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Vestibular Schwannoma with Malignant Transformation : A Case Report

We describe a rare case of malignant transformation in a vestibular schwannoma in a 33-yr-old woman. She presented herself with headache, tinnitus, and hearing loss and underwent posterior fossa explorations three times during the short period of 3 months. The clinicopathological features of the original tumor were typical of benign vestibular schwannoma. Despite a comlpete microsurgical excision, two months later, the tumor recurred locally with a rapid increase in size causing a progressive worsening of neurological symptoms. A diagnosis of malignant schwannoma was made for the recurrent tumor on the basis of the microscopic findings of high cellularity, moderate pleomorphism, and the presence of mitotic cells. Repeat magnetic resonance imaging performed a month after the second surgery unexpectedly showed definite tumor enlargement. She remained clinically stable following the third debulking of the tumor and adjuvant radiotherapy. We propose that this recurrent tumor represent malignant transformation from a benign vestibular schwannoma which was an unusual occurrence in a patient without neurofibromatosis.

Key Words : *Neuroma, Acoustic; Tumor Recurrence; Neurilemmoma*

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INTRODUCTION

The vestibular schwannoma (VS) is essentially a benign disease and its malignant transformation is to be exceptional. In this regard, malignant recurrence after surgery of VS is a very rare event and there has been only one report on malignant transformation of VS (1). Here we report a case of VS malignantly transformed 2 months after microsurgical resection.

CASE REPORT

History and Examination

A 33-yr-old woman presented with intermittent severe headache. She had a one-year history of vertigo and documented recent aggravations of gait disturbance and hearing difficulty. On admission, neurological examination was significant for nystagmus, diplopia, ataxic gait, and sensorineural hearing loss (pure tone average 65 dB, speech discrimination score 40%) in her left ear. There were neither stigmata of neurofibromatosis nor history of exposure to irradiation. Initial magnetic resonance image (MRI) demonstrated a well-enhancing large mass, measuring 3×4 cm, in the left cerebellopontine angle with an enlarged porus acousticus interna (Fig. 1A). Left external carotid artery angiography showed a moderately intense tumor blush which was supplied by meningeal vessels. The clinical diagnosis of VS was made.

Surgical Procedures and Postoperative Course

A left suboccipital retrosigmoid-transmeatal approach revealed a large well-marginated, relatively hypervascular mass at cerebellopontine angle extending into the internal auditory meatus and surrounding the eighth cranial nerve. The facial nerve was attenuated and adherent to the tumor capsule anteriorly. The lower cranial nerves and brain stem were distorted. The tumor was macroscopically totally resected with the porus acousticus being explored in the intracanicular portion. No visible residual enhancing tumor was present on postoperative computerized tomography. The patient quickly recovered after the surgery and was discharged with mild facial weakness and left-ear deafness. However, two months after the surgery, progressive facial numbness and weakness, headache, dizziness, and right-sided hemiparesis were noted. A huge recurrent tumor at original site was discovered in a follow-up MRI (Fig. 1B) which was again completely removed through the same route of the first operation. The mass was well-circumscribed with varying consistency without invasion to adjacent structures. At this point,

