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Spinal Anaplastic Ependymoma with Rapid Intracranial Ventricular Seeding - Case Report and Review of Literature

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Ependymomas are slow-growing tumors in the central nervous system. In spinal cord, ependymoma is the most common neuroepithelial tumor (15% of all spinal cord tumors). Ependymoma of the spinal cord with retrograde intracranial metastasis is rare. This study reported a 31-year-old female with thoracic anaplastic ependymoma (WHO grade III) who had received surgical intervention for removal of thoracic ependymoma twice at an interval of seven months due to local recurrence. After the second operation, rapid progression of seeding from spinal cord to brain developed in three months. Other case reports of spinal ependymoma with intracranial metastasis were reviewed and seven other cases with interval of local recurrence, location of intracranial metastasis, outcome, and pathology were also collected.

Key words: ependymoma of spinal cord, metastasis of ependymoma, seeding

INTRODUCTION

Ependymomas are slow-growing tumors of the cells that line the ventricular spaces of the central nervous system, including the central canal of the spinal cord. They are the most common neuroepithelial tumors of the spinal cord, 15% of all spinal cord tumors. In adults, ependymomas represent the most common intramedullary spinal tumors. Primary spinal cord tumors are rare, representing only 2 to 4% of all central nervous system tumors.[1,2] Neurological deficits and deterioration, including sensory loss, dorsal column dysfunction, dysesthetic syndrome, as well as bowel and bladder dysfunction are frequently observed. Ependymomas are unencapsulated lesions but are usually well circumscribed with smooth, regular margins. Consequently, gross total removal of these benign lesions is possible in most cases. This study reported a 31-year-old female with rapid progression of seeding from spinal cord to brain in 3 months.

CASE REPORT

History:

This 29-year-old female suffered from right-foot numbness since March 2010. Initially, the numbness started from her right toes, progressed to the right foot and further up to the thigh. About two weeks later, she also felt numbness over her left toes, which also progressed to the left foot and then to the thigh. Severe middle back pain happened once in May 2010. She visited Changhwa Christina Hospital for help and MRI of the lumbar spine showed no HIVD or spinal stenosis. She received rehabilitation and physical management first. However, graduate loss of sensation of low abdominal wall and anus sensation were noted after physical management. She visited St. Joseph's Hospital (Huwei, Yunlin, Taiwan) for help and MRI of the thoracic spine showed an intramedullary tumor at T6 level. Steroid therapy was prescribed for her and improvement of symptoms was noted. She was transferred to National Taiwan University Hospital Yun-Lin Branch for further management in June 2010. Urine retention developed since July 2010 and Foley's catcher was inserted on July 7, 2010. Urine retention with UTI was suspected and she then received Foley training. Detailed MRI of the thoracic lumbar spine showed an intramedullary tumor from T6 to T10 level with cystic components. She was then transferred to National Taiwan University Hospital on July 13, 2010. She had received T6 to T10 laminoplasty for intramedullary tumor excision on July 9, 2010. At first, the pathological report showed anaplastic astrocytoma (WHO grade III) and then it was revised to anaplastic ependymoma, (WHO grade III) by the pathological department of National Taiwan University Hospital.

After the operation, decreasing bilateral lower-limb muscle power developed and steroid was administered

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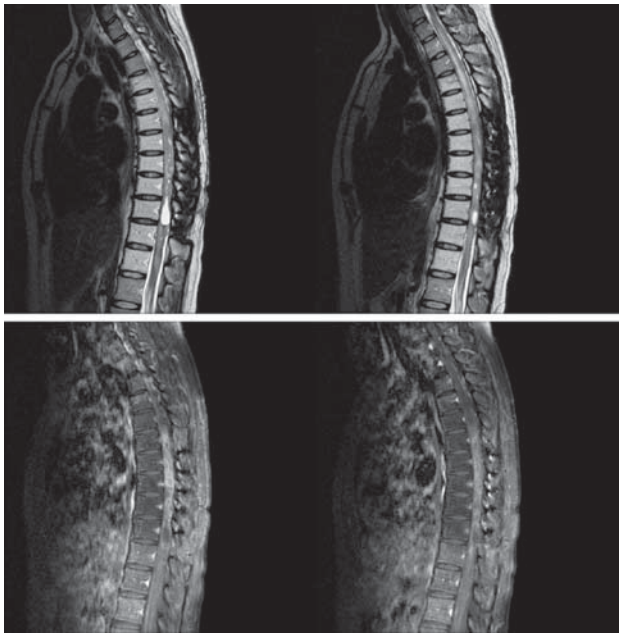

