

Primitive neuroectodermal tumour metastases mimicking neurofibromatosis type 2

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ABSTRACT

Bilateral vestibular schwannomas are the diagnostic features of neurofibromatosis type 2 (NF-2), and are the most common findings associated with the disorder. We report a three-year-old boy who presented with left facial nerve palsy and weight loss with bilateral large cerebellopontine (CP) angle masses that extended into the internal auditory canal on magnetic resonance imaging. The patient also had synchronous tumours in the lateral ventricle and intradural extramedullary spinal canal. The above findings were misinterpreted as NF-2 with bilateral vestibular schwannomas, ventricular meningioma and spinal schwannomas/meningiomas. However, a histological examination of the spinal masses revealed a primitive neuroectodermal tumour. Although bilateral CP angle masses are characteristic of NF-2, the possibility of diffuse craniospinal malignancy should be considered in a very young child who presents with weight loss and extensive tumours.

Keywords: cerebellopontine angle, magnetic resonance imaging, metastases, neurofibromatosis

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INTRODUCTION

Bilateral vestibular schwannomas are the classic features of neurofibromatosis type 2 (NF-2). However, it is important to bear in mind the differential diagnosis of diffuse craniospinal metastases if the clinical features do not correlate with the neurological imaging findings. We present a case that serves to illustrate this point.

CASE REPORT

A three-year-old Chinese boy complained of left facial weakness for three days. He was unable to close his left eye completely and had a drooping of the corner of his

mouth. He also complained of a left facial “hotness” sensation and pain in his left ear for one week; however, he did not suffer from hearing loss. On examination, the patient was fretful but afebrile, and had lost 4 kg over the previous week. Neurological examination of the patient confirmed left lower motor neuron VII nerve palsy. He had a supple neck, normal reflexes, normal extra-ocular eye movements and normal power in all limbs. Otoscopy was limited bilaterally by earwax. There were no cutaneous signs of phacomatosis, such as café-au-lait spots, axillary freckling or adenoma sebaceum, nor were there any bony deformities in the patient. Contrast-enhanced magnetic resonance (MR) imaging of the posterior fossa/internal auditory canal was performed. MR imaging showed well-circumscribed homogeneously enhancing nodular masses in the cerebellopontine (CP) angles bilaterally which extended into the internal auditory canals (Fig. 1a). A smaller, well-circumscribed enhancing mass was partly observed in the trigone of the right lateral ventricle, as the study did not cover the brain completely.

The patient was treated conservatively using oral dexamethasone and analgesic for pain. He continued to be highly symptomatic with severe uncontrollable pain in spite of the administration of multiple analgesics and intravenous morphine. The patient was highly incapacitated and was unable to sleep or take feeds orally. He subsequently complained of pain in the lower limbs as well as his mastoid area, although no deficits were observed on neurological examination. MR imaging of the brain and the full spine of the patient was performed the following day, which showed multiple enhancing intradural extramedullary masses in the spinal canal (Fig. 1b). The right intraventricular lesion (Fig. 1c) was well appreciated. No lesions were identified in the brain parenchyma. The working diagnosis of NF-2 with bilateral CP angle schwannomas, right lateral ventricular meningioma and multiple spinal schwannomas/meningiomas was made.

The patient continued to be symptomatic, with pain that worsened despite having been administered multiple analgesics. He underwent laminectomy at

