

Primary cerebellopontine angle ependymoma with spinal metastasis in an adult patient: A case report

CHENGCHENG ZHAO^{1,2}, CHUANFANG WANG^{2,3}, MENG ZHANG², TAIPENG JIANG²,
WENLAN LIU⁴ and WEIPING LI²

¹Guangzhou Medical University, Guangzhou, Guangdong 510182; ²Department of Neurosurgery, Shenzhen Second People's Hospital, Shenzhen, Guangdong 518035; ³Shantou Medical University, Shantou, Guangdong 515043; ⁴Central Laboratory, Shenzhen Second People's Hospital, Shenzhen, Guangdong 518035, P.R. China

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Abstract. Subtentorial ependymoma is a common central nervous system tumor in young children, but is uncommon in adults. Ependymoma often arises from the cells lining the fourth ventricle. The present study reports a rare case of primary ependymoma that originated from the cerebellopontine angle, with local extension to the two internal auditory canals and remote spinal metastasis, in an adult male. A 50-year-old male presented with headache, tinnitus and bilateral hearing loss that had persisted for 4 months. Magnetic resonance imaging (MRI) revealed a mass in each of the cerebellopontine angles, which had spread to each internal auditory canal and wrapped the VII/VIII cranial nerve complex. A gross total resection was performed to remove the mass in the right side. Histological examination confirmed that the tumor was a World Health Organization grade II papillary ependymoma. Notably, the patient complained of urine retention post-surgery and massive occupational lesions in T3-T4 and L5-S2 were found on full spinal cord MRI. The patient then received combination therapy consisting of temozolomide, and whole-brain and spinal cord radiation. In the final follow-up examination, performed 13 months after treatment, slight shrinkage of the T3 lesion was observed, and no progression of the left cerebellopontine angle and S5-L2 lesions were identified on MRI. In summary, although this clinical entity is rare, the diagnosis of ependymoma and the possibility of spinal cord metastasis should be considered in subtentorial tumors.

Introduction

Subtentorial ependymoma mainly occurs in young children and usually arises in the fourth ventricle (1). Although it is

a relatively benign tumor, cerebrospinal fluid (CSF) spread is found in 8-33% of patients (2,3). Moreover, subtentorial ependymoma is more inclined to exhibit CSF metastasis compared with supratentorial ependymoma (4).

Bilateral primary posterior fossa ependymoma originating from the cerebellopontine angle, termed primary cerebellopontine angle ependymoma, is a rare form of subtentorial ependymoma that predominantly occurs in infants and young children. The main symptom is headache due to progressively increasing intracranial pressure (5), while cranial nerve deficit is relatively uncommon. Surgical resection with subsequent radiotherapy is the primary treatment strategy for patients with ependymoma (6). The efficacy of conventional chemotherapy for this disease remains uncertain; however, temozolomide appears to be a promising adjuvant therapeutic approach for multifocal anaplastic ependymoma following surgical resection (7). The extent of surgical resection is the major determinant of overall survival in pediatric patients (8). However, the prognosis varies in different reports, with 5-year overall survival ranging between 50 and 64%, and progression-free survival ranging between 23 and 64% (5,9-11).

The present study reports a rare case of primary cerebellopontine angle ependymoma extending to the internal auditory canals and spinal cord in an adult man. To the best of our knowledge, this is the first such case described in the literature, with previously reported cases of primary cerebellopontine angle ependymoma limited to one side with no spinal cord metastasis (12-14). Written informed consent was obtained from the patient.

Case report

On May 3, 2013, a 50 year-old man presented to the Department of Neurosurgery of Shenzhen Second People's Hospital (Shenzhen, China) due to headache, tinnitus and bilateral hearing loss that had persisted for 4 months. A physical examination showed no facial hypo- or hyperesthesia. Muscle strength and limb tone was normal. The patient was positive for Romberg's sign and physical reflexions. Babinski's sign was negative. No significant past medical history or family history were found.

Correspondence to: Professor Weiping Li, Department of Neurosurgery, Shenzhen Second People's Hospital, 3002 West Sungang Road, Shenzhen, Guangdong 518035, P.R. China
E-mail: liweiping60@126.com

