Unusual paediatric spinal myxopapillary ependymomas: Unique molecular entities or pathological variations on a theme?

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ABSTRACT

Ependymomas are the commonest type of spinal glioma which represent a group of relatively benign tumours. Myxopapillary ependymoma (MPE) is a common variant found within the distal spinal cord around the conus. These two entities are clearly differentiated on the basis of their characteristic histological and molecular features. Rare variants of MPE's are described in the literature to have the propensity to metastasise and grow in extraspinal locations despite appearing histologically identical to their more benign relatives. Here, we describe two unusual cases of MPE and utilise DNA methylation analyses to compare their molecular signatures with known molecular subtypes of ependymoma in an attempt to distinguish whether these tumours represent a unique subset of disease.

1. Introduction

Ependymomas are the most common type of spinal cord glioma, accounting for some 60% of cases [1,2]. Myxopapillary ependymomas (MPE) are typically described as a benign subgroup, which almost exclusively involve the distal spinal cord and filum terminale. They occur much more commonly in adults than children, and in the former have an excellent prognosis. Contemporary treatment regimes in adults solely involve gross total resection, although some groups advocate for adjuvant radiotherapy [3]. MPE may rarely exhibit anaplastic features [4–6] or occur outside the spinal canal within the subcutaneous tissue [7] in both adult and paediatric patients. These unusual anaplastic variants have been reported to metastasise, both within the central nervous system and extracranially [8–10]. Dissemination prior to surgical intervention is documented in the paediatric population, but is an uncommon feature for adult spinal MPE [11,12]. Furthermore, in contrast to adults, MPEs tend to be extraspinal in children and more benign than the intra-spinal cases [13].

Classical spinal ependymomas and MPE are histologically distinct and genomic profiling has revealed that the two entities have characteristic molecular signatures that correlate with differences in their clinical behaviour [14,15]. However, what is less clear is why there is a wide variation in the phenotypic presentation of MPE in adults and children. Here we investigate two atypical cases of pediatric MPE and aim to molecular clarify if they are distinct from other ependymomas.

2. Case reports

2.1. Case 1

A previously well 12-year-old female presented with a tender mass at the superior aspect of the natal cleft, present for 2 months prior to attendance at the hospital. On the day of presentation, the patient had noticed the painful lump while lying down at school. Neurological examination was normal. Magnetic resonance imaging (MRI) revealed a well circumscribed 47 × 21 × 44 mm contrast enhancing mass intimately related to the sacrum/coccyx. (Fig. 1A). A staging CT of the chest abdomen and pelvis was normal. Blood tumour marker assessment revealed mildly elevated neuron-specific enolase (18.4 ng/ml), normal alpha-fetoprotein (AFP < 3 ng/ml) and normal beta human chorionic gonadotrophin (β-hCG < 1 ng/ml). The patient underwent a wide local excision of the lesion in continuity with the coccyx two days later.

Histopathological analysis revealed a circumscribed nodular lesion characterised by cuboidal to elongated tumour cells radially arranged in a papillary manner around vascularised stromal cores. Mucoid material was present between tumour cells and the blood vessels. There were areas of mild nuclear pleomorphism with low mitotic activity (up to two per high power field (HPF)) and no nuclear atypia or high-grade features. The diagnosis was myxopapillary ependymoma (WHO Grade I). The patient made an uneventful post-operative recovery. An MRI at 12 months after resection (Fig. 1B) revealed no evidence of local recurrence.

2.2. Case 2

A 14-year-old male presented to his general practitioner with a six-week history of worsening lower back pain, which was associated with one week of sciatic pain. Neurological examination was normal. A spinal MRI showed a well-defined 45 × 21 mm soft tissue mass filling the thecal sac and central canal at L5 level. A further small nodule at the thecal tip (S2 level) was also noted. Both lesions were mildly contrast enhancing (Fig. 2 A and B).

The patient underwent semi-elective L4 to S2 laminectomies to remove the tumours. The dura was opened midline under magnification. The filum terminale was sectioned and the blood supply to the tumour from the filum vessels was interrupted. The tumour was internally debulked with ultrasonic aspiration and gross total resection of both lesions was obtained. At the time of surgery, the surgeon described the tumour as solid and haemorrhagic, protrud-

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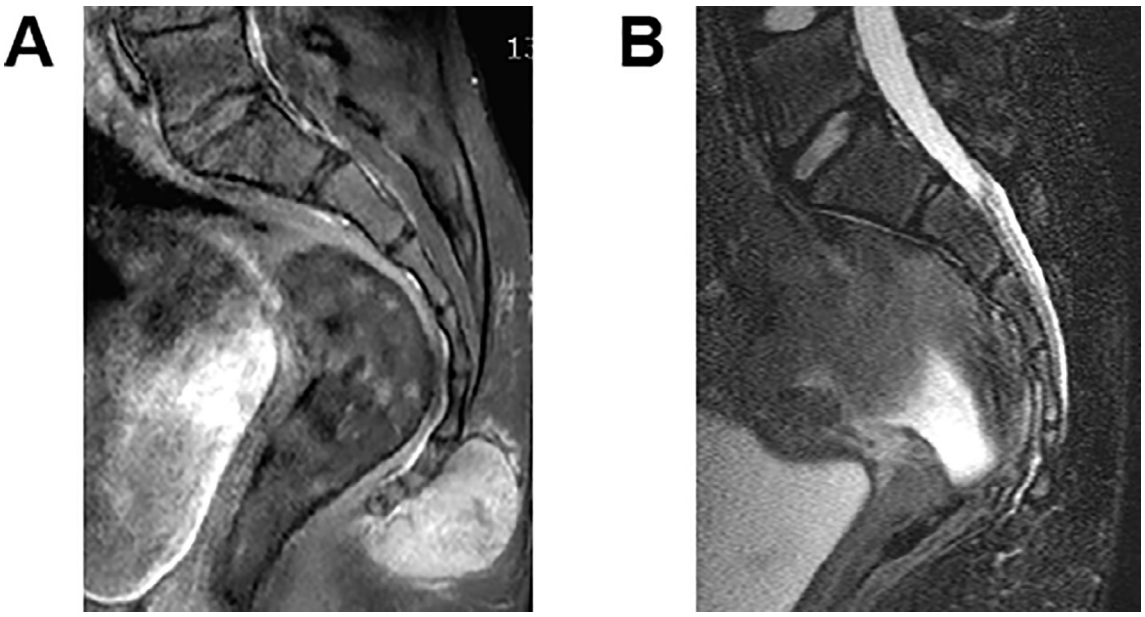

