CASE REPORT

Giant Botryoid Fibroepithelial Polyp of the Bladder in a 6-Year-Old Girl

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ABSTRACT

Fibroepithelial polyps (FEPs) of the urinary tract are a rare benign tumour in the bladder. It arises from mesoderm and is mostly found in the ureter and ureteropelvic region. The authors report a case of a six-year-old girl with no history of urogenital abnormality who presented with haematuria and suprapubic pain. Ultrasound and computed tomography showed a large multilobulated mass in the urinary bladder. The resected specimen exhibited a bulbous mass with a botryoid surface. Microscopically, the polypoidal lesion is covered by reactive transitional epithelium with the presence of cystitis cystica et glandularis with scattered spindle cells; fibroblast and smooth muscle cells. By excluding all the differential diagnoses according to histomorphology and immunostain findings, diagnosis of Giant Botyroid FEP is made. This paper also discussed the differential diagnosis for FEP.
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Keywords: Fibroepithelial polyps, urinary tract, rare, paediatric, cystitis cystica et glandularis

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INTRODUCTION

Fibroepithelial polyps (FEPs) of the urinary bladder are rare benign tumour in the paediatric age group that arises from mesoderm [1-3]. FEPs are commonly found in the ureter and ureteropelvic region, however, bladder involvement is extremely rare (less than 1%) [2]. There were only seven cases had been published in English literature consisting of four paediatrics and three adult cases with an average age of 19.7 years old [4]. The aetiology of FEPs is uncertain, however, some studies suggested acquired congenital abnormalities as one of the reasons. Other causes include infection, chronic irritation, obstruction, and trauma to the bladder [1,2,4]. Herein, the authors reported a rare case of giant botryoid fibroepithelial polyp with cystitis cystica et glandularis in a six-year-old girl who presented with a huge bladder mass mimicking rhabdomyosarcoma and its differential diagnosis.

CASE REPORT

A six-year-old girl with no known medical comorbidities presented with persistent haematuria and suprapubic pain since the age of four. On admission, her renal profile and blood gases showed uraemia with compensated metabolic acidosis which required regular haemodialysis. The abdomen examination revealed a palpable suprapubic mass up to the umbilicus. Ultrasound of the bladder revealed a bulbous lesion measuring 4.5x6.6x9.6cm. Computerized tomography (CT) scan was done with the finding of a huge heterogeneous mass within the urinary bladder (Fig. 1), that give rise to a differential diagnosis of rhabdomyosarcoma and lymphoma. Cystoscopy showed a huge, multi-lobulated mass measured 10x12cm arising from the bladder dome.

The first biopsy showed eosinophilic cystitis. A repeat biopsy was performed and exhibited polypoid cystitis. In view of unresolved symptoms, she was scheduled for an elective partial cystectomy and excision of an

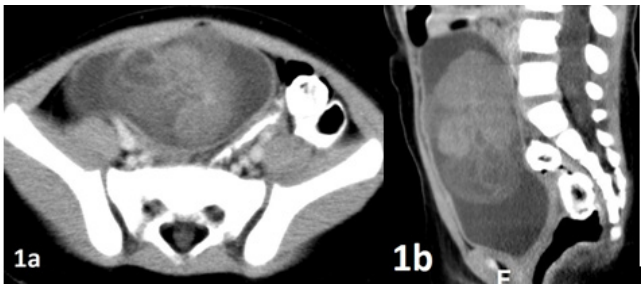

Figure 1: Contrast enhanced CT scan in axial (a) and sagittal (b) showed a huge heterogenous multilobulated lesion within the urinary bladder. No extension of the mass to the adjacent structure.

intravesical fungating bladder mass. The operation was uneventful. She recovered well postoperatively. Gross examination showed a huge multilobulated, bulbous mass (95x70x40mm) with a botryoid appearance and narrow stalk (Fig. 2). The mass was extensively sampled. The histopathology examination revealed a polypoid mass covered by inflamed urothelium with squamous metaplasia (Fig. 3 & Fig. 4). The stroma exhibited numerous Brunn nests and cystitis cystica et glandularis. Scattered benign fibroblasts, myofibroblasts, and smooth muscle cells are also appreciated with immunopositivity towards desmin, smooth muscle actin (SMA) and H-caldesmon. The spindle cells are negative for myogenin and ALK immunostains.