Fig 1 Recurrence of intramedullary tumor at T6 to T10 level and cyst (on T2WI) over T10 level were noted on MRI image.

but the muscle power did not recover. She was discharged on August 3, 2010 from NS and transferred to the rehabilitation ward. During hospitalization in the rehabilitation ward of National Taiwan University Hospital, she received radiotherapy, a total of 5000cGy in 25 fractions, and 4 courses of Temodal monotherapy (300 mg x 5 days)) from August 2010 to December 2010 under the impression of spinal anaplastic astrocytoma. Improvement of lower-limb muscle power was noted and she could walk with a walker during this period. Finally, she was discharged in December 2010.

However, progressing bilateral lower-limb weakness attacked again in February 2011 and she received MRI of the thoracic spine on February 10, 2011 at National Taiwan University Hospital Yun-Lin Branch. Recurrence of an intramedullary tumor at T6 to T10 level and a cyst over T10 level were noted on MRI images (Fig. 1). MRI of the brain was also performed for survey and there was no obvious brain tumor. She visited our NS OPD for second opinion on March 15, 2011. Almost paralysis with muscle power of bilateral lower limbs around Gr 0 -1 was noted. She was admitted on March 16, 2011 and laminectomy with duroplasty for decompression of T6 to T10 level, partial excision of the tumor, and drainage of cyst were done on March 17, 2011. The pathological report showed glioblastoma multiforme (GBM) on March 23, 2011, which was then revised to anaplastic

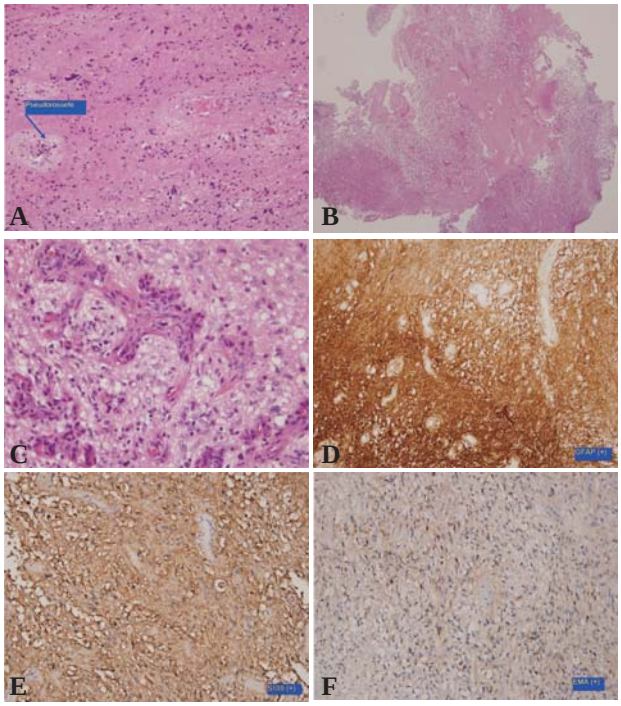

Fig.2 Inconspicuous perivascular pseudorosset characteristic of anaplastic ependymoma:
A. Perivascular pseudorosset. (200×)
B. Geographic pallisading necrosis. (40×)
C. Microvascular proliferation.
D. IHC stains: GFAP (+). S100 (+), EMA (focal +)
E. IHC stains: S100 (+).
F. IHC stains: EMA (focal +).

ependymoma (WHO grade III) on April 14, 2011 (Fig. 2).

After the operation, no obvious improvement of bilateral lower-limb muscle power was noted and neurological bladder developed. We consulted REHA for bedside rehabilitation and bladder training. She was discharged from our NS on April 12, 2011 and then transferred back to National Taiwan University Hospital Yun-Lin Branch for further treatment with Temodal and rehabilitation.

