CASE REPORT

Infantile Intravesical Malignant Rhabdoid Tumour

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ABSTRACT

Malignant rhabdoid tumour is a rare, but highly aggressive, malignancy of early childhood. Malignant rhabdoid tumour can be classified according to renal and extrarenal locations. For extrarenal lesions, the spinal cord and central nervous system are most commonly involved, although such tumours may arise in almost any site. However, malignant rhabdoid tumour of the bladder has only been reported in a few patients, mainly focusing on its pathological aspects. We report on a patient with malignant rhabdoid tumour of the urinary bladder. The clinical, radiological, and histological features of this disease entity are discussed.

Key Words: *Child; Pathology; Rhabdoid tumor; Urinary bladder neoplasms; Urogenital neoplasms*

中文摘要

嬰兒膀胱惡性橫紋肌樣瘤

譚家盈、李子飛、李醒芬、謝佩溈、彭潔儀

惡性橫紋肌樣瘤是發生於童年早期的一種罕見、具高度侵襲性的惡性腫瘤。惡性橫紋肌樣瘤依據發病部位可分為腎內型和腎外型。儘管該腫瘤可發生於任何部位，但於腎外最常累及脊髓和中樞神經系統。然而，文獻中只有少數膀胱惡性橫紋肌樣瘤的病例，且主要集中於病理方面。本文報告一宗膀胱惡性橫紋肌樣瘤的病例，並討論相關臨床症狀、影像學及組織學特徵。

INTRODUCTION

Malignant rhabdoid tumour is a rare, but highly aggressive, malignancy of early childhood. The most commonly affected site is the kidney and this tumour comprises only about 2% of paediatric renal tumours.[1] Approximately 80% of cases occur in children younger than 2 years, most of whom are diagnosed between the ages of 6 and 12 months.[1] The median age at diagnosis is 11 months.[2] Most patients present with haematuria. Due the aggressiveness of the tumour, 80% of patients develop metastases, most commonly to the lungs and, less often, to the liver, abdomen, brain, lymph nodes, or skeleton.[3] Patients may develop hypercalcaemia secondary to elevated parathyroid hormone and the serum calcium level can be normalised after tumour resection.[2] Patients have a poor prognosis, with

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mortality occurring within 12 months of diagnosis. Data for 5-year survival are barely available due to the poor prognosis. Malignant rhabdoid tumour was named for its apparent resemblance to skeletal muscle histologically. This tumour was first described as a sarcomatous variant of Wilms' tumour, but was later recognised as a distinct entity with different clinical and pathological features.[3] Malignant rhabdoid tumour can be classified based on its location as renal and extrarenal lesions. For extrarenal lesions, the spinal cord and central nervous system (CNS) are most commonly involved, although such tumours may arise in almost any site, including the extremities, brain, and heart.[4] Malignant rhabdoid tumour of the bladder has only been reported in a few patients, mainly focusing on its pathological aspects.[5-8] We report on a patient with malignant rhabdoid tumour of the urinary bladder. The clinical, radiological, and histological features of this disease entity are discussed.

CASE REPORT

A 5-month-old girl with an uneventful antenatal history was referred to the Alice Ho Miu Ling Nethersole Hospital, Hong Kong, in September 2011 with a 1-month history of haematuria. She had end-stream haematuria and was afebrile. She had been treated for a urinary tract infection with intravenous antibiotics in Mainland China before presenting to our hospital.