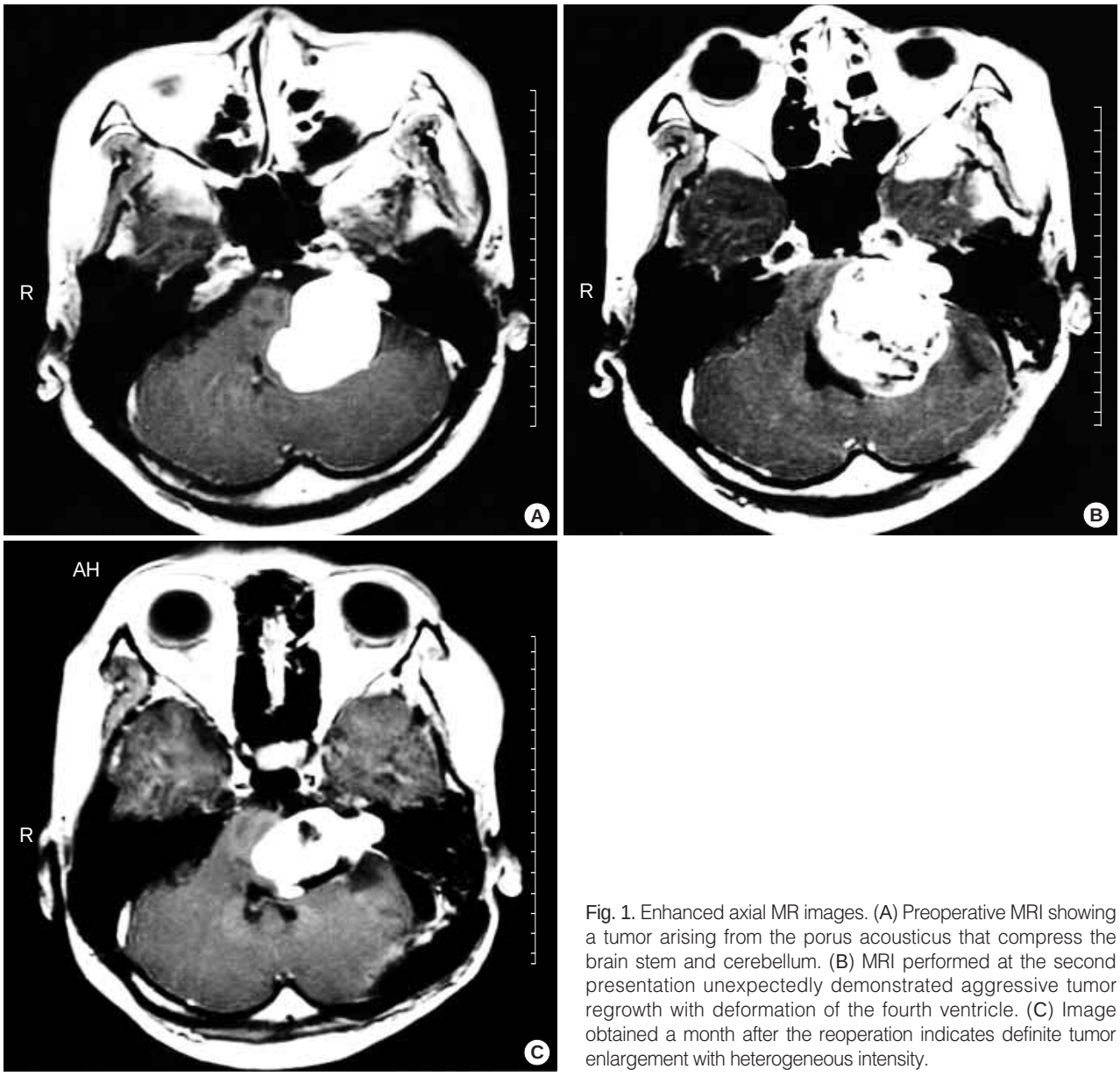

Fig. 1. Enhanced axial MR images. (A) Preoperative MRI showing a tumor arising from the porus acousticus that compress the brain stem and cerebellum. (B) MRI performed at the second presentation unexpectedly demonstrated aggressive tumor regrowth with deformation of the fourth ventricle. (C) Image obtained a month after the reoperation indicates definite tumor enlargement with heterogeneous intensity.

we considered a possible malignant transformation of schwannoma and recommended cranial irradiation as an adjuvant therapy, but she refused further treatment. A month after the reexploration, a MRI examination revealed further progression of the disease (Fig. 1C) that caused clinical deterioration. Without further workup for metastasis, a third microsurgery and adjuvant fractionated radiotherapy were performed. Postoperative subcutaneous cerebrospinal fluid leakage and suboccipital soft-tissue bulging were successfully treated with lumbar drainage. Thereafter, the patient has been clinically stable for one year until this writing without any evidence for recurrence on serial MRI.