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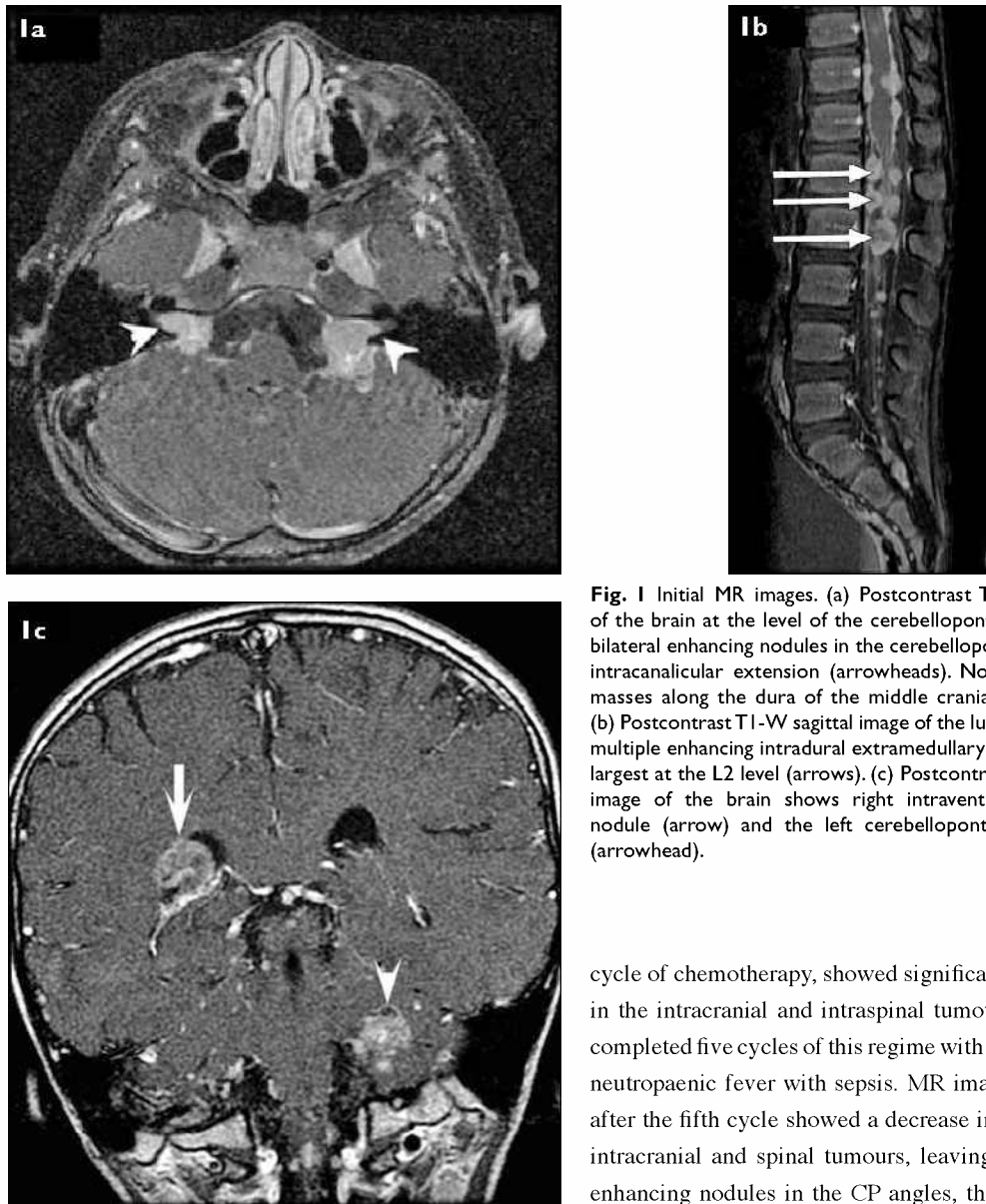


Fig. 1 Initial MR images. (a) Postcontrast T1-W axial image of the brain at the level of the cerebellopontine angles shows bilateral enhancing nodules in the cerebellopontine angles with intracanalicular extension (arrowheads). Note the enhancing masses along the dura of the middle cranial fossae medially. (b) Postcontrast T1-W sagittal image of the lumbar spine shows multiple enhancing intradural extramedullary nodules, with the largest at the L2 level (arrows). (c) Postcontrast T1-W coronal image of the brain shows right intraventricular enhancing nodule (arrow) and the left cerebellopontine angle nodule (arrowhead).

