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Case Report

Primary Intracranial Malignant Nerve Sheath Tumor in the Cerebellopontine Angle in a Woman with Neurofibromatosis Type 2

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Abstract

Neurofibromatosis type 2 is an inherited disease. The main manifestation of the disease is the development of symmetric, non-malignant brain tumors in the region of the cranial nerve VIII usually as schwannoma. We report here a 20-year-old woman with primary intracranial malignant nerve sheath tumor located in the left cerebellopontine angle. Histologically, the tumor showed malignant spindle cells in fascicular pattern with focal S100 positivity on immunohistochemistry. A subtotal surgical resection was performed followed by adjuvant radiotherapy. This is the first case of primary intracranial malignant nerve sheath tumor associated with neurofibromatosis type 2 reported in the literature. The prognosis of this potentially aggressive neoplasm is poor.

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Keywords ● Neurofibromatosis 2 ● malignant nerve sheath tumor ● cerebellopontine angle

Introduction

Neurofibromatosis type 2 or multiple inherited schwannomas, meningiomas, and ependymomas (MISME syndrome) is an inherited autosomal dominant syndrome characterized by multiple vestibulocochlear (cranial nerve VIII) schwannoma, meningiomas, and ependymomas.[1] Primary intracranial malignant nerve sheath tumors are extremely rare.[2-5] Few documented cases were reported in the literature in the setting of neurofibromatosis type 1 (von Recklinghausen's disease).[6,7] A high degree of invasiveness and tendency to recur are common features in all cases. The efficacy of adjuvant radiotherapy and chemotherapy has not been proven.[7] Here we report the first case of primary intracranial malignant nerve sheath tumor in the cerebellopontine angle associated with neurofibromatosis type 2.

Case Report

A 20-year-old woman, who was a known case of neurofibromatosis type 2, was admitted to the neurosurgery ward with left sided hearing loss, facial palsy, and dizziness. Her family history was not significant.

Magnetic resonance imaging (MRI) of the brain showed two large enhancing masses (figures 1,2). One of them was larger and located at the left cerebellopontine angle with extension into the base of the left 7^{th}-8^{th} nerve root complex. The other

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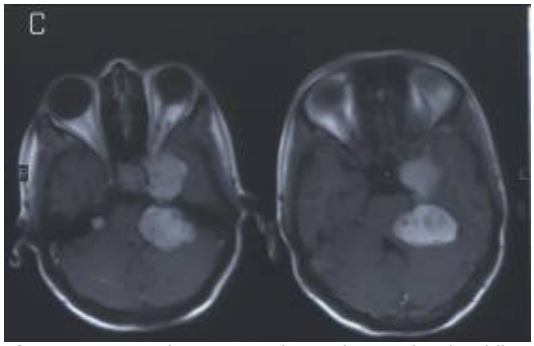

Figure 1: Coronal contrast-enhanced MRI showing bilateral cerebellopontine angel masses. Heterogeneous and more peripherally enhanced one is in the left side.

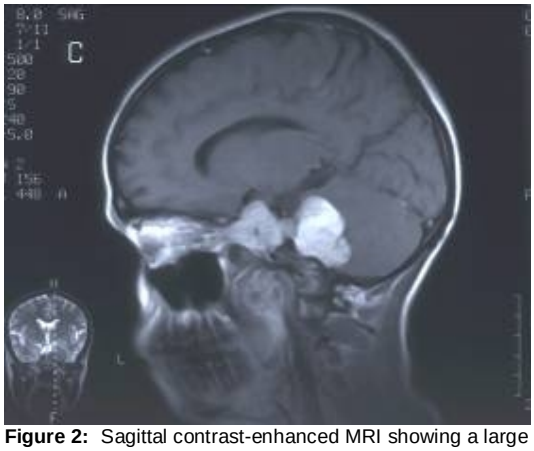

Figure 2: Sagittal contrast-enhanced MRI showing a large mass at left cerebellopontine angle.

one was at right cerebellopontine angle. There were also multiple enhancing masses within dural tail in parietal, frontal, and occipital area of the brain suggestive of multiple meningiomas (figure 1).

On physical examination, no stigmata of von-Recklinghausen's disease were noted. These findings were sufficient for the diagnosis of neurofibromatosis type 2, according to the National Institutes of Health, Manchester, or National Neurofibromatosis Foundation diagnostic criteria.[8]

However, the possibility of multiple metastatic lesions from an extracranial lesion should be considered. The results of para-clinical tests such as chest radiography, mammography, and gastric endoscopy were normal.

