Pure malignant rhabdoid tumour of the bladder

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Abstract

We present the case of a 17-year-old girl with pure malignant rhabdoid tumour of the bladder treated with a multimodal approach. She is recurrence-free at her 1-year follow-up.

Case report

We present the case of a 17-year-old female who presented with lethargy, haemoglobin of 41 g/L and an abdominal ultrasound showing a 5-cm bladder mass. She had no hematuria.

Endoscopic examination demonstrated a solid tumour resembling a transitional cell carcinoma and 42 g were resected. The tumour was poorly differentiated showing immunohistochemical positivity for pan cytokeratin, CD34, WT1 and CD56. This was interpreted as a poorly differentiated carcinoma with neuroendocrine features. The slides were sent for a second opinion to the pediatric pathologist at the Bristol Royal Infirmary and Great Ormond Street, UK. Further immunohistochemistry showed loss of INI1/BAF47 and positive vimentin staining. This was diagnostic of a malignant rhabdoid tumour (MRT). There was no evidence of deletion of the HIRA region of 22q11, assessed using in situ hybridization, although small deletions may be missed using this technique.

A staging computed tomography scan and magnetic resonance imaging (MRI) post-resection revealed localized disease. She was reviewed at both the pediatric and adult bladder cancer multidisciplinary meetings where a decision for a multimodal therapy was made.

She received 2 cycles of doxorubicin, ifosfamide, carboplatin and etopside, and a subsequent MRI demonstrated good response.

She underwent a robotic uterine, cervical and vaginal sparing cystectomy and intracorporeal formation of an ileal conduit. The decision to spare her vagina, cervix and uterus was deemed feasible from an oncological point of view and desirable for her age. The choice of reconstruction was limited by the need to keep the pelvis clear for subsequent radiotherapy. The ovaries were transposed out of the pelvis and marked with metal clips to enable future identification. Access to the vesical pedicles and bladder was achieved through 2 windows on both sides; the first between the medial umbilical ligament, round ligament and the pelvic side wall, and the second through the broad ligament inferior to the round ligament. Vaginal preservation was achieved through an incision made superiorly to the cervix with the plane of dissection between bladder and vagina guided by a vaginal swabstick. Finally, an omental flap was developed and attached to the pelvic side wall, the round ligament and to the superior surface of the uterus to prevent small bowel falling into the radiation field postoperatively. She had an uneventful recovery and was discharged on postoperative day 4. The specimen confirmed a 10-mm MRT with invasion through muscle into fat, clear surgical margins and all 17 lymph nodes were negative (pT3aN0MO).

Three weeks following surgery, she started a combination of radiotherapy and a total of 9 cycles of high-dose alkylating chemotherapy: vincristine, cyclophosphamide, actinomycin D, ifosfamide, carboplatin and etopside. MRI scans of the pelvis performed at 1, 4 and 12 months post-treatment show no recurrence.

Discussion

We present a case of a pure MRT of the bladder in a young adult. It is important to emphasize that this is histologically distinct from a genitourinary rhabdomyosarcoma or a primary bladder tumour with rhabdoid features. Rhabdoid tumours have sheets of tumour cells with round or oval cells with eccentric nuclei, prominent nucleoli and eosinophilic cytoplasm. There is a lack of immunohistochemical staining for SMARCB1/INI1. The common genetic basis for rhabdoid tumours is a deletion and/or mutation of the INI1 gene on

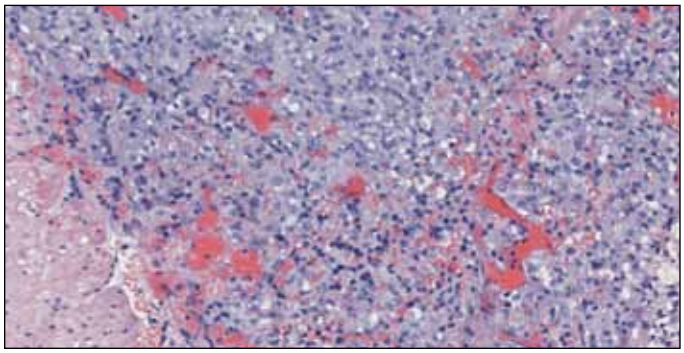

Fig. 1. Resected specimen. The tumour consisted of sheets of cells with vesicular nuclei and prominent nucleoli. There was a high mitotic index (hematoxylin and eosin).