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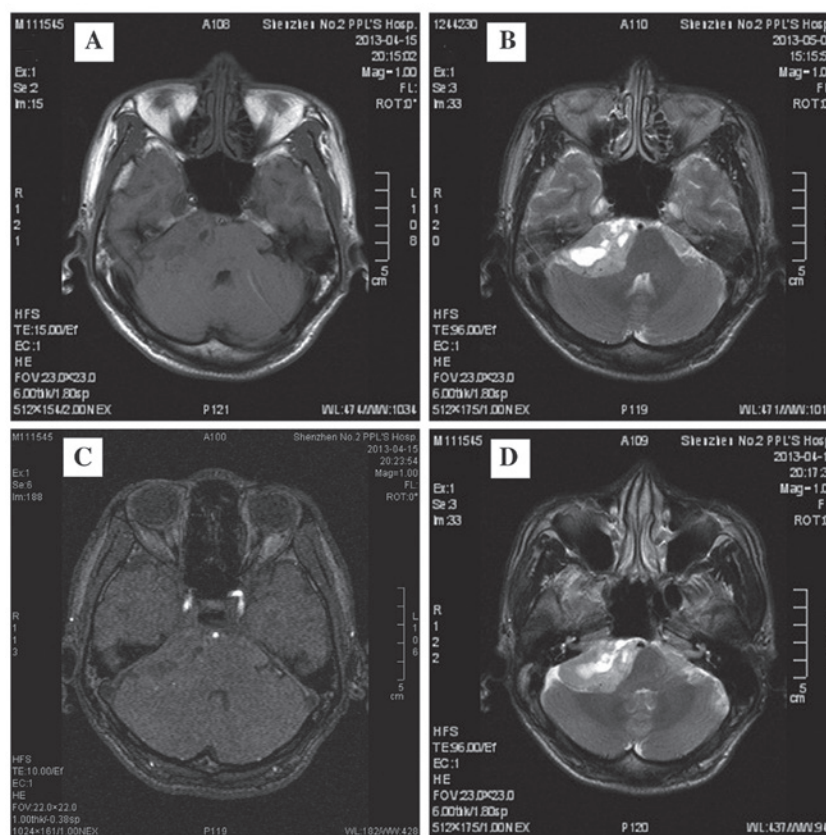


Figure 1. (A) T1-weighted magnetic resonance (MR) image showing bilateral masses in the cerebellopontine angles, with clear margins and a cyst in the middle of the right mass. (B) T2-weighted MR image showing the mass to be heterogeneous and hyperintense relative to gray matter, with an effect on the brainstem and fourth ventricle. (C) Contrast-enhanced image showing a lack of blood supply to the masses. (D) The tumors of each side protruding into the internal auditory canals.

Magnetic resonance imaging (MRI) revealed a mass in each of the cerebellopontine angles with well-defined margins and a cyst in the middle of the right mass, which presented with abnormal isointense to hypointense signals (compared with gray matter) on T1-weighted images and heterogeneous hyperintense signals on T2-weighted images. The two internal auditory canals were enlarged due to mass extension. Contrast-enhanced MRI demonstrated a lack of blood supply to the two masses (Fig. 1). The main differential diagnoses included acoustic neuroma, meningioma, glioma or lower cranial nerve schwannoma, with acoustic neuroma as the most probable preliminary diagnosis according to the clinical symptoms, MRI appearance and enlarged internal auditory canals.

A craniotomy was performed via a suboccipital retrosigmoid approach, and a gross total resection was performed to remove the tumor on the right side. During the surgery, it was found that the tumor originated from the right cerebellopontine angle and extended to the internal auditory canal. The tumor was soft, fleshy and reddish-gray, with a big cyst inside. The blood supply was poor and no apparent calcification was apparent. Notably, the tumor was wrapped around the VII/VIII cranial nerve complex and all other lower cranial nerves. Histological examination verified a papillary ependymoma, classified as a World Health Organization grade II tumor (15). The tumor featured perivascular pseudorosettes and small foci of bleeding, necrosis, degeneration and pigment deposition (Fig. 2). Moreover, the tumor was positively stained with neuron-specific enolase,

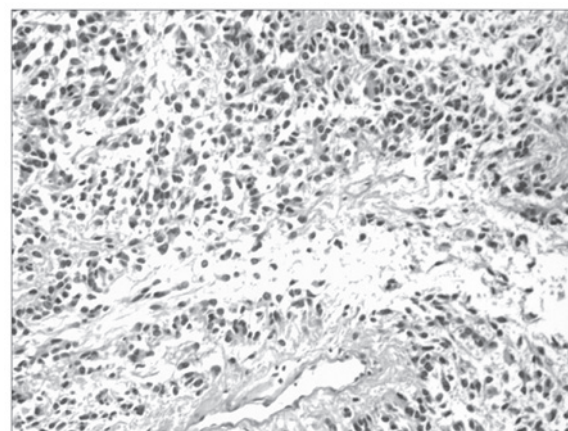


Figure 2. Histological section showing a cellular glial neoplasm with abundant perivascular pseudorosettes characteristic of ependymoma (hematoxylin and eosin staining; magnification, x100).

synaptophysin, cluster of differentiation (CD)99, glial fibrillary acidic protein, S-100, chromogranin A, CD56 and Ki-67, with a few cells with hyperchromatic nuclei.

The surgery was successful and the follow up MRI confirmed that the tumor on the right side had been completely resected (Fig. 3A). Following the surgery, the patient began to gradually recover in the period prior to adjuvant chemotherapy and radiation treatment. However, during this period, the patient started



Figure 3. (A) Post-operative magnetic resonance (MR) image showing no residual tumor in the right cerebellopontine angle (T2-weighted). Full spinal cord MR images showing (B) T3-T4 and (C) S5-L2 tumor metastasis.