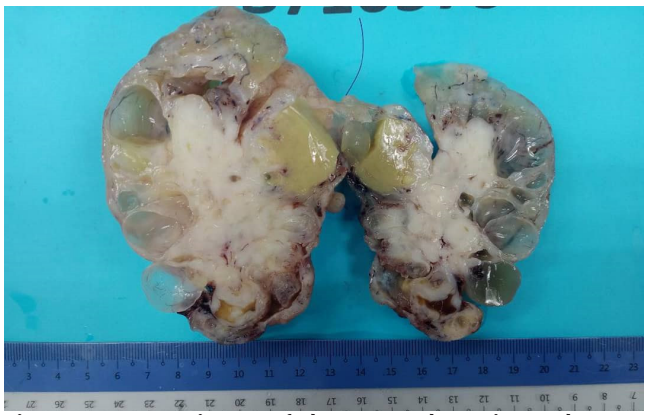

Figure 2: Gross picture of the resected specimen shows a huge, multilobulated tumour with a botryoid surface measuring 95x70x40mm.

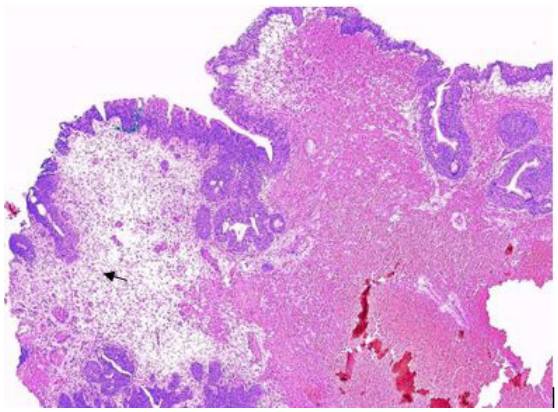

Figure 3: A polypoid structure covered by urothelial epithelium with myxoid stroma underneath (arrow) (H&E 40X).

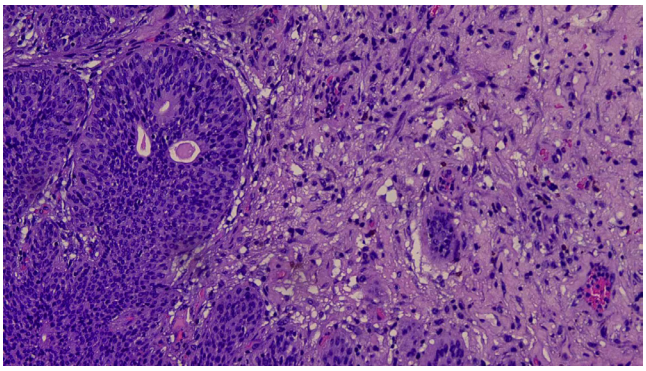

Figure 4: Cystitis cystica with fibromyxoid stroma and bland looking spindle cells (H&E 20X)

The diagnosis of giant botryoid FEP with cystitis cystica et glandularis was established. She was discharged from the ward after day seven of surgery. She was well without any symptoms during her last follow-up. She was scheduled for a repeating ultrasound in three months' time. Recent ultrasound shows no recurrent tumour.

DISCUSSION

FEPs of the urinary bladder occur predominantly in males with a wide range of ages but are extremely rare in children [1,3,4]. Half of the cases diagnosed in children are associated with urogenital malformation [2]. FEPs can arise anywhere in the urinary tract with less than 1% of cases involving the urinary bladder [3]. To the best of the knowledge, only four reported cases of paediatric bladder FEPs had been published in the English literature, diagnosed at the ages of 2, 6 (not included in the table), 11, and 14 years old (Table I).