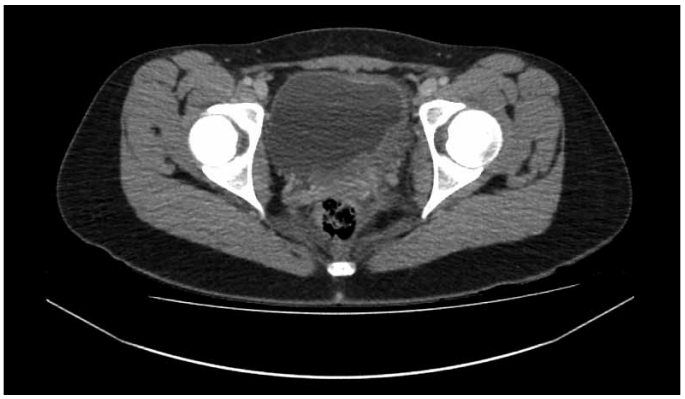

Fig. 2. A computed tomography scan performed post-initial resection shows thickening of the posterior and left lateral wall of the bladder.

chromosome 22 (22q11), inactivating the tumour suppressor gene SMARCB1, though these tumours can lack this mutation as seen in this case.[1]

Early accurate diagnosis to differentiate potentially chemosensitive MRTs from poorly differentiated transitional cell carcinoma or rhabdomyosarcoma is essential to reduce the high risk of metastasis.

MRT of the kidney are aggressive pediatric tumours accounting for 2% of renal tumours and 48% of non-central nervous system rhabdoid tumours. Extra-renal locations, such as soft tissue of the trunk, head and neck, abdomen, pelvis and retroperitoneum, have been described. MRTs metastasize early and have poor prognosis. A case series of 14 renal and extra renal rhabdoid tumours in children found that 7 died within 4 months of diagnosis.[2] Of the 106 children diagnosed in the UK with extracranial rhabdoid tumours, 1-year survival was only 31%.[3]

The previous 7 reports of pure isolated MRT of the bladder all occurred in children under 6.[1,4-6] Recently, Szymanski and colleagues have recently described a synchronous bladder and renal tumour in a 9-year-old boy.[7] These cases were managed with cystectomy, adjuvant chemotherapy and in 2 cases with additional radiotherapy. Chemotherapy regimens included combinations predominantly of vincristine, cyclophoshamide, etopside, ifosfamide with the addition of doxorubicin, actinomycin, carboplatin and cisplatin. Two of these cases, both 4-year-old children, were alive at 2 and 9 years at follow up, respectively.[4,5] The National Wilms Tumour Study showed survival increased with age in patients with rhabdoid tumours, but this 30% 1-year survival