the L2 and L3 vertebrae with excisional biopsy of the masses at these levels. A histological examination of the excised spinal masses revealed a primitive neuroectodermal tumour (PNET) (Fig. 2). The patient was treated with chemotherapy (five courses of New York University [NYU] 87-12 Head Start II Protocol). The regime consisted of induction with intravenous cisplatin, vincristine, etoposide and cyclophosphamide with mesna. This was then followed by high-dose intravenous methotrexate with leucovorin rescue. Subcutaneous granulocyte colony-stimulating factor (G-CSF) was administered 24 hours after the completion of methotrexate infusion and was continued until neutrophil recovery. This cycle was repeated every three to four weeks for five cycles. MR imaging of the patient's brain and spine, which was done after one

cycle of chemotherapy, showed significant improvement in the intracranial and intraspinal tumours. The patient completed five cycles of this regime with four episodes of neutropaenic fever with sepsis. MR imaging conducted after the fifth cycle showed a decrease in the size of the intracranial and spinal tumours, leaving residual small enhancing nodules in the CP angles, the trigone of the right lateral ventricle, the anterior spinal canal at L1 and on the spinal cord leptomeninges (Fig. 3a & b). He was pain-free and asymptomatic after treatment.

Unfortunately, six months after the completion of therapy, the patient developed signs of ataxia and irritability, and his MR imaging showed the recurrence of a large tumour in the right CP angle (Fig. 4a) and a new enhancing nodule in the thoracic cord at C7/T1 (Fig. 4b). After discussing the poor prognosis in view of tumour recurrence after a full course of chemotherapy and radiotherapy, the patient's parents opted for palliative management. The patient subsequently deteriorated, was unable to walk and eat, and was then placed on palliative treatment. He passed away three months later.

DISCUSSION

Phakomatoses are congenital malformations, mainly affecting the structures of ectodermal origin,

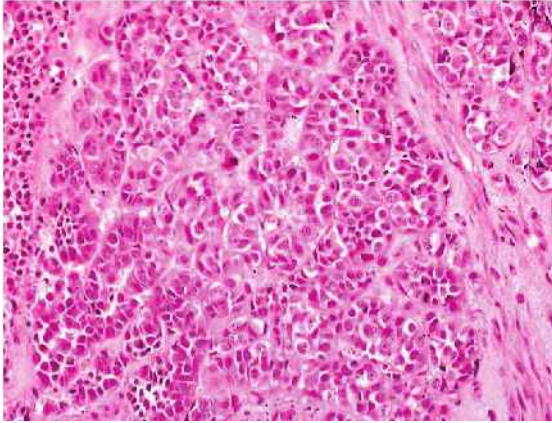


Fig. 2 Photomicrograph shows a central primitive neuroectodermal tumour featuring nests of primitive tumour cells (Haematoxylin & eosin, $\times 200$).

which typically manifest as lesions in the skin and nervous system. Neurofibromatosis is the most common phakomatosis,⁽¹⁾ comprising the classical neurofibromatosis type 1 (NF-1), also called Von Recklinghausen's disease, and the less common type 2 (NF-2). Cutaneous manifestations are common in NF-1, and the nervous system findings include neurofibromas, plexiform neurofibromas, optic gliomas, non-optic gliomas (usually low-grade astrocytomas) and hamartomas in the brain and spinal cord.⁽²⁾

On the other hand, bilateral vestibular schwannomas are the most common findings in NF-2 and are considered its main diagnostic feature. The other associated lesions are neurofibroma, meningioma, glioma or juvenile posterior subcapsular lens opacity.⁽³⁾ Café-au-lait spots may occur in NF-2, but not as frequently as in NF-1. Since cutaneous manifestations are much less common in NF-2, NF-2 patients are often older than patients with NF-1 at the time of diagnosis, with facial nerve palsy and seizures being the usual presenting symptoms in children with NF-2.

In NF-2, the diagnostic vestibular schwannomas have the characteristic appearance of typical schwannomas, including location at the CP angles, intracanalicular extension and widening of the internal auditory canal. A vestibular schwannoma typically appears as a pear-shaped mass centred in the internal auditory canal on MR imaging. Smaller lesions of up to 1.5 cm in size can appear as tubular intracanalicular masses without extension into the CP angle cistern. Medium-sized tumours of up to 3.0 cm in size may resemble an ice-cream cone, with the ice-cream being the CP angle component and the cone being the internal auditory canal component. Occasionally, some tumours can be located entirely in the CP angle cisterns.⁽⁴⁾ The internal



