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CASE REPORT

Haemangiomas in the urinary bladder: Two case reports

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Abstract

BACKGROUND

Urinary bladder haemangioma is a benign nonurothelial tumour that rarely occurs in paediatric and adolescent patients. Clinical and radiological examinations are not adequate for an accurate diagnosis. The purpose of this serial case report is to raise awareness of urinary bladder haemangioma and appropriate management.

CASE SUMMARY

We described two rare cases of urinary bladder haemangioma that were confirmed by histopathology followed by immunohistochemistry and reviewed the literature on the diagnosis and treatment of patients with this disease. The radical cystectomy was performed with open method surgery associated with an abdominal wall ostomy of the ileal outlet tract for case 1. Case 2 underwent a laparoscopic partial cystectomy. Postoperative pathology confirmed the diagnosis of urinary bladder haemangioma. Haematuria resolved postoperatively, and there was no evidence of tumour recurrence in 3 years follow-up for case 1. Postoperative urinary and pelvic ultrasonography showed no signs of recurrence in 3 mo follow-up for case 2.

CONCLUSION

Careful histopathological and immunohistochemical studies are required to establish the correct diagnosis. There is no "gold standard" treatment for urinary bladder haemangioma, and treatment options are varied for individuals with favourable follow-ups.

Key Words: Haematuria; Haemangioma; Urinary bladder; Case report

Core Tip: Urinary bladder haemangioma is a benign nonurothelial tumour that rarely

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occurs in paediatric and adolescent patients. Clinical and radiological examinations are not adequate for an accurate diagnosis. We described two rare cases of urinary bladder haemangioma that were confirmed by histopathology followed by immunohistochemistry and reviewed the literature on the diagnosis and treatment of patients with this disease.

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INTRODUCTION

Haemangiomas are benign vascular tumours that can occur almost anywhere in the human body. They more frequently occur in the skin and subcutaneous soft tissues than in the urinary bladder. Bladder haemangioma is rare and accounts for 0.6% of all bladder tumours occurring at all ages. They are more rare in childhood and adolescence. Clinical and radiological examinations are not sufficient for an accurate diagnosis. Careful histopathology and immunohistochemistry are required to establish the correct diagnosis[1,2]. Although haemangiomas in the genitourinary system occur relatively infrequently, cases of bladder haemangiomas have appeared during medical research. In this article, we describe two rare cases of urinary bladder haemangiomas (UBHs) confirmed by histopathology followed by immunohistochemistry, and we review the literature on the diagnosis and treatment of patients with this disease. Written informed consent was obtained from the patients or from his or her guardian for the publication of this case report and accompanying images.

CASE PRESENTATION

Chief complaints

Case 1: Case 1 was a 41-year-old Chinese female who presented with a sudden onset of painless gross haematuria for 1 mo and visited our outpatient clinic.

Case 2: Case 2 was an asymptomatic 30-year-old female.

History of present illness

Case 1: Cystoscopy and biopsy were performed by an outside hospital and showed a bluish ovoid mass with blood clots on the anterior wall of bladder. Transurethral resection of the bladder tumour (partial resection) was performed. The initial histopathological studies showed gland cystitis and local urothelial hyperplasia with nodule formation, but no clear cancer cells were found (Figure 1A and 1B).

Case 2: A large urinary bladder haemangioma in a 30-year-old female who visited our outpatient clinic presented without any symptoms. It was found during a routine examination at an outside facility.

History of past illness

Neither case had past illnesses.

Personal and family history

Neither case had specific family history.

Physical examination

In these two cases, the vital signs and observation results of the physical examination were normal.