Fig. 1. Case 1: 12-year-old female. (A) T1 weighted gadolinium-enhanced sagittal MRI revealing a contrast enhancing mass intimately related to the sacrum/coccyx, which is no longer visible following complete surgical resection (B).

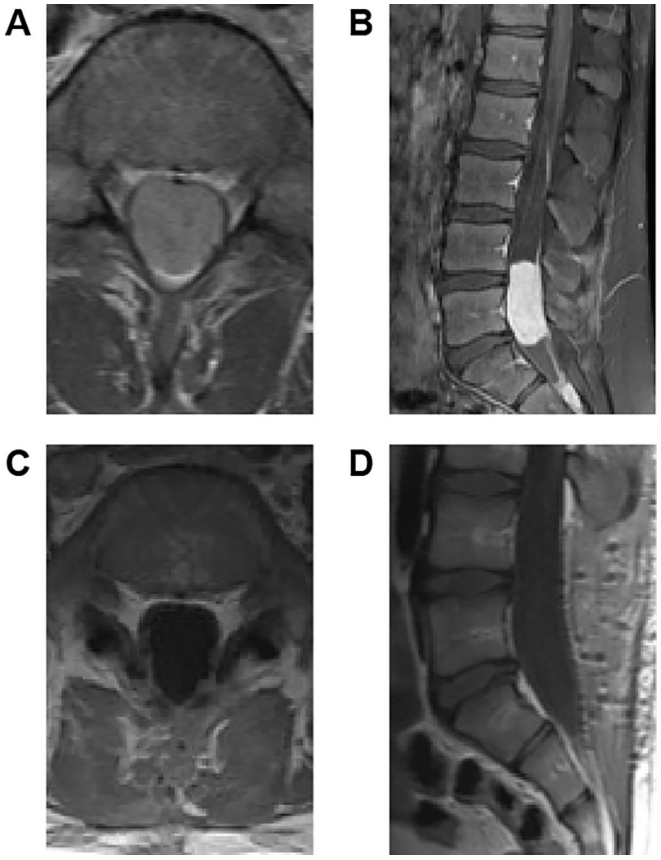

Fig. 2. Case 2: 14-year-old male. Coronal (A) and sagittal (B) T1-weighted gadolinium contrast-enhanced images showing two intradural lesions adjacent to L5 and S2. T1-weighted coronal (C) and sagittal (D) images with gadolinium contrast enhancement obtained seven weeks after surgery showed complete excision of both lesions.

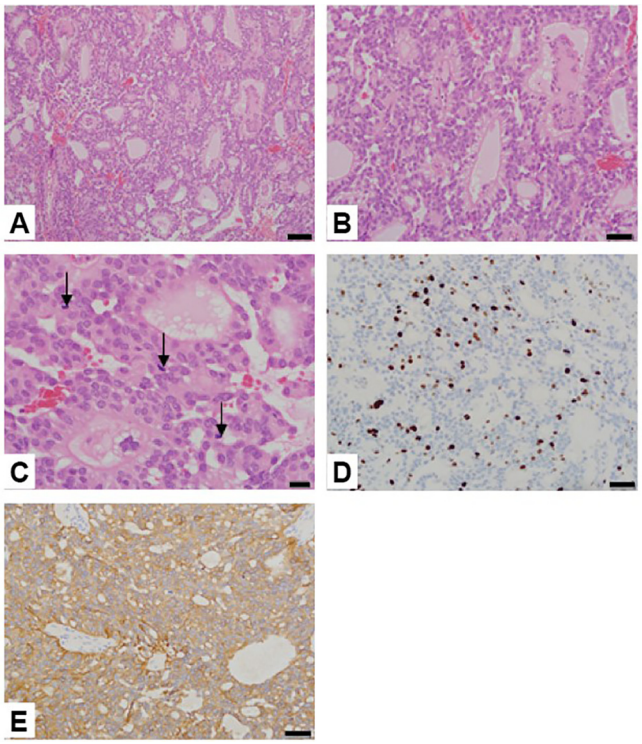

Fig. 3. Case 2 – Histological features of the tumour were generally consistent with MPE. H&E staining shown in low (A) and high (B) power revealed layers of tumour cells around vessels with mucoid degeneration (scale bars represent 275 and 100 μm, respectively). In addition, unusual mitotic figures (arrows) were observed (C), as was a high proliferative index indicated by Ki67 immunohistochemistry (D) and extensive perivascular GFAP positivity (E). Scale bars in C-E represent 25, 50 and 50 μm, respectively.

ing initially through the dural sac and requiring ultrasonic aspiration and suction to remove. The postoperative period was unremarkable, and the patient was discharged well with no neurological deficits. A follow-up MRI seven weeks after surgery confirmed a complete resection (Fig. 2C and D).

Pathological examination of the lesion revealed a grey-tan solid tumour. Microscopic sections showed a cellular neoplasm with a predominantly pseudo-papillary architectural growth pat-