Fig. 3 MR imaging at six months post chemotherapy. (a) Postcontrast T1-W axial image of the brain shows a partial response of the tumour to chemotherapy, with a reduction in the size of the cerebellopontine angle lesions bilaterally (arrows). (b) Postcontrast T1-W sagittal image of the lumbar spine also shows the regression of most spinal nodules with residual enhancing nodules at the L1 and L2 levels (arrow), and linear "sugar-coating" of the spinal cord from subarachnoid tumour deposits (arrowheads).

auditory canal may be eroded or enlarged due to tumour expansion. On MR imaging, the typical appearance of a schwannoma is iso- to hypointense on T1-weighted and iso- to hyperintense on T2-weighted images, and has a strong but heterogenous contrast enhancement. The heterogeneity of these tumours is secondary to cystic degeneration and haemorrhage, which are the common features of these tumours. Intracranial meningiomas, which are often multiple, are also common in NF-2.⁽⁵⁾ Hence, in our patient, the bilateral CP angle tumours with intracanalicular extension were misinterpreted as

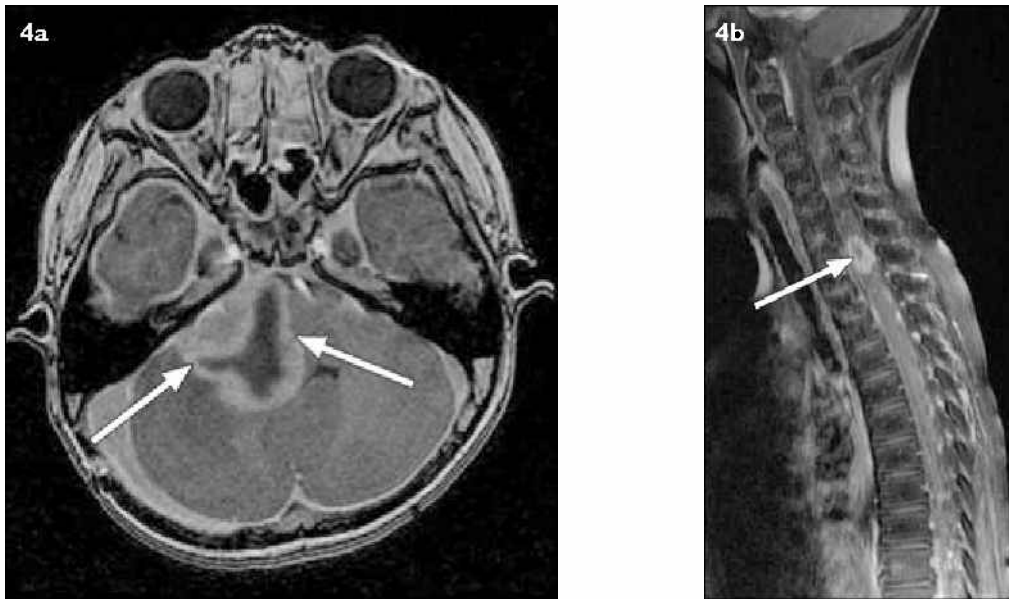


Fig. 4 Follow-up MR imaging at six months after the completion of therapy. (a) Postcontrast T1-W axial image of the brain shows a large recurrent necrotic mass in the right cerebellopontine angle (arrows). (b) Postcontrast T1-W sagittal image of the cervical spine shows a new enhancing nodule in the cervicothoracic cord (arrow).

vestibular schwannomas, and the ventricular mass was misinterpreted as a meningioma as part of the NF-2 syndrome.

Intraspinal tumours are not uncommon in patients with NF-2; they typically comprise multiple intradural extramedullary schwannomas or meningiomas.⁽⁶⁾ Schwannomas are usually hyperintense relative to the spinal cord on T2-weighted images and show avid contrast enhancement, while meningiomas are typically isointense relative to the spinal cord on all sequences and also enhance strongly following gadolinium administration. Schwannomas and meningiomas are typically intradural extramedullary tumours that form discrete nodules on the existing spinal nerve roots and nerve root sheaths. Although many spinal meningiomas have a broad dural attachment that is similar to their intracranial counterparts, the typical dural tail sign for intracranial meningioma is less frequently detected in spinal meningiomas, and it is difficult to distinguish between these two tumours preoperatively.⁽⁷⁾ Therefore, the finding of multiple intradural extramedullary discrete tumour masses on MR imaging in our patient was thought to be consistent with our primary diagnosis of NF-2.