Laboratory examinations

Case 1: The blood cell count results were as follows: erythrocyte count, 3.84 × 10^{12}/L;

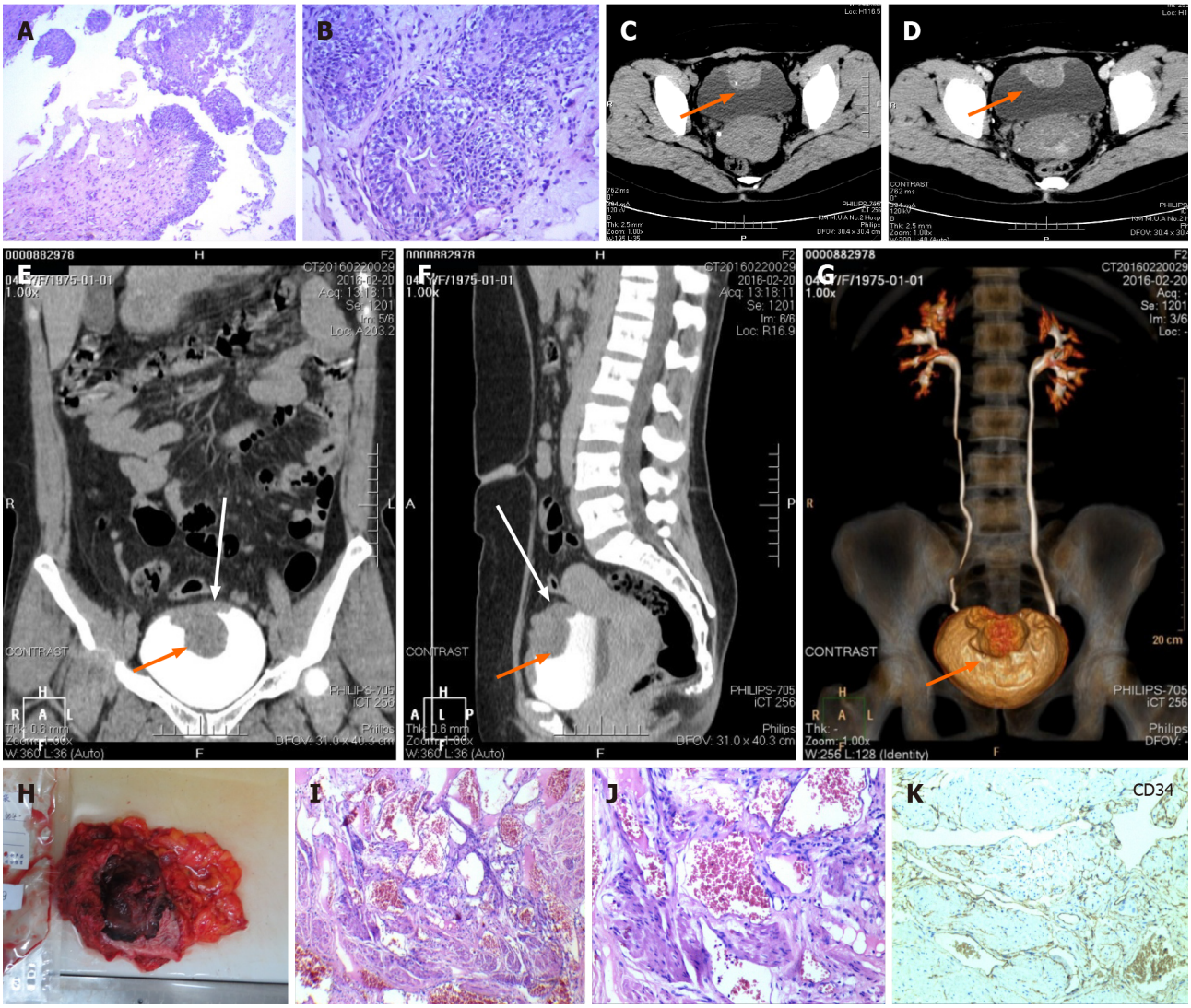

Figure 1 Cystoscopy and biopsy, multislice spiral computed tomography urography scanning, and histological and immunohistochemical characteristics of case 1. A and B: The initial pathological report of cystoscopy and biopsy. Haematoxylin and eosin staining showed gland cystitis and local urothelial hyperplasia with nodule formation, but no clear cancer cells were found (A: 40 ×, B: 100 ×); C-G: Multislice spiral computed tomography urography of the urological system showed a 5.0 cm × 3.1 cm × 4.0 cm mass (orange arrow) arising from the superior and anterior wall of the urinary bladder with visible calcification and uneven enhancement; H: A specimen of the en bloc resected tumour. Macroscopically, it was a 10.0 cm × 7.0 cm × 4.0 cm partial cystectomy specimen, which on cut section showed a large, soft to firm haemorrhagic tumour mass measuring approximately 6.0 cm × 5.0 cm × 5.0 cm; and I-K: Histological and immunohistochemical characteristics of the *en bloc* resected tumour. Haematoxylin and eosin staining exhibited the urothelium of the bladder mucosa in the resected specimen and dilated thin-walled vessels in the detrusor muscle layer (I: 40 ×). The lesion was composed of small irregular angiomatous spaces lined by a simple layer of endothelial cells (J: 100 ×), and endothelial cells were CD34-positive (K: 100 ×).

