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CASE REPORT

Multiple intradural-extramedullary spinal ependymomas including tumors with different histological features

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Abstract
Introduction We report a rare case with multiple intradural-extramedullary spinal ependymomas with different histological features.
Case report A 26-year-old female presented to our hospital because of difficulty in walking due to progressive paresis. Magnetic resonance imaging of the thoracic spinal cord showed multiple spinal cord tumors. Surgical resection of these tumors was performed and a different histological diagnosis including World Health Organization Grade III anaplastic ependymoma and Grade II ependymoma was obtained using the resected specimen. Additional radiotherapy and chemotherapy were also performed, and a successful outcome has been maintained for at least 3 years after surgery.
Conclusion Surgical resections and subsequent radiotherapy and chemotherapy for cases with multiple intradural-extramedullary ependymomas can result in a good postoperative course.

Keywords Multiple spinal cord tumor · Ependymoma · Mixture of different histology

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Introduction

Spinal ependymoma typically occurs in a solitary fashion as intramedullary tumors at the spinal cord level, or as exophytic tumors in the conus medullaris or filum terminale [1, 2]. However, to the best of our knowledge, multiple intradural-extramedullary spinal ependymomas which are histologically confirmed to be composed of two subtypes of ependymomas have not yet been reported.

Case report

We report a 26-year-old female case presented to our hospital complaining of difficulty in walking due to progressive paresis, pain in the trunk and numbness in the lower limbs. She had no medical history or family history including neurofibromatosis. At the first visit, a neurological examination revealed muscle strength of lower limbs of grade 3–5/5 and hypesthesia in the trunk and lower limbs, with hyperreflexia of the muscle stretch reflex, indicating the pyramidal tract sign.

Magnetic resonance imaging (MRI) of the thoracic spinal cord demonstrated multiple spinal cord tumors with low signal intensity changes on T1, T2 and short-T1 inversion recovery images (Fig. 1).

We performed laminectomies of T3 and T4 and gross total resection of the two intradural-extramedullary tumors located at the upper thoracic level to confirm the histology of the tumors and improve the neurological status. The histological studies revealed that proliferation of small cells with round-to-oval nuclei, formation of perivascular pseudorosette, increased cellularity, numerous mitoses, and microvascular proliferation in hematoxylin and eosin staining for those resected tumors and also revealed that

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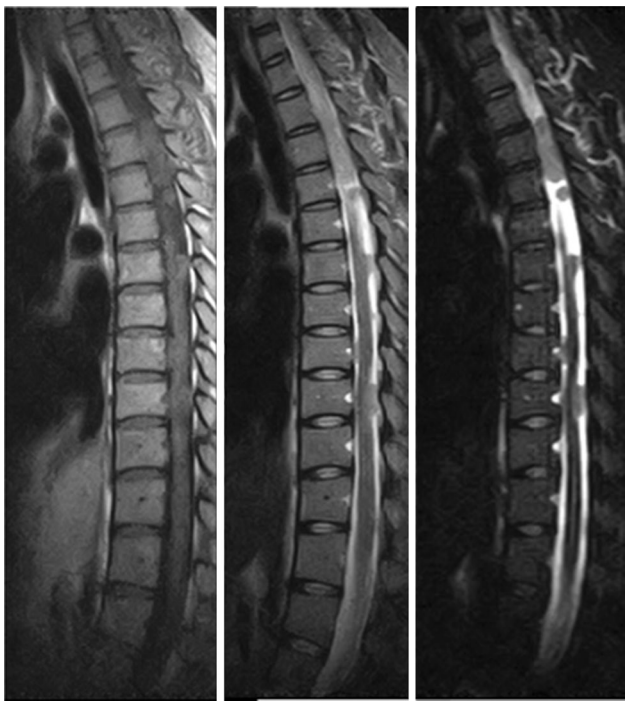