PNETs, on the other hand, are highly cellular malignant tumours with presumed neural crest origin, which predominantly affect children below five years of age. The term “primitive” is derived due to the presence of more than 90%–95% of undifferentiated cells with few focal areas of differentiation along

neuronal and glial lines.⁽⁸⁾ The commonest type of PNET is medulloblastoma, which is sometimes considered to be an infratentorial PNET and is termed PNET-MB. Supratentorial PNETs are rare and make up less than 5% of all paediatric supratentorial tumours.⁽⁹⁾ Although they show histological similarities to medulloblastoma, they are generally considered to be more aggressive in behaviour.⁽¹⁰⁾ They frequently occur in the deep white matter, and necrosis, haemorrhage, cysts and calcification are seen in more than half of the cases of supratentorial PNET. This gives a heterogeneous appearance on imaging, with mild to moderate contrast enhancement. Intraventricular PNET has also been rarely described. In children, the differential diagnosis of an intraventricular tumour should include PNET, teratoma, choroid plexus papilloma and choroid plexus carcinoma. On MR imaging, PNET signal characteristics approximate the appearance of choroid plexus papilloma, but typically, PNET shows more avid enhancement on postcontrast imaging.⁽¹¹⁾

Similar to medulloblastoma, supratentorial PNET often spreads through the cerebrospinal fluid (CSF) and metastases to the craniospinal leptomeninges.⁽¹²⁾ Distant metastases of PNET to the liver, lungs and bones have also been reported. Intracranial metastases to the subarachnoid space may involve multiple or bilateral cranial nerves and usually present as nodular or linear enhancing leptomeningeal lesions. Leptomeningeal metastases (or carcinomatosis) to the spinal canal typically result in diffuse enhancement of the

leptomeninges of the spinal cord and is generally termed a “sugar-coating” or “zuckerguss” (German for sugar icing) appearance. Nodular enhancement of the spinal cord surface or nerve roots, clumped nerve roots and diffuse enhancement of the thecal sac are also common findings in leptomeningeal spread.⁽¹³⁾ Other primary brain tumours affecting children and those that can cause craniospinal leptomeningeal metastasis include medulloblastoma, astrocytoma, pineal germinoma and choroid plexus carcinoma. In adults, glioblastoma multiforme, anaplastic astrocytomas and extensive metastatic disease outside the brain from melanoma, breast or lung cancer, acute lymphoblastic leukaemia and lymphoma can all cause spinal metastasis. These conditions were unfortunately not considered in this patient, as the intraspinal tumours were labelled schwannomas/meningiomas to fit the presumptive diagnosis of NF-2.

In this patient, there were many imaging features that appeared to be consistent with NF-2, but there were also some subtle clues that were not typical of NF-2. Most cases of NF-2 with bilateral vestibular schwannomas present with progressive hearing loss, tinnitus and ataxia in the second to third decade of life, and hence, the very young age of our patient was unusual for NF-2, especially in the absence of any family history. The youngest diagnosed case of NF-2 described in the literature is a 21-month-old child, who had characteristic ophthalmic and skin lesions, but no intracranial lesions on MR imaging.⁽¹⁴⁾ The loss of weight, although nonspecific, should also have alerted the physicians to a sinister malignant cause, as should the appearance of spinal lesions in such a young patient. On the other hand, the imaging features were not entirely characteristic of PNET either. Since the commonest type and location of PNET in the infratentorial compartment is medulloblastoma in the fourth ventricle, the imaging findings of large CP angle tumours with a bilateral symmetrical appearance and a third synchronous intraventricular lesion are not typical of supratentorial PNET or medulloblastoma. Although it may be argued that the homogenous signal intensity and enhancement was more consistent with PNET than schwannoma, this was not appreciated at the time.

In conclusion, although bilateral CP angle masses are typically diagnostic of NF-2, and ventricular

meningiomas and intraspinal nodular tumours may be present, these would be very unusual in a very young child who presents with significant weight loss. Hence, diffuse craniospinal metastatic malignancy, especially the atypical presentation of PNET, should be considered in the differential diagnosis.

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