haemoglobin, 113 g/L; haematocrit, 34.2%; and platelet, 206/L. Random urinalysis with microscopic examination showed haematuria, > 100 red blood cells, 0-3 white blood cells per high-powered field, and no proteinuria or pyuria.

Case 2: The blood cell count results were within a normal range, and the results of 11 tumour markers were negative. However, urinalysis showed > 100 red blood cells and 3-6 white blood cells per high-powered field.

Imaging examinations

Case 1: Multislice spiral computed tomography urography in the urological system showed the anterior and superior wall of the bladder was thickened and multiple nodules and masses. The larger one was about 5.0 cm × 3.1 cm × 4.0 cm mass, exhibited multiple punctate calcifications, and marked uneven enhancement, which was suspected as urachal (bladder) cancer (Figure 1C-G).

Case 2: Computed tomography scan of the abdomen and pelvis with contrast was also performed to evaluate the extent of the lesions and pelvic lymphadenopathy. The

computed tomography images indicated a soft tissue mass arising from the right anterior and upper wall of the urinary bladder (Figure 2A and 2B). The results of contrast-enhanced magnetic resonance imaging scan of the abdomen confirmed that a large 6.2 cm × 6.9 cm × 5.2 cm soft tissue mass arose from the right anterior and superior wall of the bladder, which suggested the possibility of a benign bladder tumour, and several enlarged lymph nodes were seen in the pelvic cavity (Figure 2C-E). We performed cystoscopy and pathological examination of the tissue sample. Cystoscopy confirmed that blue to reddish sessile lesions of a large 6.0 cm × 6.0 cm × 5.0 cm were visualized on the right anterior superior wall of the bladder. The initial pathological report showed gland cystitis, but no characteristic tumour tissue was identified (Figure 2F and 2H).

FINAL DIAGNOSIS

Postoperative pathology and immunohistochemistry confirmed the diagnosis of urinary bladder haemangioma for both cases.

TREATMENT

Case 1

Under suspicion of urachal cancer, radical cystectomy was performed with open method surgery associated with an abdominal wall ostomy of the ileal outlet tract (in February 2016).

Case 2

Based on imaging results and the pathological results, the patient underwent a laparoscopic partial cystectomy (in November 2018).

OUTCOME AND FOLLOW-UP

Case 1

The final pathological results indicated a cavernous haemangioma of the urinary bladder extended into the deep muscular layer of the bladder wall adjacent to the adventitia (an ill-defined, soft, and brown tumour measuring 6.0 cm × 5.0 cm × 5.0 cm in size was seen outside the anterior bladder wall) (Figure 1H-K). Haematuria resolved after surgery, and no evidence of tumour recurrence was found during the 3-year follow-up.

Case 2

The resected partial cystectomy specimen was sent for histopathological examination. The pathological diagnosis was given as bladder angioma consisting of a mixture of cavernous lymphangioma and haemangioma components. The gross histopathology revealed a mass that was well-circumscribed, vesicles-like, 7.0 cm × 5.0 cm × 4.0 cm, and grey-brown cut surface. These anatomical characteristics supported the diagnosis of bladder haemangioma (Figure 2I-L). Postoperative urinary and pelvic ultrasonography showed that the bladder wall was smooth. No abnormal echoes were found in the lumen in 3 mo follow-up (Figure 3). Haematuria was not noted on postoperative urinalysis.

DISCUSSION

Most bladder tumours are epithelial. Nonurothelial neoplasms occur very rarely in the bladder and usually increase the diagnostic challenge for urologists. To the best of our knowledge, the present research about UBHs are mostly congenital malformation of capillaries and blood vessels, and nonurothelial neoplasms are rarely reported clinically, accounting for only 0.6% of all urinary bladder tumours[3,4].

