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Review article

Inflammatory myofibroblastic tumour of the bladder in children: A review

Michael Collin [a], Adrian Charles [a], Andrew Barker [a], Japinder Khosa [a], Naeem Samnakay [a,b]

[a]Princess Margaret Hospital for Children, Roberts Road, Subiaco, Western Australia, 6008, Australia

[b]University of Western Australia, Hackett Drive, Nedlands, Western Australia 6009, Australia

Correspondence to: N. Samnakay, Princess Margaret Hospital for Children, Roberts Road, Subiaco, Western Australia, 6008, Australia, Tel.: +61 (0) 8 9340 8188; fax: +61 (0) 9 9340 8396

mcollin@me.com (M. Collin)
Adrian.Charles@health.wa.gov.au (A. Charles)
Andrew.Barker@health.wa.gov.au (A. Barker)
Japinder.Khosa@health.wa.gov.au (J. Khosa)
Naeem_samnakay@hotmail.com (N. Samnakay)

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Summary

Introduction
Inflammatory myofibroblastic tumours of the bladder (IMTB) are rare, and feature a benign and reactive proliferation of myofibroblasts. 25% of the reported IMTB cases in the literature occur in children. The present study presents a review of IMTB in children.

Discussion
The data from 42 reported cases of paediatric IMTB in the world literature are summarised, including two recent cases from the present centre. Paediatric IMTB equally affects males and females. It mainly presents with haematuria, dysuria or abdominal pain. Lesions can vary in size, but mean size is 5.5 cm. Mean age is 7.5 years.

The aetiology of IMTB is poorly understood, but includes infective or traumatic aetiologies, or a possible clonal lesion. IMTB may specifically show clonal gene rearrangements involving the anaplastic lymphoma kinase (ALK-1) gene. To differentiate IMTB from rhabdomyosarcoma, tissue diagnosis and careful histological analysis are essential. Tumour biopsy can be achieved by a transurethral approach or a transcutaneous approach with ultrasound guidance.

Between 35 and 89% of cases of IMTB express ALK-1 by immunohistochemistry. ALK-1 expression is much less common in other bladder soft tissue tumours. ALK-1 is thus useful in the diagnosis of IMTB.

The treatment of choice for IMTB is complete surgical resection of the lesion. In children, no proven recurrent or metastatic IMTB episodes are reported after excision. However IMTB recurrences are reported in adults, likely due to incomplete excision. Follow-up after excision is therefore recommended.

Conclusions
Paediatric IMTB is uncommon. Tissue biopsy is essential for diagnosis. Careful histological assessment is required to differentiate IMTB from malignant paediatric bladder tumours such as rhabdomyosarcoma. ALK-1 expression is useful in confirming the diagnosis of IMTB. Treatment of choice is complete surgical resection of the lesion. Recurrence is reported in adult IMTB. Follow-up is therefore recommended.

Table Paediatric inflammatory myofibroblastic tumour of the bladder (IMTB) reports in world literature, to date, including two recent cases from the present centre.

Paediatric inflammatory myofibroblastic tumour of the bladder cases (*n*)	Mean age (years)	Male: Female	Commonest inflammatory myofibroblastic tumour of the bladder location	Commonest presentation	Mean tumour size (cm)	Treatment
42	7.5	21:21	Bladder dome	Haematuria	5.5	Surgical resection – 41 Medical – 1

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Introduction

Bladder tumours are uncommon in children. A bladder mass in a child is most likely to be malignant, and is usually a malignant rhabdomyosarcoma. Other masses that may occur in children's bladders are benign fibroepithelial polyps and nephrogenic adenomas. Less common paediatric bladder lesions include transitional cell carcinomas, acute lymphocytic leukaemia, phaechromocytoma and inflammatory myofibroblastic tumours of the bladder (IMTB).

An inflammatory myofibroblastic tumour of the bladder involves a generally benign and reactive proliferation of spindle cells (myofibroblasts) with inflammatory cells. The tumour may be recurrent and may be associated with specific genetic changes [1]. The malignant potential for IMT in general is debated, but is not specifically reported for IMTB. The diagnosis and management of IMTB differs from the more common paediatric malignant neoplasms of the bladder.

Discussion

Inflammatory myofibroblastic tumours are an uncommon, benign and reactive proliferation of myofibroblasts, and are classed under the umbrella of soft tissue tumours. In the past they have been known as pseudosarcomatous tumours, atypical fibromyxoid tumours, plasma cell granuloma or spindle cell tumours. The current World Health Organization soft tissue sarcoma classification recommends that the term inflammatory myofibroblastic tumours (IMT) be used. Inflammatory myofibroblastic tumours have been reported to occur in the lung, liver, heart, orbit, pancreas, mesentry, uterus and other soft tissues of the body. Some of these tumours, especially pulmonary IMT, have been reported to metastasise. There is a thought that IMT, although considered to be histologically benign, may carry a risk of sarcomatous change.