The mass was incompletely resected. Microscopically, the tumor was moderately to highly cellular, consisting mainly of spindle cells in interlacing and intertwining fascicles of varying sizes. No Antoni A or B areas or Verocay bodies were present (figure 3). The tumor was entirely solid without any cystic areas. Individual cells had a spindle shape with tapering edges and eosinophilic cytoplasm. Moderate pleomorphism was noted and the mitotic activity was variable, with up to 2-3 mitoses per 10 high-power fields. No rhabdomyoblastic differentiation was present. Immunohistochemistry showed focal immunoreactivity for S-100 and diffused staining for vimentin in the spindle cells (figure 4). Stains for epithelial membrane antigen, glial fibrillary acidic protein (GFAP), synaptophysin and cytokeratin were negative in the tumor cells. On the Basis of these findings, the tumor was diagnosed as a primary intracranial malignant nerve sheath tumor.[9] Clinically, the left-sided hearing loss and left facial paresis were still noted. The patient received a course of cranial radiotherapy. Unfortunately, her clinical condition was deteriorated, caused by local recurrence of the tumor that was confirmed by a new MRI. The patient died within 5 months after surgery.

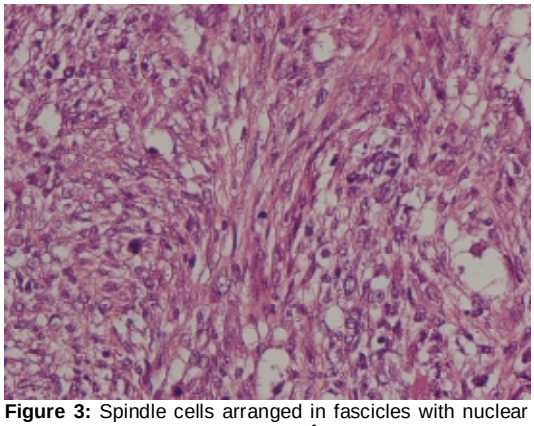

Figure 3: Spindle cells arranged in fascicles with nuclear atypia and mitosis. (H&E staining Í 400)

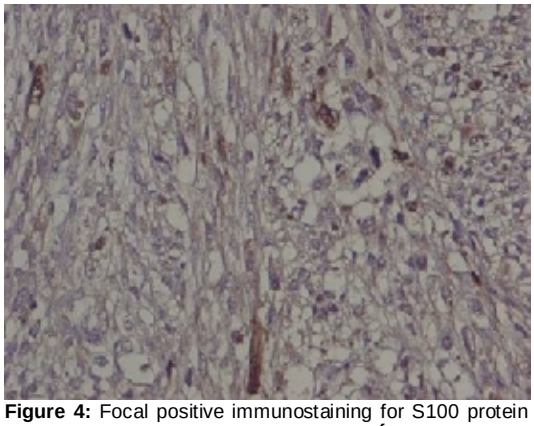

Figure 4: Focal positive immunostaining for S100 protein in malignant cells. (Avidin-Biotin complex Í 400)

Discussion

Neurofibromatosis type 2 or central neurofibromatosis is inherited in an autosomal dominant mode with high penetrance. From neurological point of view, the disease is more devoting than neurofibromatosis type 1. The classic

features of neurofibromatosis type 2 include bilateral 8th nerve schwannoma, as well as multiple ependymoma and meningioma.[9,10]

Schwannomas are benign neoplasms arising from the peripheral nerve sheath cells. They account for about 8% of all primary brain tumors.[11] 80-90% of all intracranial schwannomas arise from the vestibular component of the vestibulocochlear nerve.[11] Malignant peripheral nerve sheath tumors, which comprise 5% to 10% of all soft tissue sarcomas, often arise from neurofibromas in the setting of neurofibromatosis type 1.[4] However, few cases of primary intracranial malignant nerve sheath tumors have been reported in the literature.[5,12-14] Among those cases, the occurrence with neurofibromatosis type 1 is exceptional.[3,11] Intracranial nerve sheath tumors characteristically occur in relation to cranial nerves, most commonly the 8th cranial nerve, in the cerebellopontine angle.[12] It is difficult to make an accurate diagnosis with routine histological study. The main differential diagnoses of these tumors in this area include malignant meningioma and gliomas with mesenchymal differentiation.[4,14] Immunohistochemical analysis is useful to distinguish malignant nerve sheath tumors from other lesions.[9]