Pathological Findings

The surgical specimens obtained at the first resection consisted of multiple pieces of pale to yellow-tan, homogeneous, soft tissue and measured $2.5 \times 2.2 \times 0.9$ cm in aggregates. Microscopic finding demonstrated a tumor predominantly composed of spindle cells that are arranged in interlacing fascicles admixed with more loose textured cells (Fig. 2A). Multiple sections failed to show any evidences of malignant features and immunostaining for S-100 protein was strongly and uniformly positive in the spindle cells (Fig. 2B). On the basis of these findings, the histopathological diagnosis of a benign VS was made. At the first recurrence, the fea-

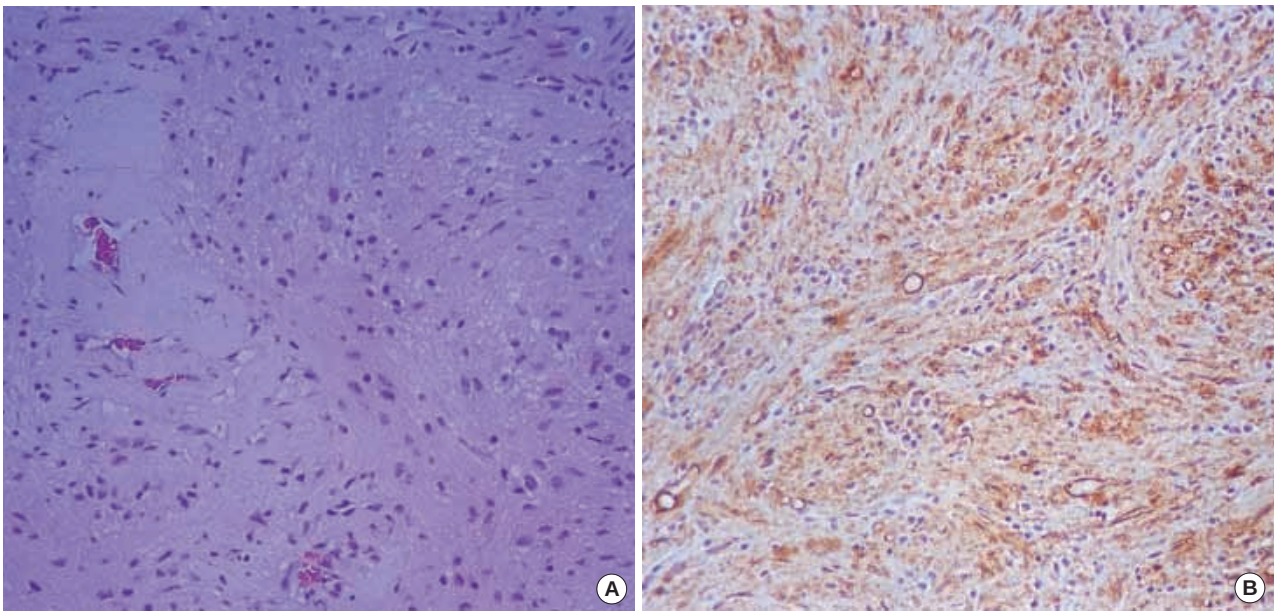

Fig. 2. Neuropathology (H&E) (A) and immunohistochemistry (B) of the initial neoplasm display diffuse proliferation of spindle-shaped Schwann cells which are strongly immunoreactive for S-100 protein. Some hyalinized blood vessels within the hypocellular myxoid areas are also noted ($\times$200).