She visited our ER on May 13, 2011 with the chief complaint of blurred vision and deterioration of visual acuity exacerbated for 10 days. MRI of the brain, cervical and thoracic was performed. Tumor with CSF seeding over left frontal horn, 4th ventricle and C-T-L spine were suspected on the basis of image findings. Recurrence with seeding of tumor and obstructive hydrocephalus were diagnosed and she was admitted to our NS ward. After admission, conservative and palliative management were performed on her. Conscious change was noted beginning from May 22, 2011 and progressed to loss of consciousness on May 29, 2011. She was expired the following day under the impression of central failure.

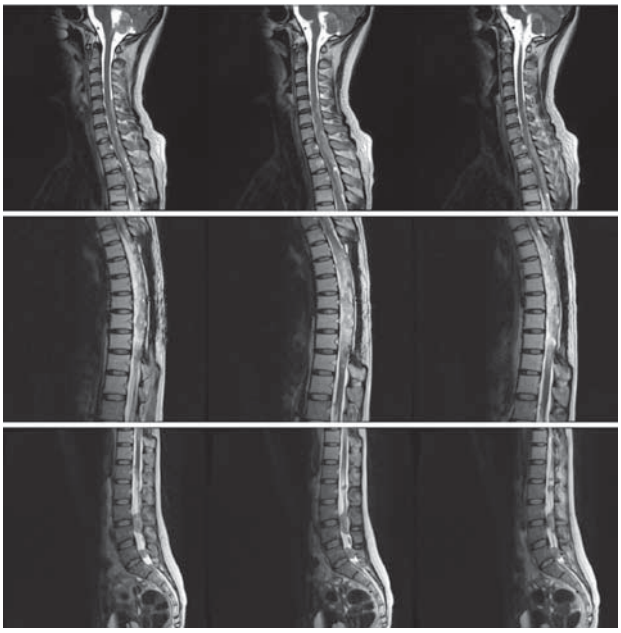

Fig. 3 MRI of the spine on May 13, 2011 showed numerous intramedullar and intradural extramedulrary mass and nodular lesions on cervical, thoracic lumbar, and sacrum spine. Tumor mass over 4th ventricle can be seen on sagittal view of C-spine image. Laminectomy status of T6 to T10 was also noted on T-spine image.

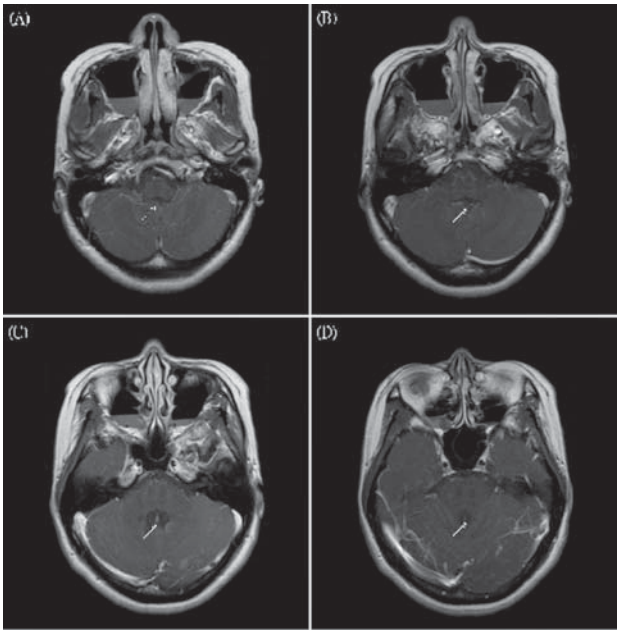

Fig. 4 MRI (T1WI with contrast) of brain on February 16, 2011 showed no tumor mass over 4th ventricle.

Physical and Neurological Examination:

Neurological examination demonstrated that her cranial nerves and upper limbs had normal function. On examination, the patient was found to have almost paralysis of bilateral lower limbs (only minimal movement of bilateral 1st toes), decreasing DTR (bilateral 1+) and absence of Babinski's sign. Normal bilateral upper-limb muscle power with absence of Hoffman sign and loss of sensation from abdomen around T6 dermatone level were noted. No lymphadenopathy was identified. An examination of the cardiovascular and respiratory systems yielded unremarkable findings. An abdominal examination revealed a distended bladder.