Fig. 1 Preoperative sagittal MRI of the thoracic spinal cord demonstrated multiple spinal cord tumors with low signal intensity changes on T1, T2 and short-T1 inversion recovery images

cells with strongly positive GFAP and vimentin and dot-like and ring-like structures with positive EMA in immunostaining, respectively. Those histological findings consisted with World Health Organization (WHO) Grade III anaplastic ependymoma. Cranial MRI after the first operation showed no intracranial mass lesion. Although the neurological condition improved after the first operation, 5 weeks later, we resected five residual tumors which were detected on MRI images via T5–T10 laminectomies. All five tumors were also intradural-extramedullary tumors in the spinal cord and gross total resection was performed. A histological assessment of these five tumors revealed WHO grade III anaplastic ependymoma (1 tumor) whose histological findings were similar to upfront resected two tumors and WHO Grade II ependymoma (4 tumors) whose histological studies showed moderate cellularity without mitotic figures or microvascular proliferation, apparently different from the upfront tumors (Fig. 2). After the second operation, we added craniospinal radiation in consideration of the existence of nonvisible dissemination of the tumors, in addition to chemotherapy using temozolomide [11].

Three years after this operation, further improvement in the neurological condition was obtained in the postoperative course and the patient was able to walk without any support. No apparent recurrence or dissemination was detected in MRI images using gadolinium contrast agent (Fig. 3).

Discussion

There have been only a few reports regarding multiple spinal ependymomas, especially multiple intradural-extramedullary ependymomas at the initial visit [3–5, 9, 10]. Furthermore, to the best of our knowledge, cases with multiple ependymomas consisting of tumors with different histological subtypes have not been reported. We herein reported a case of multiple intradural-extramedullary ependymomas including WHO Grade III anaplastic ependymomas and WHO Grade II ependymomas. Vural et al. reported a case with multiple intradural-extramedullary ependymomas in which the histological assessment of all resected tumors revealed WHO Grade II ependymomas, and confirmed that the condition was a result of dissemination according to a genetic analysis [5]. Additionally, it is known that anaplastic transformation can occur in intradural-extramedullary ependymomas [6–9]. In

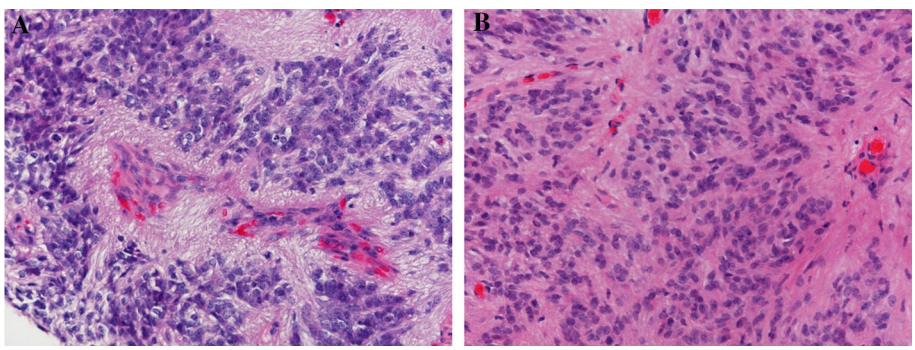

Fig. 2 Photomicrographs of the resected tumors showed different histological features: anaplastic ependymoma, WHO grade III, or ependymoma, WHO grade II. **a** Anaplastic ependymoma, WHO grade III, at the level of T9 showed increased cellularity, numerous mitoses, and microvascular proliferation with perivascular pseudorosettes (H&E, original magnification, ×20). **b** Ependymoma, WHO grade II, at the level of T7 showed moderate cellularity without mitotic figures or microvascular proliferation (H&E, original magnification, ×20)