Ultrasonography showed a lobulated intravesical mass adhering to the left posterior wall of the urinary bladder, measuring 2 cm in size at its maximal dimension.
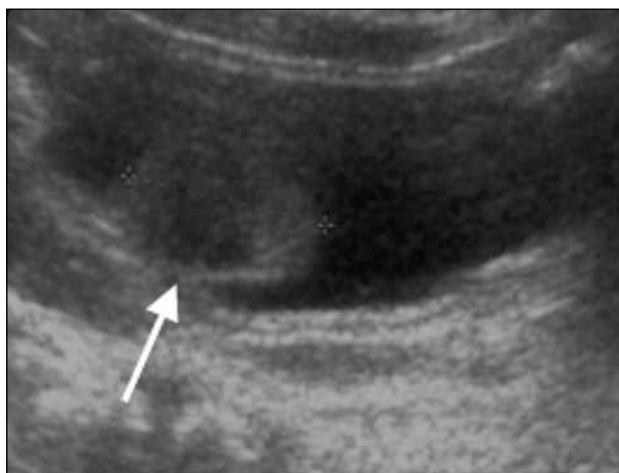
Figure 1. A transabdominal ultrasound scan of the pelvis in longitudinal section shows a lobulated soft tissue mass (arrow) attached to the left posterior aspect of the urinary bladder wall. Of note are internal hypoechoic areas that may suggest the presence of tumour necrosis.

Intralesional hypoechoic areas were present (Figure 1). No significant vascularity was noted within the mass. No focal renal mass or proximal dilatation of the ureters and collecting systems was detected on either side. Computed tomography (CT) scan showed a lobulated soft tissue mass with broad attachment to the left superoposterior wall of the urinary bladder (Figure 2). Internal hypoenhancing areas were suggestive of cystic or necrotic components. The kidneys were unremarkable. No pelvic or retroperitoneal lymphadenopathy was identified. No evidence of

Figure 2. Contrast-enhanced computed tomography scans of the abdomen and pelvis: (a) axial and (b) coronal reformatted images show a lobulated soft tissue mass (arrows) with broad attachment to the left superoposterior wall of the urinary bladder. Internal hypoenhancing areas that suggest the presence of cystic or necrotic components are present. No intralesional calcification is identified.

distant metastases was detected on the CT scan. She subsequently underwent cystoscopy, which showed a large intravesical mass arising from the posterior part of the dome of the urinary bladder. The mass had an irregular shape with a rough papillary surface and appeared vascular.

Partial cystectomy was performed. Intraoperatively, the tumour measured approximately 3 cm in maximal dimension and was attached by a stalk to the dome of the urinary bladder (Figure 3). Additional necrotic tumour fragments were present within the bladder. The rest of the urinary bladder was unremarkable macroscopically. Pathologically, the tumour was confirmed to be extrarenal malignant rhabdoid tumour.
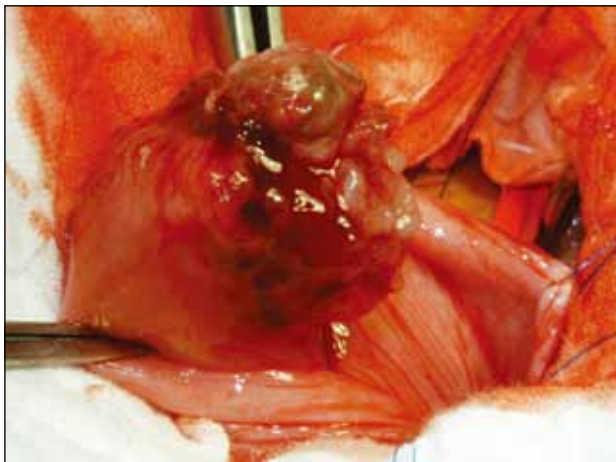

Figure 3. Intraoperatively, the tumour is attached to the dome of the urinary bladder, with evidence of necrosis.

The ulcerated tumour consisted of diffuse sheets of malignant cells exhibiting large vesicular nuclei, prominent nucleoli, and a moderate-to-large amount of eosinophilic cytoplasm. A rhabdoid appearance with eccentrically located nuclei with inclusion-like cytoplasmic features was noted. Mitotic activity was frequent with tumour necrosis (Figure 4). The tumour invaded deep into the muscularis propria without evidence of lymphovascular permeation. The resection margin was clear. Immunohistochemical staining of the tumour cells exhibited loss of integrase interactor 1 (INI-1) staining.