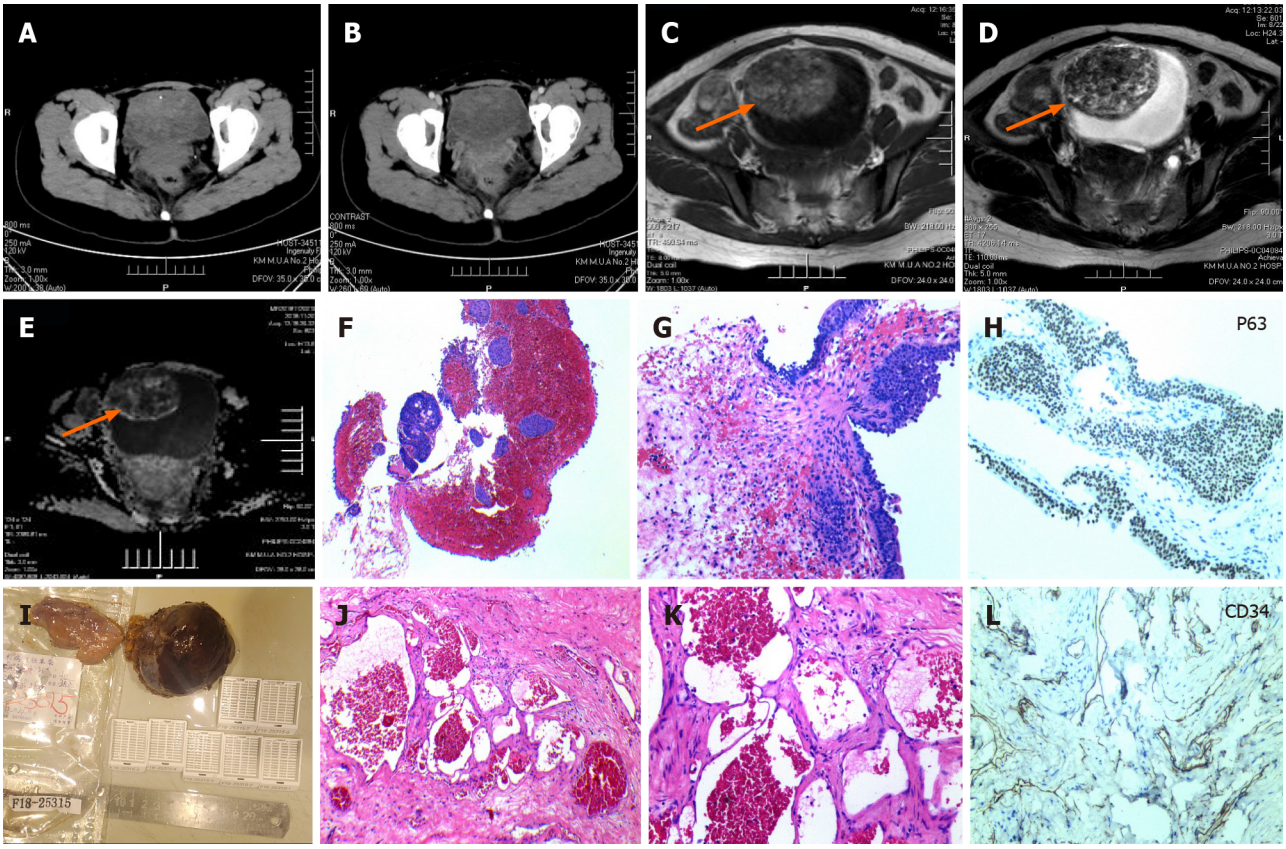

Figure 2 Computed tomography scanning, magnetic resonance imaging scanning, cystoscopy and biopsy, and pathological analysis of case 2. A and B: Preoperative computed tomography scan image showed that the bladder wall was thickened, and patchy soft tissue density shadows and punctate calcifications could be seen in the cavity (A) along with uneven enhancement (B); C-E: Preoperative pelvic magnetic resonance imaging. The tumour was a large 6.2 cm × 6.9 cm × 5.2 cm sharply defined lesion on the right anterior and upper bladder wall, which showed intermediate signal intensity on T1-weighted images (C), heterogeneous signal intensity with a predominance of hyperintensity on T2-weighted images, and marked enhancement of the lesion (D). Diffusion weighted imaging showed a slightly higher signal, Apparent Diffusion Coefficient (ADC) showed a slightly lower signal, and the enhancement was slight (E). F and H: Cystoscopy and biopsy. The initial pathological report of haematoxylin and eosin showed gland cystitis and a single-layer flat endothelium with no nuclear atypia (F: 40 ×, G: 100 ×); endothelial cells were P63-positive (H: 100 ×); I: A specimen of the resected tumour: The gross histopathology revealed a well-circumscribed tumour bearing a vesicle-like shape with a size of 7.0 cm × 5.0 cm × 4.0 cm and a grey-brown cut surface; and J-L: Histological and immunohistochemical characteristics after partial cystectomy. Haematoxylin and eosin staining showed that the tissue structure was predominantly formed by large and dilated vessels that were engorged with blood and covered with a thin wall (J: 40 ×) but with no clear atypia of endothelial cells (K: 100 ×). Endothelial cells were CD34-positive (L: 100 ×).

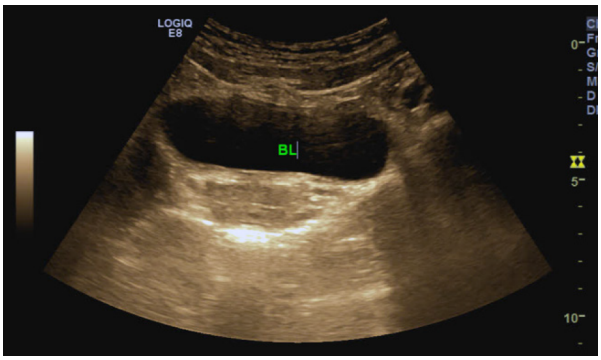

Figure 3 Postoperative urinary and pelvic ultrasonography image taken within 3 mo of surgery for case 2.