Neuroimaging Findings:

MRI of the spine on February 10, 2011 showed evidence of hetergenious and irregular signal from T6 to T9 level on T1WI with contrast and cyst formation over T10 level and syringomyelia on T2WI. MRI of the spine on May 13, 2011 showed numerous intramedullar and intradural extramedulrary mass and nodular lesions with hypo- to isointese on T1WI and intermediate T2WI hyperintensity, and contrast enhancement are noted (Fig. 3).

MRI of the brain on February 16, 2011 (Fig. 4) showed no obvious tumor lesion over T1WI with contrast but a mass lesion size about 31×20 mm with isointese T1 signal intensity and intermediate T2 hyperintensity over the 4th ventricle with mildly heterogeneous contrast enhancement was found on May 13, 2011 (Fig. 5).

Operation and Postoperative Course:

The patient underwent the first operation of laminectomy and laminoplasty T6 to 10 and the spinal lesion was debulked on July 9, 2010 at National Taiwan University Hospital. With the first diagnosis of spinal anaplastic astrocytoma, she received radiotherapy, a total of 5000cGy in 25 fractions and 4 courses of Temodal monotherapy (300 mg×5 days) from August 2010 to December 2010. Improvement of lower-limb muscle power was noted under rehabilitation.

After the second operation of laminectomy with duroplasty for decompression of T6 to T10 level, partial excision of the tumor and drainage of cyst were performed on March 17, 2011, she received rehabilitation therapy but the lower-limb muscle power and urination condition did not improve. She was transferred back to National Taiwan University Hospital Yun-Lin Branch for further Temodal monotherapy and rehabilitation on April 12, 2011.

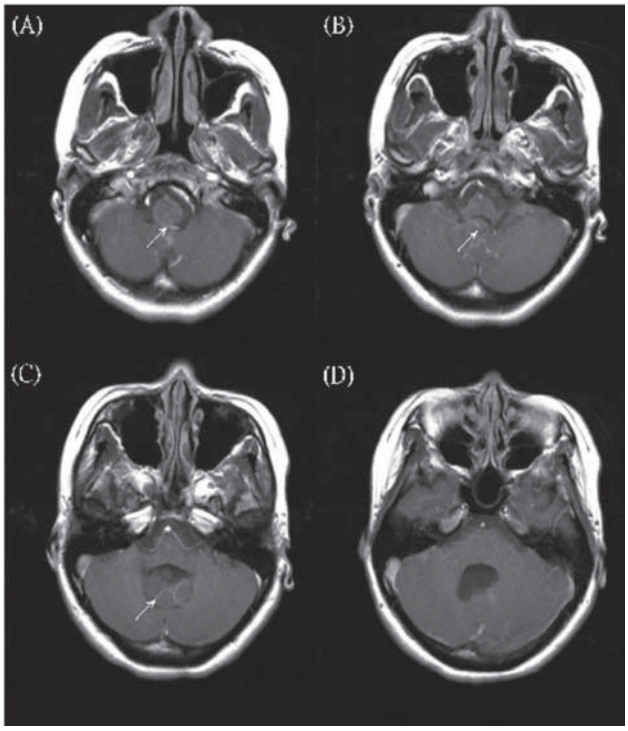

Fig. 5 MRI of brain (T1WI with contrast) on May 13, 2011 showed tumor mass over 4th ventricle with dilatation.

