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Pseudotumoral Eosinophilic Cystitis in 2 Children From India

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ABSTRACT

Eosinophilic cystitis is a rare form of bladder inflammation. Fewer than 30 pediatric cases have been described in the literature. The current report is about 2 children, ages 11 years and 4 years. Both patients presented with irritative voiding disturbances and a bladder mass lesion that was seen on imaging. The diagnosis of eosinophilic cystitis was confirmed by cystoscopic biopsy. The children were treated with antihistamines, which resulted in complete clinical and radiological resolution of the lesion.

INTRODUCTION

Eosinophilic cystitis (EC) is a rare form of noninfective cystitis. Fewer than 30 cases have been reported in the pediatric population [1]. The cause of EC remains unclear, although it has been associated with various etiological factors such as allergy, bladder tumor, bladder trauma, parasitic infections, and chemotherapeutic agents [2]. EC is thought to be caused by an antigenic stimulus that produces an immunoglobulin E (IgE) mediated attraction of eosinophils throughout the bladder wall, with subsequent mast cell degranulation and release of inflammatory mediators [1]. Affected children present with a combination of irritative voiding symptoms with or without hematuria and suprapubic discomfort [3]. Imaging and cystoscopy may indicate a bladder mass, raising a suspicion of malignancy. Various medical, surgical, and combined forms of therapy have been used for managing the condition. The present report is about 2 children with EC who presented with irritative voiding disturbances.

CASE REPORTS

Case 1. An 11-year-old male presented with increased diurnal frequency of urination, urgency, urge incontinence, nocturnal enuresis, dysuria, and suprapubic pain for 2 months duration. No abnormality was found on clinical examination. Routine blood investigations were within normal limits. Urine examination showed 3-4 pus cells/hpf. Culture was negative for growth. Ultrasound examination showed a suspicious mass lesion or thickened urinary bladder wall (Figure 1). The location was the posterior wall, with extension into the left lateral wall of the bladder. Computed tomography (CT) scan of the abdomen and pelvis showed a minimally enhancing mass lesion involving the posterior wall, part of the dome, and the left lateral wall. The upper tracts were normal. Diagnostic cystoscopy revealed an irregular lobulated mass with an intact bladder mucosa (Figure 2). The mass involved the area of the trigone, posterior wall, left lateral wall, and part of the dome. The ureteric orifices were normal. Multiple biopsies

KEYWORDS: Bladder; Cystitis; Eosinophilic inflammation; Pseudotumor

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Abbreviations and Acronyms
CT = computed tomography
EC = eosinophilic cystitis
IgE = immunoglobulin E

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case report

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Figure 1. Ultrasound Showing the Bladder Mass.
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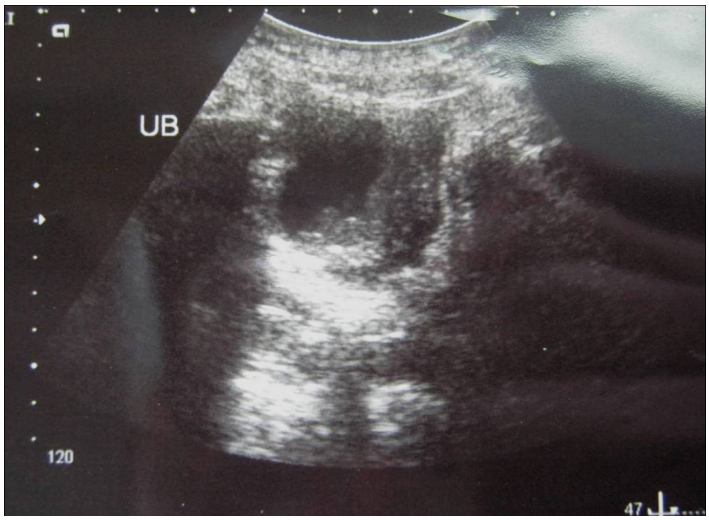