Although UBH can occur in all age groups, the most common age group is under 30. In a review of the literature, most bladder haemangiomas are solitary (66%), varying from a few millimetres to 10 cm in diameter, and mostly occurred in the dome, posterior wall, and trigone of the bladder, which has increased the diagnostic challenge of intramural tumours of the bladder[5]. Because many bladder haemangiomas occasionally coexist with cutaneous haemangiomas, varicose veins, Sturge-Weber syndrome, or Klippel-Trenaunay-Weber syndrome (both of which predispose

patients to their development), systemic evaluation in these patients is highly recommended[6,7].

UBHs are mostly congenital benign tumour formations of angiogenesis. Nevertheless, several studies have confirmed increased risks of developing soft tissue tumours related to radiation therapy for cancer[8,9]. The predominant clinical symptom of a UBH is the painless recurrence of isolated gross macroscopic haematuria with or without irritative urinary symptoms and abdominal pain[10]. However, hypovolemic shock can be present in cases with massive haemorrhage. Ureteric obstruction by the mass can cause hydroureteronephrosis, and a haematoma can obscure the mass in the bladder when there is massive bleeding[11].

Here, we conducted a thorough English literature review focusing on literature about UBHs published up to January 2019, and we identified 16 cases published from 2000 to 2019 after strict selection stored in the PubMed database (Table 1)[5,6,9,12-22]. The following key words were used for literature retrieval: ("case report") and ("Urinary Bladder Hemangioma" or "Bladder hemangioma" or "Hemangioma of the urinary bladder"). Including our two cases, these cases occurred in a wide range of ages, from 2 years to 85 years (mean 27.8), with a median age of 18 years, and the male-to-female ratio was 0.8 with no sex predominance. It was typical with the size of lesions ranging from 1.0 cm to 7.0 cm in diameter, although the characteristic of multiplicity was not usual. In our two cases, the systemic evaluations of all cases were grossly normal, with no cutaneous haemangioma or palpable scrotal varicocele.