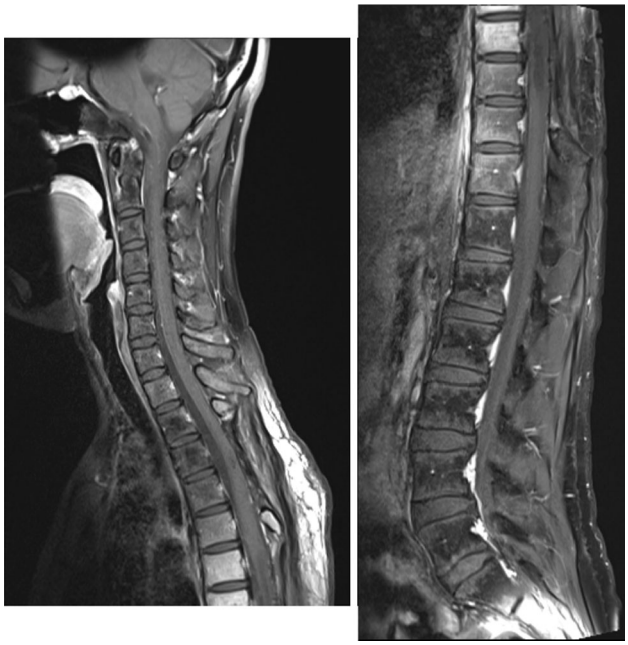

Fig. 3 No enhanced lesion indicating recurrence or dissemination was detected on sagittal MRI of the spinal cord using gadolinium contrast agent at 3 years after the operation

this case, we speculated two hypotheses regarding the pathogenesis. First, primary WHO GradeII intradural-extramedullary ependymoma may have disseminated to other spinal cord levels via the cerebrospinal fluid. Thereafter, some of the tumors, including the primary tumor, underwent anaplastic transformation. Second, the tumors may have occurred at multicentric foci. A further genetic analysis is needed to confirm the pathogenesis of tumor multiplicity.

Regarding the treatment for multiple intradural-extramedullary ependymomas, surgical treatment was adopted in all the previous reports cited in this study [3–5, 9, 10], although additional chemotherapy and/or radiotherapy was also performed in some cases [3, 9, 10]. Furthermore, there have been some reports supporting activity of temozolomide in ependymoma and glioblastoma [11, 12]. In this case, we first performed surgery in order to improve the neurological symptoms and obtain histological diagnosis. Subsequently, we added surgical resection for residual tumors and craniospinal radiation and chemotherapy using temozolomide. Although this treatment strategy resulted in a successful postoperative course for at least 3 years after the treatment, a greater accumulation of case reports is warranted to establish the appropriate treatment strategy for multiple intradural-extramedullary ependymomas.

Conclusion

Surgical resections and subsequent radiotherapy and chemotherapy for multiple intradural-extramedullary ependymomas resulted in a good postoperative course. This case report provides useful information to establish an appropriate treatment strategy for this very rare pathology.

Compliance with ethical standard

Conflict of interest The authors declare no conflicts of interest.

References

1. Duffau H, Gazzaz M, Kujas M et al (2000) Primary intradural extramedullary ependymoma: case report and review of the literature. Spine 25:1993–1995
2. Fourney DR, Siadati A, Bruner JM et al (2004) Giant cell ependymoma of the spinal cord. Case report and review of the literature. J Neurosurg Spine 100:75–79
3. Iunes EA, Stávale JN, de Cássia Caldas Pessoa R et al (2011) Multifocal intradural extramedullary ependymoma. Case report. J Neurosurg Spine 14:65–70
4. Landril F, Ajler P, Tedesco N et al (2012) Multicentric extramedullary myxopapillary ependymomas: two case reports and literature review. Surg Neurol Int 3:102
5. Vural M, Arslantas A, Ciftci E et al (2010) Multiple intradural-extramedullary ependymomas: proven dissemination by genetic analysis. J Neurosurg Spine 12:467–473
6. Cerase A, Venturi C, Oliveri G et al (2006) Intradural extramedullary spinal anaplastic ependymoma. Case illustration. J Neurosurg Spine 5:476
7. Graca J, Gultasli N, D'Haene N et al (2006) Cystic extramedullary ependymoma. Am J Neuroradiol 27:818–821
8. Robles SG, Saldana C, Boto GR et al (2005) Intradural extramedullary spinal ependymoma: a benign pathology? Spine (Phila Pa 1976) 30:E251–E254
9. Schuurmans M, Vanneste JA, Verstegen MJ et al (2006) Spinal extramedullary anaplastic ependymoma with spinal and intracranial metastases. J Neurooncol 79:57
10. Pomeraniec IJ, Dallapiazza RF, Sumner HM et al (2015) Anaplastic extramedullary cervical ependymoma with leptomeningeal metastasis. J Clin Neurosci 22:1871–1876
11. Stupp R, Mason WP, van den Bent MJ et al (2005) Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. N Engl J Med 352:987–996
12. Gramatzki D, Roth P, Felsberg J et al (2016) Chemotherapy for intracranial ependymoma in adults. BMC Cancer 16:287