no leakage. The patient was able to void successfully after the catheter was removed.

The patient's last follow-up 6 months after surgery showed that all wounds had healed and she was normotensive without any medication. Her pheochromocytoma screen showed normal values of urinary metanephrine (592 nmol/day), normetanephrine (549 nmol/day), and vanillylmandelic acid levels (14.2 umol/day) over 24 hours. A repeat CT scan showed no recurrent or residual disease.

DISCUSSION

We report our initial experience of successful laparoscopic partial cystectomy without precipitation of a hypertensive crisis.

Paraganglioma of the bladder occur more commonly in young women aged between 30-40 years [1]. Hematuria is the most common presentation, occurring in 55-60% of the symptomatic patients. About half of the patients have hypertensive episodes that are precipitated by micturition and are associated with headaches, palpitations, and anxiety [2-4]. These symptoms occur after contraction of the bladder wall and changes in bladder pressure during micturition, which lead to the release of catecholamines [3]. Hence, alpha and beta-adrenergic blockade are necessary before the operation.

The reported cases are mostly solitary and occur at the lateral or posterior walls of the bladder. They might appear submucosal on cystoscopy [1]. The diagnosis of hormonally active tumors can be established by the measurement of catecholamines and catecholamine metabolites (metanephrine and normetanephrine) in plasma and 24-hour urine samples. Most of the paragangliomas of the bladder (83%) are hormonally active. The diagnosis can be difficult if the levels of catecholamines and metabolities are normal. An iodine-I3I-MIBG should be performed to search for multifocal tumors or metastases. If the MIBG scan is negative, positron emission tomography (PET) imaging with specific ligands should be considered [5].

Five to 19% of these paragangliomas have been reported to be malignant and there are no reliable histological features to differentiate malignant from benign tumors. Malignancy can only be confirmed after local invasion or distant metastases have occurred [2,4]. Histologically, paragangliomas of the bladder are indistinguishable from those involving other sites. There is a typical Zellballen pattern of growth and positive staining with S-100, chromogranin, NSE and synaptophysin.

Genetic testing should be offered to patients because up to 50% of the paragangliomas are hereditary and may be associated with familial paraganglioma, neurofibromatosis type 1, von Hippel-Lindau disease, and the Carney triad. These patients may have germ-line mutations of genes encoding for succinate dehydrogenase (SDH) subunits B, C, and D [6]. If they are tested positive, they are at increased risk of extraadrenal or metastatic pheochromocytoma as well as recurrence [7,8].

A laparoscopic approach was initially demonstrated and proven feasible by Kozlowski et al in 2001 [9] and recently Huang et al [10] performed preperitoneal laparoscopic partial cystectomy for a paraganglioma of the bladder. Due to its rarity, a standard operative method has not been described in the literature although the general recommendation was for open partial cystectomy [2]. The argument against a laparoscopic approach for the present case was concern over precipitating a hypertensive crisis intraoperatively [3]. Although more experience is needed to justify the safety of a laparoscopic approach to bladder paraganglioma, we believe that with adequate alpha- and beta-blockade, a hypertensive crisis can be avoided regardless of the surgical approach. Case selection is crucial. In our case, a single dome/ lateral wall tumor was ideal when compared to one at the trigonal or base of the bladder. In addition, technical factors for laparoscopic approach to

partial cystectomy of bladder paraganglioma can also be extrapolated from experiences in laparoscopic adrenalectomy for paragangliomas/pheochromocytomas. In these series, the authors concluded that minimal manipulation of the tumor, close anesthesia monitoring and preoperative alpha-adrenergic blockers were important for safe and feasible laparoscopic approach to pheochromocytomas [11,12]. Robotic-assisted urological surgery is fast gaining worldwide acceptance and Nayyar et al [13] performed the first case of robotic partial cystectomy for a patient with symptomatic paraganglioma of the bladder. Because this tumor is very rare, the role of robotic-assisted partial cystectomy can be inferred from robotic management of adrenalectomy. Brunaud et al [14] and Desai et al [15] have independently shown that robotic-assisted adrenalectomy is technically feasible and the perioperative outcomes are comparable to laparoscopic adrenalectomy. Improved magnification with 3-dimensional view of the tumor during robotic surgery will reduce unnecessary manipulation of the lesion and this will help to reduce catecholamine release that might otherwise cause the blood pressure to fluctuate. Hence, we believe that robotic management of this case is definitely possible and the outcome will be similar.

The laparoscopic approach required specific technical points to ensure success. With simultaneous cystoscopic and laparoscopic visualization and localization of the tumor, manipulation can be minimized and margins can be delineated easily. This allows for wide and accurate margins to be taken around the mass. Laparoscopic intracorporeal suturing was important for the repair of the bladder. Attention should be given to tension-free closure of healthy tissue edges because this is crucial for good healing. A flexible cystoscopy can be used in place of a rigid scope for margin delineation if there is difficulty with the insertion of the scope due to the Trendelenburg position of the patient. Bilateral ureteric stenting should be considered if the tumor is at the trigonal area, which is one of the common sites for bladder paragangliomas.

Anesthesia for laparoscopic partial cystectomy of bladder paraganglioma is definitely challenging [16]. Due to the prolonged lithotomy and steep Trendelenburg position, there are risks of nerve injuries and cardiovascular and respiratory compromise. On creation of the pneumoperitoneum, catecholamines will be released and the hemodynamic status might fluctuate. Hence, carbon dioxide insufflation for the creation of the pneumoperitoneum should be performed gradually. The duration of the surgery for laparoscopic and robotic approaches will usually be longer than an open approach and this may have an impact on the patient's hemodynamic status. Care has to be taken during cystoscopy because even external pressure on the abdominal wall can cause hemodynamic fluctuations. Other recommendations include adequate hydration of the patient and the use of epidural analgesia. If the patient is elderly, problems such as decreased perfusion of the lower extremities due to the positioning, increased intracranial vascular congestion, decreased cardiac output, reduced perfusion of other organs, and respiratory compromise will not be well tolerated. The anesthetic team will have to take more measures to prevent and minimize these concerns.

If local invasion or distant metastases have occurred, radical cystectomy with pelvic lymphadenectomy or surgical debulking might be a better choice [4]. Chemotherapy and radiotherapy have limited value in the treatment of these patients. The bladder paraganglioma series from Mayo clinic showed that patients with T1 or T2 disease had favorable outcome after complete resection of the tumor, whereas those with T3 or T4 disease were at risk of tumor recurrence or metastases [17]. The data on long-term outcome and recurrence rate are limited due to the rarity of these tumors. Because there is always a risk of local recurrence and metachronous metastasis, lifelong follow-up annually is recommended [2,4].

CONCLUSION

Laparoscopic partial cystectomy for paraganglioma is safe and feasible with good case selection and good surgical technique with minimal manipulation of the tumor to prevent a hypertensive crisis.

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