Few cases of intracranial neuraxial nerve sheath tumors, which were histologically malignant, have been reported in the literature.[3-5,9,11,14] The prognosis of primary intracranial malignant nerve sheath tumor seems to be equally poor. All but two of these patients had postoperative tumor recurrences despite complete surgical resections, which were performed in all documented cases.[3-5,9,11,14] Two patients, 4- and 8-year-old girls, were recurrence-free for 17 and 19 months after surgery, respectively.[3,14] For three patients with a primary intracranial malignant nerve sheath tumor, the time of first recurrence clearly predicted the survival: the earlier first recurrence, the worse overall survival.[9,11,14] Despite adjuvant radiotherapy and/or chemotherapy, the tumor recurred 5 and 10 months after surgery in the first and second patients and the patients died 9 and 18 months after the initial diagnosis, respectively.[11,14] One patient,[9] had a third and final recurrence 5 years after the first surgery; the last resection was incomplete because of deep tumor invasion. Hence, it is apparent that the prognosis of primary intracranial malignant nerve sheath tumor seems to be equally poor and the intrinsic biological behavior of the tumor is quite variable.

A few aspects of our observations that differ from previously reported cases are noteworthy. This is the first case report in a patient who is suspected for neurofibromatosis type 2. Our patient was older than previously reported patients, who were very young. The location of the tumor was uncommon: it was located infratentorial and involved the cerebellopontine angel region. All but one of the previous lesions were supratentorial.

It is still unknown whether survival is influenced by tumor location, size, and grade. A high degree of invasiveness and a tendency to recur have been common features in all of the patients like our case.[3-5,9,11,14] The 5-year survival rate in malignant spinal schwannomas ranges between only 23% for patients without neurofibromatosis and 0% for patients with neurofibromatosis.[7,15] Accurate histologic diagnosis and a well-planned, extensive surgical resection with adjuvant therapy appear to be the key elements in the management of these tumors. However, it is still unknown whether survival is influenced by this approach. In our patient, treatment was unsuccessful.

Conflict of Interest: None declared

References

1 Goutagny S, Bouccara D, Bozorg-Grayeli A, et al. Neurofibromatosis type 2. *Rev Neurol (Paris)* 2007; 163: 765-77

2 Akimoto J, Ito H, Kudo M. Primary intracranial malignant schwannoma of trigeminal nerve. A case report with review of the literature. *Acta Neurochir (Wien)* 2000; 142: 591-5.

3 Singh RV, Suys S, Campbell DA, Broome JC. Malignant schwannoma of the cerebellum: Case report. *Surg Neurol* 1993; 39: 128-32.

4 Tanaka M, Shibui S, Nomura K, et al. Malignant intracerebral nerve sheath tumour with intratumoral calcification: Case report. *J Neurosurg* 2000; 92: 38-41.

5 Yamashiro S, Nagahiro S, Mimata C, et al. Malignant trigeminal schwannoma associated with xeroderma pigmentosum.case report. *Neurol Med Chir (Tokyo)* 1994; 34: 817-20.

6 Best PV. Malignant triton tumour in the cerebellopontine angle. Report of a case. *Acta Neuropathol* 1987; 74: 92-6.

7 De Cauwer H, Bogers JP, Duwel V, et al. An intracerebral intraparenchymatous triton tumor in a man with neurofibromatosis. *J Neurol* 2007; 254: 1009-11.

8 Baser ME, Friedman JM, Wallace AJ, et al. Evaluation of clinical diagnostic criteria for neurofibromatosis 2. *Neurology* 2002; 59: 1759-65.

9 Bruner JM, Humphreys JH, Armstrong DL. Immunocytochemistry of recurring intracerebral nerve sheath tumor. *J Neuropathol Exp Neurol* 1984; 43: 296
10 Fisher LM, Doherty JK, Lev MH, Slattery WH 3rd. Distribution of nonvestibular cranial nerve schwannomas in neurofibromatosis 2. *Otol Neurotol* 2007; 28: 1083-90.
11 Stefanko SZ, Vuzevski VD, Maas AIR, van Vroonhoven CCJ. Intracerebral malignant schwannoma. *Acta Neuropathol (Berl)* 1986; 71: 321-5.
12 Comey CH, McLaughlin MR, Jho HD, et al. Death from a malignant cerebellopontine angle triton tumor despite stereotactic radiosurgery. Case report. *J Neurosurg* 1998; 89: 653-8.
13 Horie Y, Akagi S, Taguchi K, et al. Malignant schwannoma arising in the intracranial trigeminal nerve. A report of an autopsy case and a review of the literature. *Acta Pathol Jpn* 1990; 40: 219-25.
14 Sharma S, Abbott RI, Zagzag D. Malignant intracerebral nerve sheath tumor: a case report and review of the literature. *Cancer* 1998; 82: 545-52.
15 Hanemann CO. Magic but treatable? Tumours due to loss of merlin. *Brain*. 2008; 131: 606-15.