The foremost clinical presentations of FEPs are urinary hesitancy, obstruction, and haematuria which latter is the most typical symptom [2,3]. In addition to haematuria, FEPs may also cause hydronephrosis and severe pelvic pain [2,3]. Ultrasound, CT, or intravenous urogram could not give a definite diagnosis for FEPs [4]. This is due to a lack of consensus on standard imaging reports in diagnosis of FEP in the bladder. Hence, distinguishing bladder FEPs from other benign and malignant neoplasms by imaging findings alone is challenging [4].

The aetiology of FEPs is uncertain. FEPs are congenital abnormalities either acquired or triggered by an infection, chronic irritation, obstruction, or trauma. Congenital abnormalities are more common in children, whereas inflammation or infections are common in adults [2].

The pathogenesis of FEPs remains unclear despite of few studies anticipating genetic mutation involvement. The previous authors proposed that DICER1 mutations play a crucial role in the pathogenesis of bladder FEPs [3]. DICER1, is ribonuclease III family, which involved in the biogenesis of microRNAs. Hence, it has an effect towards gene expression regulation [5].

Table I: Reported cases of FEPs in children

Authors	Age (years)	Symptoms	Radiological and cystoscopy findings	Histological findings
Natsheh et al., 2008	2	Hematuria	- Ultrasound: Irregular mass arises from the bladder neck - Cystoscopy: Polypoid mass at bladder neck protruding into proximal urethra	- Polypoid lesion with papillary fronds, lined by unremarkable transitional epithelium. - Submucosal stroma consists of benign fibrous tissue admixed with mild chronic inflammatory cells with no cambium layer. - IHC: None
Lum et al., 2007	11	Hematuria	- MRI: Well circumscribed solitary papillary lesion (24x20x16mm) arising from the left anterolateral aspect of the bladder floor - Cystoscopy: Botryoid mass with narrow stalk arise from anterolateral aspect of left side bladder.	- Polypoid lesion covered by benign urothelium with significant inflammation. Prominent cystitis cystica and cystitis glandularis. Scattered enlarged stromal cells noted. No rhabdomyblast or strap cells. No mitosis or necrosis. - IHC showed the large stromal cells are strongly positive for vimentin, desmin, oestogen receptor and progesterone receptor, focally positive for SMA and CD34. IHC are negative for pancytokeratin, S100, CD68, factor XIIIa, CD117, myoD1 and MYF-4.
Zachariou et al., 2005	14	Hematuria	- Ultrasound: Papillary lesion at the posterior surface - Cystoscopy: Exophytic papillary tumor in the left posterior surface of the bladder.	- Papillary lesion with epithelial layers of normal transitional cells with extensive submucosal edema, dilated blood vessels, chronic inflammatory cells, and fibrous stroma. - IHC: None

IHC immunohistochemistry, MRI magnetic resonance imaging

Meanwhile, other authors suggested that congenital malformation is one of the contributing factors to the development of FEPs in children [2]. Regardless of the aetiologies, the prognosis of FEPs is good with rare rate of recurrence. However, malignant transformation into bladder carcinoma has been reported in early studies [2,3]. Histologically, bladder FEPs are covered by unremarkable urothelium with underlying myofibroblast mixed with spindle cell components [1,5]. Despite of no specific immunohistochemistry marker for FEPs, Eckstein et al. reported, that desmin, SMA, estrogen receptor (ER), and CD56 immunohistochemical markers are found to be positive in the stromal cells and in favour of FEPs rather than polypoid cystitis [5]. Hence, a panel of immunohistochemical markers is essential in establishing the diagnosis. In addition, the presence of florid cystitis cystica is in favour of the diagnosis of FEPs as reported by the previous cases [1]. The differential diagnosis of FEPs includes polypoid cystitis (PC), eosinophilic cystitis (EC), botryoid embryonal rhabdomyosarcoma (ERS), inflammatory myofibroblastic tumor (IMT) and urothelial carcinoma (UC) (Table II).