Postoperative bone scan and CT scan of the thorax and abdomen at 1 month after operation showed no evidence of metastases. Due to the association of the tumour with the CNS, the patient underwent magnetic resonance imaging (MRI) of the brain and whole spine, which was negative for metastases. The patient was cared for by the paediatric oncologists and scheduled for chemotherapy.

DISCUSSION

Malignant bladder tumour in childhood is commonly mesenchymal in origin. The most common entity is rhabdomyosarcoma, either arising directly from the bladder wall or originating from other pelvic or perineal structures. Rhabdomyosarcoma usually presents in the first 2 decades of life, with an older age of presentation than rhabdoid tumour. Rhabdomyosarcoma usually arises from the trigone or urethral orifice when located within the urinary bladder.[9] Other less common bladder
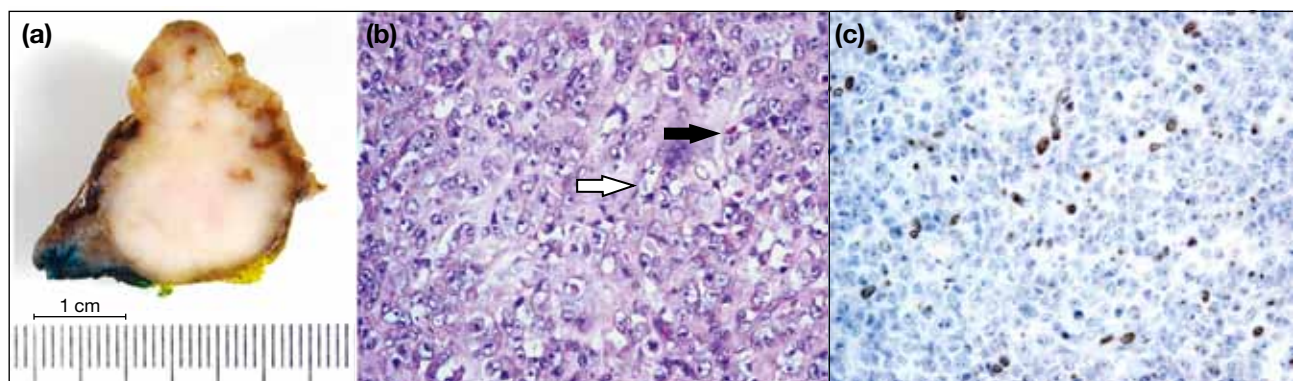
Figure 4. Rhabdoid tumour of the bladder specimen: (a) longitudinal sagittal section of the ulcerated polypoid mass that protruded from the bladder mucosal surface is shown. The cut surface reveals a solid whitish fleshy tumour measuring 2.8 cm in maximum dimension. The tumour is close to most of the circumferential margins and the deep margin. (b) Histological section shows diffuse sheets of malignant cells with large eccentric vesicular nuclei, prominent nucleoli (white arrow) and a moderate-to-large amount of eosinophilic cytoplasm (black arrow). Mitotic activity is frequent (H&E, original magnification x 400). (c) Integrase interactor 1 (INI-1) immunostain shows loss of INI-1 staining in the tumour cells (H&E, original magnification x 400).

tumours include pheochromocytoma, which is usually suspected in the presence of biochemical abnormalities. Imaging study is performed primarily to locate the tumour rather than to make the primary diagnosis. Transitional cell carcinoma of the bladder is rarely found in the first 2 decades of life and is exceptional in children younger than 10 years.[10] Other rare bladder tumours include cavernous haemangioma and neurofibroma, which show no specific imaging features. Infantile intravesical malignant rhabdoid tumour is exceedingly rare, and has been reported in only a few patients,[5-8] but it should be considered as a differential diagnosis in infants presenting with a bladder mass.

While the imaging features of renal and CNS malignant rhabdoid tumour have been well described,[11,12] those of malignant rhabdoid tumour within the bladder are rarely reported. Imaging features of renal malignant rhabdoid tumour include a subcapsular fluid collection and a lobulated appearance surrounded by haemorrhage or necrosis. Calcifications are more common in rhabdoid tumour than in Wilms' tumour. Vascular and local invasion is not uncommon.[11] In this patient, the tumour appeared lobulated in outline both on ultrasonography and CT, with central hypoechoic/low attenuating areas highly suggestive of tumour necrosis. Although there was no calcification or evidence of local invasion, the overall appearance was similar to its renal counterpart, which is prone to necrosis and haemorrhage.