It is postulated that IMT in the adult and paediatric populations are different entities. Harik et al. suggested that the paediatric IMT had a more aggressive course with greater recurrence than the adult population [2], with cases of recurrence in pulmonary and abdominal IMT reported in paediatric patients [3].

Occurrence in the bladder (IMTB), while reported, is rare. The nomenclature of these bladder tumours has also been contentious and confusing in the past, with different authors using different names for similar entities [2,4]. Inflammatory myofibroblastic tumours of the bladder are reported in both adult and paediatric populations; 25% of the reported cases occur in children [1,5].

The aetiology of IMTB is not completely understood; suggestions include an infective aetiology, chronic cystitis or intra-operative trauma. Iatrogenic trauma following transurethral resection of transitional cell carcinoma is more commonly described in adults. The aetiology in children is less obvious, often with no predisposing infective or iatrogenic trauma. In some cases, the argument for infective aetiology is supported by the presence of Ebstein Barr Virus (EBV) and Human Herpes Virus 8 (HHV-8) DNA on immunohistochemistry analysis of the lesions [6]. Inflammatory myofibroblastic tumours of the bladder may show a range of different genetic changes, specifically: clonal gene rearrangements involving the Anaplastic lymphoma kinase (ALK-1) gene seen commonly in IMTB. These are more often seen in children and young adults with IMTB, and are uncommon in adults over 40 years of age. The recurring finding of the ALK-1 gene change suggests a clonal lesion. The different genetic changes may be associated with different prognoses. It should be noted that some authors consider paediatric IMTB to be a different entity to the tumour in adults. This genetic heterogeneity may explain some of the variations in reported tumour behaviour. The expression of cytokeratin is comparatively more frequent in adult IMTB [2].

In the present study, data from reports of the 42 cases of paediatric IMTB in the world literature are summarised, including two recent cases from the present centre (Table 1). The mean age of paediatric IMTB in this collated data is 7.5 years (range 2—15 years). Inflammatory myofibroblastic tumours of the bladder usually present with gross haematuria, irritated or obstructive dysuria, and abdominal pain. If the lesion is confined to the submucosa, haematuria may be absent [7]. Presentation with a palpable abdominal mass but no other symptoms has also been described [7]. Constitutional symptoms (such as fever and weight loss) have also been described and are postulated to be due to the release of cytokines [5]. In the summarised paediatric cases, males and females seem to be equally affected (21 males and 21 females).

The tabulated summary shows that paediatric IMTB lesions range in size from 1.8 to 13 cm, with the mean size being 5.5 cm in the largest diameter. Lesions as large as 37.5 cm have been reported in adults [8]. Lesions may be pedunculated, nodular, lobular or frondy in appearance (Fig. 1). The commonest site of IMTB in children is the dome of the bladder, compared to the lateral bladder wall in adults [5].

Ultrasound evaluation of the renal tract and staging computed tomography (CT) scanning are important base investigations to evaluate any bladder mass in children (Fig. 2). Inflammatory myofibroblastic tumours of the bladder are usually indistinguishable from true malignant bladder lesions on imaging and cystoscopy alone, necessitating biopsy for tissue diagnosis. Tissue diagnosis will guide appropriate management. Tumour biopsy can be achieved by a transurethral cystoscopic approach or via a transcutaneous approach with imaging guidance such as ultrasound.

The malignant potential in general of IMT in paediatrics is undetermined. Whilst the tumour is thought to be benign and inflammatory in nature, in adults, local recurrence has been described in IMTB and metastases have been described in pulmonary IMT. No local recurrence or metastases have been described in IMTB in the paediatric population.

Histopathology of IMTB, although benign, may show cytologic atypia, an infiltrative pattern and mitotic activity. Therefore, there is a significant overlap with the malignant spindle-cell-type tumours of the bladder: sarcomatoid carcinoma, leiomyosarcoma and malignant rhabdomyosarcoma [9]. The main differential of IMTB in children is malignant rhabdomyosarcoma. Careful review of the histology with the lack of a cambium layer, the cellular morphology and the inflammatory infiltrate, together with the immunohistochemical profile is important. The management of malignant rhabdomyosarcoma versus IMTB is very different: rhabdomyosarcoma