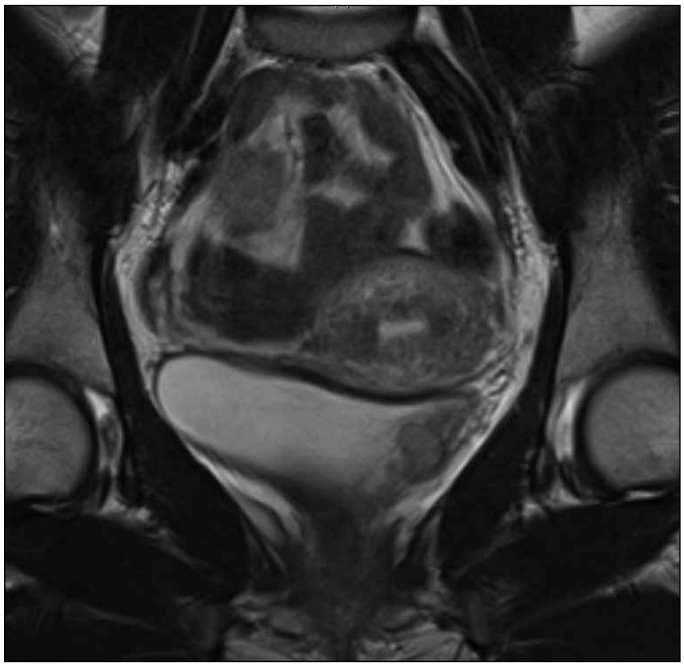

Fig. 3. Staging magnetic resonance imaging before chemotherapy.

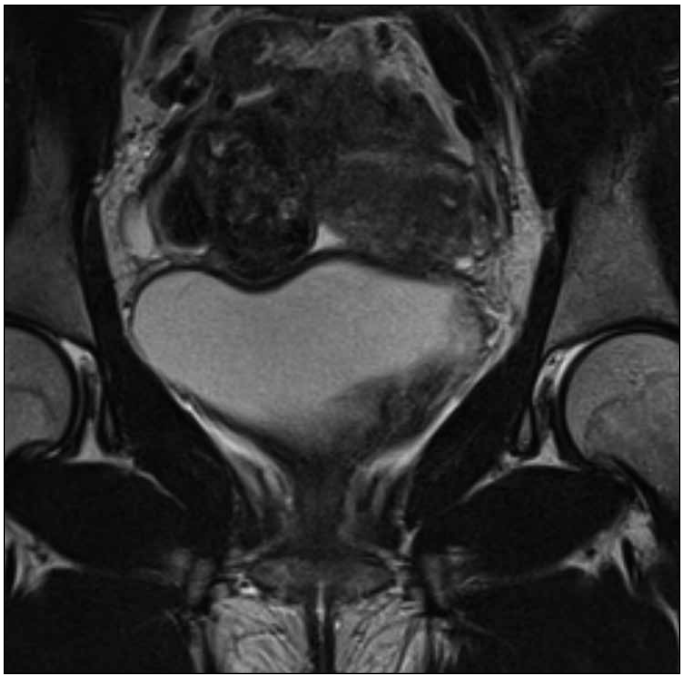

Fig. 4. A magnetic resonance image after 2 cycles of chemotherapy.

has not improved since 1993.[8] Our case supports the possible relationship between better prognosis and age >3 years for MRTs in general, although the numbers of bladder MRTs remain too low to draw definitive conclusions.

There are no standard pathways of treatment for managing extra cranial rhabdoid tumours due to the rarity of the disease.[9] Evidence on the treatment of extra renal MRTs is based predominantly on patients with atypical teratoid/rhabdoid tumours (AT/RT). They appear to have the same initial chemosensitivity, early recurrence and poor prognosis as renal MRT and AT/RT. Historical case studies of renal rhabdoid favour alternating courses of vincristine, doxorubicin, cyclophosphamide, ifofosfamide and etopside. Szymanski and colleagues used the AREN0321 protocol for their chemotherapy combination to manage high-risk renal tumours.[10] Surgical resection and chemotherapy, including actinomycin, apprear to have a positive effect on survival. In a systematic and meta-analysis, actinomycin was shown to improve survival by 73%.[11] Older patients (>3 years) appear to have a better response to high-dose alkylating therapy.[1,6,11,12] Radiation therapy has been reserved for older patients in managing extracranial rhabdoid tumours, but appears to have a positive effect. Future management in the form of targeted therapies to induce cell cycle arrest in the rhabdoid cell lines, in addition to a standard chemotherapy regimen, are being explored.[9]

Conclusion

This case is, to the best of our knowledge, the first of a pure MRT of the bladder in a young adult managed with a combination of surgery, high-dose alkylating chemotherapy and radiotherapy, with 1-year recurrence-free follow-up.

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This paper has been peer-reviewed.

Competing interests: Ms. Warren, Mr. Oxley and Mr. Koupparis all declare no competing financial or personal interests.

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