PC is a reactive process related to indwelling catheters that may lead to polypoid formation due to chronic inflammation. It has a few gross appearances such as broad stalk and rounded elevation. Another variant is papillary cystitis exhibit thin and filiform in configuration. In comparison with FEPs, PC shows normal to hyperplastic urothelium with underlying congested, chronically inflamed and markedly oedematous stroma with less of spindle cells proliferation [4].

EC usually occurs in women and children. In comparison to FEPs, EC is associated with allergic conditions of the bladder and parasitic infestation. Patients usually present with recurrent episodes of dysuria and haematuria. The cystoscopic examination revealed ulcerated mass with necrosis which can be suspicious for carcinoma. It also harbours diffuse erythematous mucosa with broad-based polypoid growth. The microscopic features of EC include the presence of dense inflammatory infiltrate rich in eosinophils, often with fibrosis, muscle necrosis and occasional giant cells. Previous study emphasized the diagnosis of EC can be made if the eosinophils are more than 25 per high power field. They also described that a significant elevation of peripheral eosinophilia with the mucosa and submucosa was seen in the acute stage of EC, while chronic mucosal inflammation was usually observed in the chronic stage.

ERS is a malignant soft tissue tumour that harbouring the embryonic of skeletal muscle either by its morphology or immunophenotyping. The majority of ERS occurs in head and neck region as well as in the genitourinary system. Patients may present with urinary retention when it occurs in the bladder. This sarcoma is commonly found in children and adolescents. Molecularly, ERS involves RAS mutation in less than 50% of cases, NF1 and TP53 mutations in about 10% of cases. The gross findings of ERS exhibited botryoid appearance as seen in botryoid FEPs but the presence of a subepithelial cambium layer with atypical cells in microscopic examination is a favour in toward rhabdomyosarcoma rather than botryoid FEP. Furthermore, rhabdomyosarcoma is positive in Myogenin immunostain while not in FEP [5].

IMT comprise of myofibroblast and fibroblast accompanied by inflammatory cells infiltration. This disease occurs in wide anatomical distribution including bladder and uterus. Patients also may present with non-specific symptoms such as fever and weight loss. IMT primarily affects children and young adults. It involves rearrangement of ALK gene which found in 50 % to 60% of cases. IMT appear as nodules with circumscribed, whorled, fleshy or myxoid surface. The histopathology examination showed either myxoid, hypercellular or hypocellular pattern of fibroblastic-myofibroblastic cells proliferation with inflammatory cells. These patterns may mimic FEPs, but the positivity of ALK immunostaining warrant the diagnosis of IMT [5].

Another differential for FEPs is UCs. It is extremely rare in children with a mean age of 13.7 years. Only four cases of UCs in children were reported from the year 2001 to 2015. Most of the UCs in children presented with haematuria with fewer cases experienced with dysuria, abdominal pain, pyelonephritis and incidental findings during radiological procedures for other reasons [1-4]. In a small biopsy UCs, may be misdiagnosed as FEPs

because of a variety of histology variants in UCs.

The initial treatment for FEPs includes open exploration and resection. Later, a transurethral (TUR) operation has become more popular because of less traumatic procedures and faster recovery. Therefore, TUR is highly recommended as the first choice of treatment for bladder and urethral FEPs [4]. However, there is no consensus on long-term follow-up in patients with FEPs post-operatively. In view of this disease has a tendency to progress into bladder carcinoma, therefore, a long-term follow-up with cystoscopy examination is recommended.

CONCLUSION

FEPs are rare entities with infrequent malignant transformation. The authors need to consider FEPs as one of the differential diagnoses of fungating bladder mass in children who presented with haematuria and urinary obstruction. Identifying the characteristic features of FEPs is essential to avoid misdiagnosis. The most common characteristic features in FEPs include unremarkable urothelium without a cambium layer, spindle cells in the stroma and numerous cystitis cystica et glandularis with the help of ancillary studies. The prognosis is good, and long-term follow-up with regular cystoscopy is highly recommended.

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