DISCUSSION

Ependymomas are usually benign tumors of the central nervous system derived from the liquor-filled spaces of ependymal cell lining, and also the most frequent spinal cord tumors in adult patients.[1] Ependymomas are rarely found in the spinal cord and comprise 15% of all spinal cord tumors.[3,4] Ependymomas are usually slow-growing neoplasms amenable to complete surgical resection that tend to compress adjacent structures rather than infiltrate cord parenchyma, resulting in associated symptoms. The most common symptoms and signs of spinal cord emedymoma are presentation of neck or back pain, sensory deficits, motor weakness, as well as bowel and bladder dysfunction.[5] Ependymomas can occur at any age; when they occur in children, they are more frequently located in the brain, whereas they are more often found in the spinal cord of affected adults. The WHO classified ependymomas into three distinct subtypes: subependymomas (WHO grade I), myxopapillary (WHO grade I) ependymomas, classic ependymomas (WHO grade II), and anaplastic ependymomas (WHO grade III).[5,6] Most ependymomas are classified as either WHO grade I or II, while malignant (grade III) types are rare. The mean age at presentation for ependymoma is 38.8 years.[7] Postoperative radiotherapy (> 45 Gy) of spinal cord in patients with residual tumor was suggested.[3] Rezai *et al*.[1] reported a disseminating rate of primary spinal ependymoma of 12.5% (11 of 88 patients). In the population of patients aged above 50 years, thoracic ependymomas are the most common intramedullary spinal cord tumors that present characteristically with sensory symptoms, and safe gross-total resection or subtotal resection can result in low perioperative morbidity and mortality as well as excellent functional outcome in the long run (more than 10 years).[8]

In 1985, Davis *et al*.[9] reported three primary spinal lumbosacral ependymomas with intracranial metastasis. The first case was a 40-year-old male with first onset of L1-2 level primary ependymoma (pathological report: myxopapillary ependymoma by postmortem examination). He received surgical resection but the tumor recurrence was noted over L1 level 5 years later. After 12 years from onset, left frontal-lobe metastasis was confirmed under ventriculography with symptoms of intellectual deterioration, bilateral papilledema, and paraplegia. He never recovered consciousness and died shortly afterward.

The second case was a 46-year-old male with first onset of L3-4 level (pathological report: papillary ependymoma). During operation, a large mass of tumor was found densely adhered to the lumbar nerve roots and was incompletely removed. Four years later, recurrent ependymoma was found to extend from L-2 to the sacrum and he received the second operation with a moderate removal of tumor tissue. Eight years later, he suffered from bilateral papilledema, nystagmus on lateral gaze, and ataxia of cerebellar type. Angiograms showed the appearance of a posterior fossa mass and, at operative exploration, a mass of tumor was found in the right cerebellar hemisphere spreading toward the vermis. Following partial tumor removal, the patient was given a further course of local radiotherapy and his intracranial symptoms were relieved. Three years after intracranial metastatsis was found, he developed a rapidly progressive weakness of the right arm, with pain in both shoulders. Myodil ventriculography outlined a tumor mass at C-3 and he received laminectomy extending from C-2 to C-6, which revealed a very vascular tumor, 3.5 cm in length, wrapped around the spinal cord. One year later, the patient deteriorated rapidly, became completely paraplegic, and then died one month after complete paralysis.

The third case was a 26-year-old man with L-3 level ependymoma (pathological report: myxopapillary

Table 1 Summary of cases of spinalependymomas with intracranial metastasis

Author	Sex & age	Local Recurrence	Intracranial Metastasis	Outcome	Pathology
Charles Davis	M, 40	6 years later	Left frontal, 12 years from onset	Die	Myxopapillary ependymoma
Charles Davis	M, 46	4 years later	Cerebellar, 8 years from onset	Die 11 years from onset	Papillary ependymoma
Charles Davis	M, 26	7 years later	Cerebellar, 5 years from onset	Alive & well 32 years later	Myxopapillary ependymoma
Matthew D. Smyth	M, 41	Unknown	Found at the same time	Unknown	Low-grade myxopapillary ependymoma
Mohanpal S. Dulai	F, 8	2 years later	Right cerebellum and left temporal lobe 4 years from onset	Stable tumor deposits in the brain and spine 9 years later	Papillary ependymoma, WHO grade II
Xing Su	M, 20	Unknown	Found at the same time	Unknown	Myxopapillary ependymoma, WHO grade I
Mascha Schuurmans	F, 29	Nil	Intracranial extrac erebral, 2 years from onset	Unknown	Intradural extramedullary anaplastic ependymoma, WHO grade III
Our case	F, 31	7 months later	4th ventricle 8 months later	Died 10 months from onset	Anaplastic ependymoma, WHO grade III

ependymoma). Most of the tumor was removed by surgery, and only fine strands were left on the nerve roots. Five years later, he developed frontal headache, nausea, vomiting and collapsed on the street. Tumor mass was found in the right cerebellar hemisphere and partially removed. Two years after intracranial metastasis, signs of tumor recurrence appeared in the lumbar region, and a further operation was performed. The patient was staying alive and well 32 years after first onset.