Figure 4. Follow-up magnetic resonance images showing no increase in the size of the tumor in (A) the left cerebellopontine angle, and at (B) T3-T4 and (C) S5-L2.

to complain of urine retention, which had not been present prior to the surgery. This was initially considered to be due to irritation by the urinary catheter and prostate hypertrophy. As spinal metastasis is one of the features of papillary ependymoma, full spinal cord MRI was performed and massive occupational lesions were found at T3-T4 and L5-S2 (Fig. 3B and C). It was speculated that these spinal tumors were of ependymomal origin, but a histological examination was not performed since the patient refused to undergo a biopsy procedure. Combination therapy using single dose temozolomide chemotherapy (4 cycles of 150 mg/m² administered for 5 days in a 28-day therapeutic) and radiation therapy (3,600 cGy whole-brain and spinal cord radiation treatment administered in 20 fractions over 28 days, and 1,620 cGy focal irradiation administered in 9 fractions over 13 days at the surgical incision site) was selected to control tumor growth. A slight shrinkage of the T3 lesion was observed, and no progression of the left cerebellopontine angle and S5-L2 lesions were identified on follow-up MRI performed 13 months later (Fig. 4).

Discussion

Ependymomas are relatively rare, with an incidence of ~0.2 per 100,000 person-years. Men and Caucasians are more susceptible to ependymomas compared with women and other

ethnicities (16). Particularly, subtentorial ependymomas typically arise in the fourth ventricle from the roof, floor, lateral medullary velum or its lateral recesses, and the majority of the tumors appear in young children (1). Through the foramina of Luschka and lateral Magendie, ependymomas may extend into the cerebellopontine angle or subarachnoid space (17). Typical MRI features of ependymomas are hypointense to isointense on T1-weighted images and hyperintense on T2-weighted images, with irregular enhancement and marked heterogeneity due to hemorrhage, calcification, necrosis or cystic components (18).

To date, radical resection is the widely accepted therapy for ependymoma (19). Adjuvant radiotherapy and chemotherapy have been used post-operatively to prevent tumor recurrence. Chemotherapy has also been used to decrease the tumor size prior to surgery and reduce the radiotherapy dosage post-surgery. However, the potential for adjuvant radiotherapy to improve the prognosis of a patient with ependymoma remains under debate (19-21).

The prognosis of patients with ependymomas depends on various factors, including tumor grade, therapeutic regimes, extent of resection, Ki-67 index, gene type, location, age and gender. Among them, radical removal of the tumor is the most significant prognostic factor (22). The prognosis of adults is significantly better than that of children, with a 5-year-survival-rate of 55-90% compared with 14-60% (23).

For ependymoma, metastasis is relatively common for the anaplastic type, subtentorial tumors and young patients (24,25). In addition, surgery can potentially cause tumor dissemination (26). Therefore, it is important to avoid tumor dissemination and spillage during surgery in cases of suspected ependymoma in order to avoid CSF metastasis and recurrences. Moreover, full spinal cord MRI is necessary for ependymomas, particularly subtentorial ependymomas, as the tumor cells may migrate to other places through the CSF.

In the present case, bilateral primary posterior fossa ependymomas that originated from the cerebellopontine angles with local invasion to the fourth ventricle and the internal auditory canals, and with remote metastasis to the spinal cord were reported in a 50-year-old male. This was an extremely rare case of adult ependymoma with the following features: i) Cerebellopontine angle origin; ii) wrapping of the VII/VIII cranial nerve complex; and iii) extension into the internal auditory canals, with remote metastasis to the spinal cord. These features could easily lead doctors to form a diagnosis of neurofibromatosis type II acoustic neuroma. The present case clearly suggests that ependymoma should be considered as a differential diagnosis among the cerebellopontine angle tumors. Another notable fact is that the patient complained of a new symptom of urine retention shortly after surgery, which was found to be caused by massive occupational lesions in T3-T4 and L5-S2. Although a biopsy examination could not be performed, it was highly speculated that these lesions were metastases from the ependymoma in the brain. Apparently, these metastasized lesions were unlikely due to surgical dissemination in this case, as it is impossible to develop such large metastasized lesions within a short period of two weeks (the time prior to performing follow-up MRI).

To the best of our knowledge, this is the first reported case of bilateral primary posterior fossa ependymomas originating from the cerebellopontine angle and extending to the internal auditory canals, with spinal cord metastasis. Although primary cerebellopontine angle ependymoma is extremely rare and difficult to diagnosis, pre-operative suspicion of ependymoma is important for surgical planning, given its more malignant nature and poorer prognosis compared with acoustic neuroma. The present study also suggests that full spinal cord MRI is extremely important to rule out spinal cord metastasis in ependymoma patients.

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