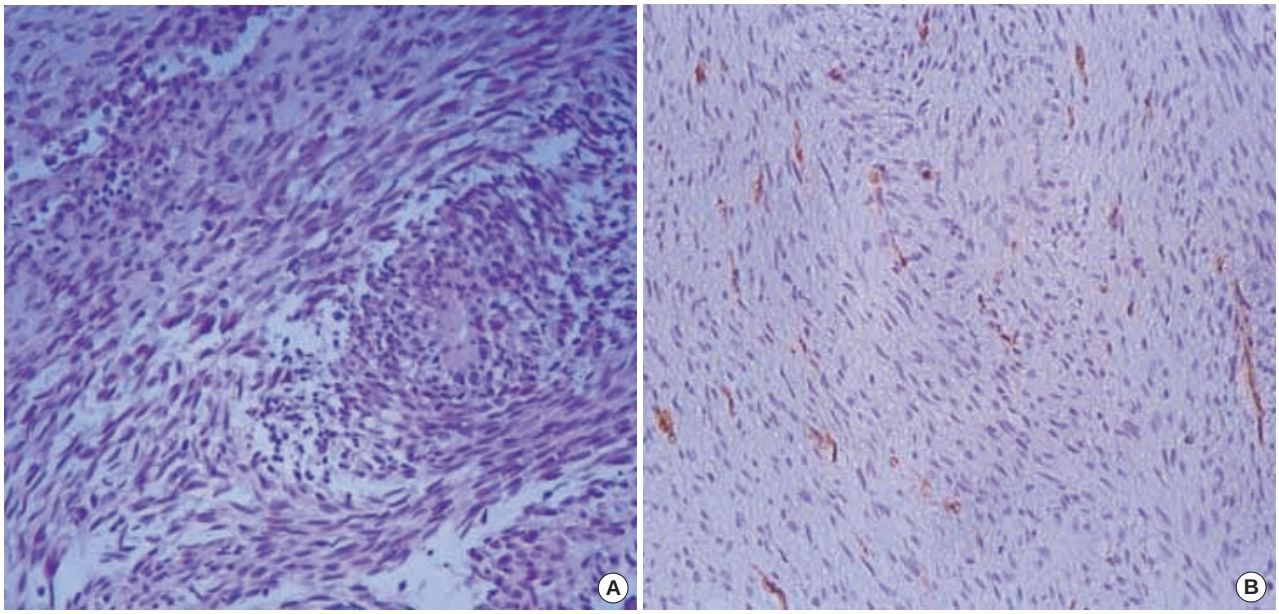

Fig. 3. Photomicrographs of the first recurrent tumor. (A) This view shows a fascicular arrangement of atypical spindle cells with hyperchromatic nuclei and frequent mitoses and increased cellularity compared with the original tumor (H&E, $\times$200). (B) Immunostaining reveals focal positivity of the tumor cells with anti-S-100 protein antibody (H&E, $\times$200).

tures of the tumor was quite different from those of the original mass and were compatible with low-grade malignant schwannoma. Gross examination of the second specimen revealed several irregular hard fragments of pale-tan tumor mass measuring 5.5 $\times$ 3.0 $\times$ 3.0 cm in aggregates. The recurrent tumor was characterized by extreme hypercellularity, moderately pleomorphic spindle cells with hyperchromatic nuclei, and frequent mitoses (Fig. 3A). There were 2-3 mitotic figures per 10 high-power fields at the active hypercellular area of recurrent tumor. No focus of hemorrhage or necrosis was present. Immunohistochemical findings of the recurrent tumor demonstrated scattered MIB-1-positive cells with 3%

proliferation index and intranuclear deposits of p53 protein suggesting the tumor recurrence. The second recurrent tumor showed the similar features both in the histologic composition and immunohistochemical result: the first recurrent tumor had weakly and focally positive immunoreactivity for S-100 protein (Fig. 3B). The third specimen looked white, firm fibrous tumor and measured $4.5 \times 3.0 \times 1.0$ cm in aggregates. We did not measure specimen weight.

DISCUSSION

Malignant cranial nerve schwannomas are rare and occur most commonly in the trigeminal nerve (2, 3). In recent reviews, approximately five cases of malignant tumors arising in the eighth cranial nerve has been reported (1, 4-6), of which four were malignant triton tumors which consisted of distinct schwannian and rhabdomyoblastic cell components and were first described by Kudo et al. (7). The remaining one case (1) was malignant vestibular nerve tumor of pure schwannian origin. Those tumors were usually larger than classic benign VS on presentation. In spite of adjuvant combination therapy, all malignant VS including the malignant triton tumors exhibit aggressive biological behavior marked by multiple local recurrence, frequent neuroaxis dissemination and need for reoperation. They usually present in a fashion typical of more common benign VS, but have distinguishable clinical features by multiple cranial nerve palsy due to the tumor progression. Regardless of complete surgical removal, the reported cases of malignant VS showed marked regrowth after a mean interval of 5 months. The patient described here also showed trigeminal and facial nerve dysfunctions at the second admission with malignant recurrence. For the management of patients with malignant VS, total resection is preferred to reduce the possibility of recurrence and prompt radiotherapy or radiosurgery is needed for the control of any residual tumor (5, 8). Unfortunately, however, no long-term survival has been previously reported. For the five reported cases of malignant vestibular schwannoma, treatment in every case consisted of a surgical excision preceded or followed in only one instance by radiation therapy. Four of those patients with recurrent tumor underwent reoperations and resulted in fatal clinical course postoperatively. Two cases demonstrated drop metastasis at tumor recurrence. The mean survival in the those five patients dying with disease was 11 months. We successfully performed operations three times and anticipate that she will survive longer than previously reported cases. On the basis of the previous studies, we would only resort to the option of stereotactic radiosurgery for any tumor progression on the follow-up MRI.