Clinically, imaging examinations, such as ultrasonography, pelvic arteriography, computed tomography scan, and magnetic resonance imaging, are helpful in defining the extent and location of a haemangioma[2]. The cystoscopic features of a bluish, sessile mass with gross haematuria are highly suggestive of a haemangioma. The endoscopic differential diagnostic of pigmented raised lesions includes endometriosis, melanoma, and sarcoma. The final accurate diagnosis requires confirmation by biopsy[23].

Because bladder haemangiomas are not commonly seen in the genitourinary tract, it is important for pathologists and clinicians to carefully differentiate them from malignant nonurothelial neoplasms as they have vital prognostic characteristics as well as therapeutic strategies[20]. Clinical and radiological examinations are not enough for an accurate diagnosis. Careful histopathology and immunohistochemistry are required to establish the correct diagnosis. Histologically, bladder haemangiomas can be classified into cavernous, capillary, and arteriovenous types. Nearly 80% are cavernous type, while the capillary or arteriovenous types occur much less frequently[23]. Bladder haemangiomas are histologically similar to haemangiomas found in other sites and are formed by numerous proliferative capillaries mixed with thin walled, dilated blood-filled vessels lined with flat endothelial cells. The vessels are sometimes thickened by adventitial fibrosis. The histological depth of a bladder haemangioma may be within the submucosa layer or even extend to the muscular layer or perivesical tissues[5].

Malignant vascular tumours, such as angiosarcoma, have highly aggressive potential with the features of infiltrative growth, clear cytological atypia, high cellularity, and poor prognosis. By contrast, bladder haemangiomas are typically characterized by the proliferation of vessel walls with a clear boundary and spreading between the normal vasculature, which lack typical endothelial atypia or multilayering and have a satisfying prognosis[24]. The differential diagnosis of a polypoid bladder mass found in children with painless gross haematuria includes haemangioma, rhabdomyosarcoma, other vascular tumours, inflammatory pseudotumours, leiomyoma, neurofibromatosis, pheochromocytoma, transitional cell papilloma, transitional cell carcinoma, and pseudotumoural cystitis[25,26].

The treatment options for UBHs vary according to the individual, and follow-ups show favourable outcomes. The treatment of patients with UBHs is still controversial, and the considered factors include the size, location, and depth of penetration[22]. For small lesions and asymptomatic haemangiomas, surveillance is enough. Therapy is necessary only when the lesions threaten organ function or the patient's performance condition, such as haematuria resulting in anaemia and the suspicion of some malignant lesions. Optional therapeutic strategies include observation, transurethral resection, electrocoagulation, radiation, systemic steroid administration, the injection of a sclerosing agent, interferon-a-2 therapy, Yttrium-aluminium-garnet-laser therapy, and partial cystectomy or complete cystectomy[5,12,22]. Transurethral endoscopic surgery resection has become the gold standard for the treatment of small bladder cavernous haemangiomas. The risk of uncontrollable bleeding is inconsiderable when the lesion is small (≤ 3 cm), and follow-ups show satisfactory outcomes[2,18]. Biopsy and fulguration do not create severe bleeding and can adequately treat small lesions.

Table 1 Literature review of the reported cases of clinicopathologic characteristics of haemangioma in the bladder