Malignant rhabdoid tumour has the worst prognosis among malignant urinary tract tumours of infancy and childhood. The tumour is aggressive, with early metastasis, and patients commonly have advanced disease at presentation, with death ensuing within 12 months of diagnosis.[3] The 18-month survival rate is only 20%.[13] The association of rhabdoid tumour with synchronous or metachronous primary intracranial tumours or metastases has been well established as a distinctive feature. Rhabdoid tumours are commonly midline lesions in the posterior cranial fossa, and include primitive neuroectodermal tumour, ependymoma, and cerebellar and brainstem tumours.[2] Hence, it is justifiable for patients with tissue confirmation of infantile intravesical rhabdoid tumour to undergo evaluation of the CNS. This patient underwent MRI of the CNS, which showed no evidence of distant metastases or intracranial lesions. Recent studies have also investigated the use of tracer fluorine-18 fluorodeoxyglucose (F18-FDG) positron emission tomography (PET) for malignant extrarenal rhabdoid

tumours, which accumulate F18-FDG avidly. PET/CT is helpful in the initial staging, assessing response to treatment, and clinical decision making at various stages of disease management.[14]

The treatment approach is different for rhabdoid tumour than for other bladder tumours, usually involving partial cystectomy and chemotherapy,[7] as for this patient. Radiotherapy is commonly given for rhabdomyosarcoma together with chemotherapy, which incurs a radiation hazard during early childhood.

The misleading name of rhabdoid tumour was originally suggested because of the morphological resemblance to other skeletal muscle tumours. However, neither ultrastructural nor immunohistochemical features support a myogenic origin for this tumour.[15] Histologically, rhabdoid tumour is characterised by a monotonous population of large, non-cohesive cells with vesicular nuclei and large nucleoli. The eccentric nucleus contains vesicular chromatin and prominent nucleoli, and eosinophilic cytoplasmic hyaline inclusions are present. Immunostaining is variable, but the tumour cells may be immunoreactive to vimentin, which may show paranuclear staining, cytokeratin, epithelial membrane antigen, desmin, and neurofilament. Extrarenal rhabdoid tumours generally have a histological appearance similar to renal rhabdoid tumours. The prognosis is poor for children with malignant rhabdoid tumour, therefore, making an early and accurate diagnosis is essential. Homozygous truncating mutations of the *hSNF5/INI1* gene have been known to predispose patients to malignant rhabdoid tumour and a variety of tumours of the CNS since 1999.[16] Patients with rhabdoid tumours have homozygous deletions or mutations of the *INI1* gene in chromosome band 22q11.2.[17] Thus, molecular genetic analysis of the INI1 locus has clinical utility in a diagnostic setting. The *INI-1* gene is a tumour suppressor gene that alters the conformation of the DNA histone complex so that transcription factors have access to the target genes. INI-1 is a nuclear antigen that is normally expressed in nucleated cells. The diagnostic feature of a rhabdoid tumour is the loss of normal nuclear INI-I expression. Thus, a positive INI-1 stain result will show loss of nuclear INI-1 staining. The cystectomy specimen of this patient exhibited loss of INI-1 staining. The *INI-1* gene mutation has also been reported to be associated with germline mutation and predisposition to familiar cancers.[18] Early diagnosis can aid family screening and counselling.[19]

CONCLUSION

Malignant rhabdoid tumour is an aggressive malignancy of early childhood that should be considered as a differential diagnosis in infants with a bladder mass. The imaging findings of malignant rhabdoid tumour are non-specific, although the histological and immunochemical findings are distinctive. CNS screening is essential as malignant rhabdoid tumour is highly associated with CNS tumours. Imaging can help to stage the disease and monitor treatment response.

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