There were four other case reports of primary spinal ependymoma with intracranial metastasis. Smyth, *et al.*[10] reported a 41-year-old man with primary multiple intradural low-grade myxopapillary ependymoma over the lumbosacral region with metastasis to the right C-P angle region, which was similar to vestibular schwannoma on MRI image findings. It was assumed that the intracanalicular tumor arose from subarachnoid seeding from a primary myxopapillary spinal lesion and low-grade ependymomas can present with disseminated disease. Another author reported an 8-year-old girl presented with a papillary ependymoma (WHO grade II histology) in the thoracic spinal cord with multiple metastasis over the thecal sac at L-5 and S1-2, right cerebellum and left temporal lobe.[11] The patient received first treatment of subtotal resection of an intramedullary T8-10 spinal ependymoma in April 2001. The second treatment involved surgical removal of a L-5 tumor in September 2004 and full-spine external beam radiotherapy for S1-2 level residual tumor due to abnormal finding of low thoracic spine on MRI image. The third treatment was given 22 months after the second treatment. The patient received Cyberknife radiotherapy for both right cerebellar hemisphere and well-circumscribed lesion in the left temporal lobe and 6 cycles of oral etoposide over 6 months. She received the fourth treatment of gross-total resection of an enlarging left temporal tumor in June 2007 and subsequent Cyberknifera-diosurgical treatment for left cerebral lesion. The fifth treatment of whole-brain radiation (3750 cGy in total) was administered in January 2008 because some lesions had progressed. The sixth treatment involving 8 cycles of intravenous topotecan and oral cyclophosphamide was prescribed in March, 2008 for new tumor consisting of 3-4 nodules throughout the lower lumbar and sacral spine. At the age of 17 years, the patient had multiple, stable tumor deposits in the brain and spine. The third case report was a 20-year-old man with C4 myxopapillaryependymoma, WHO grade I with intracranial dissemination and distal spinal column of lumbar and sacrum.[12] The fourth case was described by Schuurmans *et al.*[13] Cervical spine revealing an extramedullary tumor with severe spinal cord compression was noted on a 29-year-old woman. Further imaging showed a second lumbar spinal tumor and both tumors was removed by surgery. During surgery, an intradural extramedullary tumor was found. Pathologic report

showed that both tumors were anaplastic ependymomas. Two years after surgery, an intracranial extracerebral metastasis was found, without evidence of spinal recurrence

The summary of these eight cases and our case of spinal ependymoma with intracranial metastasis is presented in Table 1. Most of these cases with primary spinal epedymomas were WHO grade I or II (or low grade). Local recurrence developed more than two years (from 2 to 7 years) later in four of these seven cases. If intracranial metastasis was not found at the same time with spinal lesion, it developed from 3 months to 12 years from onset. In our case, local recurrence developed 5 months after first surgery with nearly total resection of T6-T10 intramedullary ependymoma as well as postoperative radiotherapy and oral chemotherapy. When local recurrence and extended tumor were suspected, brain image survey of MRI was also performed for evaluation of intracranial metastasis. No image evidence showed intracranial metastasis at that time. Intracranial metastatsis was noted on brain image 10 months after onset (3 months after local recurrence was found) and she died soon due to severe IICP and central failure symptoms and signs. Before she died, she did not recover neurological function of lower limbs or bladder and bowel function, and was in total paralysis and incontinence status.

The anaplastic ependymoma cells may have migrated cranially with the CSF circulation, leading to the formation of other spinal subdural metastasis.[13] A similar mechanism may have led to the development of intracranial metastasis, although an additional role of spinal surgery, favoring the spread of malignant cells within the subdural space, cannot be excluded.

CONCLUSION

When a patient presents with an intramedullary tumor, an ependymoma should be included in the differential diagnostic list of spinal tumors. In patients with an ependymoma, performing an MRI of the entire neuraxis is mandatory in order to exclude metastases at distant sites. In patients with an anapalsticependymoma, rechecking MRI of the brain should be considered if IICP signs, local neurological deficit, and unclear conscious level develop.

DISCLOSURE

All authors declare no competing financial interests.

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