Ref.	Case No.	Sex/Age in yr	Clinical manifestation	Site	Tumour size	Pathologic examination	Treatment	Follow-up (mo)
Kato *et al*[12], 2000	1	F/8	Gross haematuria, Klippel Trenaunay Syndrome	The apex of the bladder	4.0 cm	NA	Nd: YAG laser	NED (10)
Pratap *et al* [13], 2007	2	M/5	Gross haematuria accompanied by lower abdominal pain	The dome and the posterolateral bladder wall	5.0 cm	Cavernous haemangiolymphangioma	Partial cystectomy	NED (8)
Tavora *et al*[5], 2008	3	F/19	Haematuria alone	Not mentioned	1.1 cm	Cavernous haemangioma	Biopsy	LFU
	4	M/67	Haematuria combined with pain	Not mentioned	3.2 cm	Capillary haemangioma	Biopsy	NED (24)
	5	F/85	Asymptomatic	Not mentioned	2.4 cm	Capillary haemangioma	Biopsy	NED (4)
Macedo *et al*[14], 2010	6	F/7	Mild haematuria with clots	Supratrigonal lateral and posterior bladder wall	Numerous haemangiomas	NA	Electrocautery	NED (6)
Ashley *et al*[15], 2010	7	F/3	Gross haematuria	Posterior and left lateral bladder wall	4.0 cm	Cavernous haemangioma lymphangioma	Cystoscopic illuminated partial cystectomy	NA
Takemoto *et al*[16], 2011	8	M/4	Gross haematuria	Anterior wall, dome, and right lateral bladder wall	Covered about 60% of the bladder	NA	Nd: YAG/ holmium: YAG laser	NED (24)
Mager *et al*[17], 2014	9	M/46	Disabling lower urinary tract symptoms	Prostate, the seminal vesicle, and the bladder neck	Not mentioned	NA	Interventional superselective coiling of the arterial feeder	NED (6)
Jibhkate *et al*[18], 2015	10	M/3	Gross haematuria accompanied by lower abdominal pain	The dome of the bladder	7.0 cm	Cavernous haemangioma	Partial cystectomy	NED (12)
Kim *et al*[6], 2015	11	M/4	Intermittent and recurrent painless gross haematuria	The bladder dome and along the lateral aspects	1.3 cm	Cavernous haemangioma	Coagulated with a holmium laser	NA
Lahyani *et al*[19], 2015	12	M/60	Macroscopic haematuria	The dome of the bladder	Not mentioned	Cavernous haemangioma	Partial cystectomy and augmentation cystoplasty	NA
Jin *et al*[20], 2016	13	M/46	Asymptomatic	The right bladder wall	1.4 cm	Intramural anastomosing haemangioma	Partial cystectomy	NA
de Sousa *et al*[21], 2017	14	M/2	Persistent gross haematuria	The dome of the bladder	Not mentioned	Cavernous haemangioma	Partial cystectomy	NA
Hu *et al*[9], 2018	15	F/49	Painless haematuria	The superior posterior wall	1.0 cm	Cavernous haemangioma	Transurethral tumour resection	NED (18)
Syu *et al*[22], 2019	16	M/17	Painless gross haematuria	The superior anterior wall	3.5 cm	Cavernous haemangioma	En bloc resection of the urachus and bladder tumour with opened surgery	NED (24)
This report	17	F/44	Painless gross haematuria	The superior anterior wall	5.0 cm	Cavernous haemangioma	Open radical cystectomy	NED (36)
	18	F/31	Asymptomatic	The right anterior wall	6.9 cm	Cavernous lymphangioma and haemangioma	Laparoscopic partial cystectomy	NED (12)

LFU: Lost to follow-up; NA: Not available; Nd: Neodymium; NED: No evidence of disease; YAG: Yttrium-aluminium-garnet.

Neodymium: yttrium aluminium garnet laser irradiation is another effective and less invasive therapy option, and it allows complete coagulation of the whole bladder thickness[16]. In cases of > 3 cm masses or multiple tumours or those that extend deep into the bladder. However, a transurethral biopsy or the resection of a bladder haemangioma is contraindicated because of the iceberg nature of this tumour and the significant possibility of gross haemorrhage. Open resection of the lesion or partial cystectomy is effective[5,11]. Whereas partial cystectomy may reduce storage function, partial cystectomy and bladder augmentation can preserve storage function, but this treatment may make voiding function worsen[19].

Although UBHs have a benign course, postoperative follow-up is mandatory for the detection of tumour recurrence or residual disease, and ultrasonography, computed tomography, and even flexible cystoscopy can be used to detect recurrence[18,19].

CONCLUSION

In conclusion, UBHs are benign, nonurothelial tumours that rarely occur in paediatric and adolescent patients. The accurate diagnosis of UBH is usually confirmed by histopathology and immunohistochemistry due to the difficulty of definitive diagnosis by clinical and radiological examination. It is critical to distinguish UBH from malignant vascular tumours because the required treatment approach and the prognosis may differ dramatically. Due to the limited number of reported cases, there is no "gold-standard" therapy for UBH. Treatment options vary according to the individual, and follow-ups show favourable outcomes. Although the prognosis of patients with UBH is usually excellent, follow-up is necessary to detect evidence of tumour recurrence or residual disease.

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