Figure 2. Ultrasound Showing the Bladder Mass.
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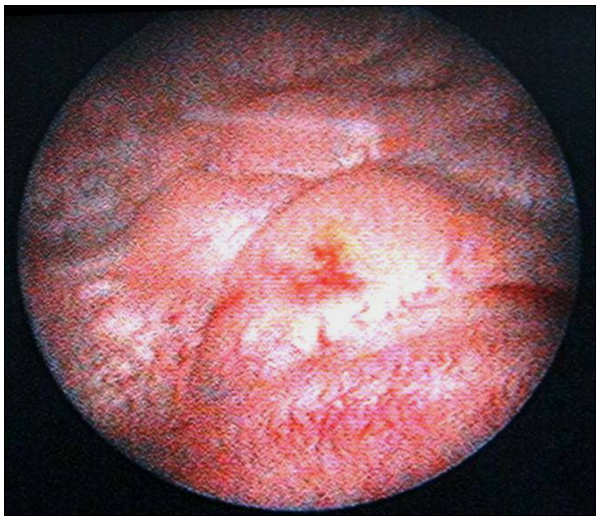

were taken from the lesion. Histopathologic examination revealed normal mucosal architecture. There was edema and inflammation of lamina propria with many eosinophils (Figure 3). Eosinophilic infiltrate was also seen in the muscular layer. The absolute eosinophilic count was 650/mm^3; serum IgE levels were within normal limits. The child was put on anti-inflammatory (ibuprofen, 100 mg, 3 times/day), antihistaminic (terfenadine, 1 mg/kg, twice daily), and anticholinergic (oxybutynin, 2.5 mg, twice daily) drugs for 6 weeks. Six months later, he was relieved of all symptoms and an ultrasound showed complete resolution of the mass lesion.

Case 2. A 4-year-old male had developed frequency, dysuria, and suprapubic discomfort of 1 month duration. He had 2 episodes of hematuria. Urinalysis showed traces of protein; the culture was sterile. Routine blood investigations were unremarkable. Ultrasound revealed a severely thickened bladder wall with a mass-like lesion at the trigone and normal upper tracts. A CT scan confirmed an enhancing mass lesion in the trigone area with thickening of the bladder wall. Cystoscopy showed a submucosal mass in the trigone and diffuse infiltration of the remaining bladder mucosa. Biopsy suggested EC with characteristic infiltrate of the lamina propria. The absolute eosinophil count was marginally raised; the serum IgE levels were normal. The patient was treated with an antihistaminic drug (terfenadine, 1mg/kg, twice daily) for 6 weeks. There was complete resolution of symptoms after 2 weeks of treatment. A follow-up ultrasound at 3 months showed complete regression of the bladder lesion.

DISCUSSION

EC is a rare inflammatory disorder of the urinary bladder. It was first described by Brown in 1960 [4] in a 50-year-old woman with severe atopy. In the same year, Palubinskas [5] described a case occurring in a 31-year-old woman with eosinophilic gastroenteritits. Several reports have been published since then, but only a few cases have involved children [1].

Figure 3. Microphotograph Showing Eosinophilic Infiltration of the Lamina Propria and Muscularis Layers (40x).
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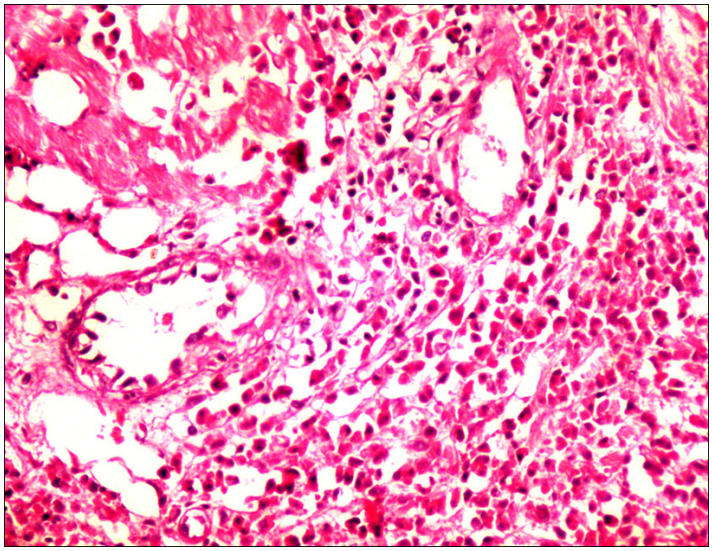

The mean age at presentation in children is around 10 years; boys are more commonly affected than girls [1]. The exact cause remains obscure. A number of individuals with EC have had preexisting allergies (eg, asthma, rhinitis) [1]. Several drugs have been reported to induce EC in adults: cyclophosphamide, warfarin (Coumadin; Bristol-Myers Squibb Co, Princeton, NJ, USA), tranilast (an antiallergic drug), penicillin, and clometacin. Intravesical instillations with mitomycin and thiotepa can cause eosinophilic infiltration of the bladder wall [6]. Goble et al [7] found urothelial eosinophilic infiltration in response to catheterization. Engler et al [8] reported EC at the site of chromic catgut sutures. The disease is mediated by IgE, which binds to various antigens that activate granulation of mast cells, attraction of eosinophils, and release of damaging cytokines. Hematoxylin and eosin staining of the pathological specimen shows a predominantly eosinophilic infiltration of the lamina propria, submucosal edema, muscle necrosis, and replacement of the superficial muscle by fibrous tissue. Geimsa staining may help quantify the number of eosinophils [9].

Dysuria, frequency of urination, diurnal and nocturnal enuresis, suprapubic pain, and recurrent hematuria are the usual manifestations of EC [10]. Ten percent of patients have been reported to present with acute retention of urine [10]. Eosinophils are rarely identified in the urinary sediment because they are rapidly degraded or there is little mucosal shedding. Peripheral eosinophilia has been noted in about 30-40% of the patients [2]. High serum IgE levels have also been reported, but the levels are not in the range of hyper-IgE syndrome [2]. Rarely, the disorder may progress to a complete fibrosis of the urinary bladder with secondary involvement of the rest of the urinary tract. This progression results in obstructive nephropathy with variable degrees of renal insufficiency [9].

Ultrasound and CT imaging show variable thickening of the bladder wall that may mimic a tumor-like infiltrative lesion. Definitive diagnosis needs to be obtained by cystoscopy and bladder biopsy. Cystoscopic features described in the literature range from mucosal erythema to raised velvety polypoid, edematous and frankly fungating, invasive-appearing masses [9]. In adults, 25% of EC has been reported to occur metachronously in a bladder with a previous transitional cell carcinoma; EC has even been reported to coexist with carcinoma in-situ [9]. However, there are no known reports of associated malignancy in the pediatric population.

EC has been found to be self-limiting in some children and tending to chronicity with relapses in others. Treatment is largely empirical [1]. Various management options include observation, antihistamines, anti-inflammatory drugs, and antibiotics in the presence of infection. Corticosteroids (prednisolone, 20 mg daily for 6-12 weeks) have been found to be useful in nonresponsive patients [1]. Cyclosporine A (6 mg/kg/day for 8 months) induced complete regression in 1 child with EC that was refractory to oral prednisolone treatment [2]. Surgical treatment such as transurethral resection of the lesions, partial cystectomy, or total cystectomy is reserved for patients who remain refractory to multiple oral medications (eg, anticholinergics, antihistaminics, antibiotics, steroids) and have unremitting symptoms [1,11]. The outcome of surgical treatment has been found to be good [11].

CONCLUSIONS

EC is a rare entity with uncertain causes. The presentation is variable and can clinically mimic a bladder mass. Cystoscopy and biopsy are essential to diagnosing the condition. Because no guidelines exist for optimum treatment or follow-up, management should be tailored to the symptoms and severity or extent of the disease. In the pediatric population, the condition usually has a benign course and complete resolution occurs in most cases. However, underlying rare progression to chronicity necessitates long-term follow-up of these children.

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