Malignant schwannomas are rarely derived from a preexisting benign solitary schwannoma except for the cases in association with neurofibromatosis type 1 (9). Postradiation sarcomatous change is well known but, schwannomas rarely undergo spontaneous malignant transformation. Woodruff et al. (10) described only nine cases of spontaneous malignant transformation in all parts of the body. In this series, two cases showed malignant transformed schwannomas one and 2 months after the first operation, respectively. Akimoto et al. (2) also reported the malignant recurrence of the intracranial trigeminal nerve schwannoma 4 months later initial resection. In rare cases (8, 9, 11), VS displayed rapid growth, but its malignant transformation following microsurgery is very unusual and thus hardly expected. In McLean's report (1) of the first case of malignant transformed VS after removal, the patient developed a recurrence 11 months postsurgery and the histology revealed malignant features. But the histopathologic findings of the original tumor was not enough to definitely convince the benign nature because of its increased cellularity and mitoses, albeit in a small focus. In present case, one might suggest that the original tumor did harbor a malignant component which was not removed at the first surgery, although the clinicopathological findings are certainly consistent with rapid malignant progression of a schwannoma. But we fulfill grossly complete resection of the tumor at the first surgery and confirmed total excision on the postoperative imagings. Although an alternative explanation that the initial tumor had both benign and malignant components, and that due to with incomplete resection, the malignant component rapidly recurred was also considered, retrospective careful examinations of the slides of the original tumor showed no presence of any foci of malignant schwanoma. Therefore the possibilities of intratumoral heterogeneity and insufficient tissue due to sampling errors of the first surgical specimen could be in the discard. Han et al. (6) reported a case of VS transformed into a malignant schwannoma with rhabdomyosarcomatous differentiation 10 months after near-total removal of the original tumor. Although the histogenesis of such change remains uncertain, some physicians have suggested the possibility of a dedifferentiating potential for malignant Schwann cells in schwannomas (1, 8-11). Furthermore, the postoperative irradiation or surgical trauma may exacerbate the malignant progression in the partially removed cases, such as malignant progression of cerebral astrocytic tumors (9). Difficulties in establishing the pathogenesis of malignant nerve-sheath tumors include the extreme rarity of such tumors arising from a previously benign schwannoma and the presence cells other than Schwann cells that give rise to a malignant tumor (1).

In microscopic examination of benign VS, varying degree of cellular polymorphism is acceptable, but mitotic figures are mostly infrequent (4, 9, 10, 12). For the histological diagnosis of a malignancy, some insisted on the requirements of increased cellularity, atypical mitoses, poor cellular differentiation, high mitotic rate, and/or extensive invasion in a previously unoperated field. Alternatively, the use of cell prolif-

eration markers might be useful. Yokoyama et al. (11), and Tanabe et al. (8), mentioned that VS with high MIB-1 staining index greater than 2% showed rapid growth, had a higher tendency to recur, and suggested the usefulness of this index for the management planning of VS. In our case, MIB-1 index was 3% and 2% in the specimens at first and second recurrence, respectively. Intranuclear deposits of the p53 protein is demonstrated in the majority of malignant schwannomas and this expression indicates mutation in the *TP53* tumor suppressor gene (9). Analysis of the reported cases of malignant schwannoma or benign schwannoma with malignant transformation of the cranial nerves did not demonstrated the molecular evidence of biological malignancy or genetic mutation of the recurrent tumor. In our case, neither electron microscopy nor immunohistochemical stainings for desmin, myosin, vimentin, or myoglobin was carried out because the surgical specimens showed uniform histologic features and did not contain any heterogeneous cellular components such as rhabdomyoblasts on the microscopic findings. Immunohistochemically, the schwannian origin of nerve sheath tumors can be confirmed by their positive staining for S-100 protein, but the immunostaining results for the malignant Schwann cells are variable and often negative (7, 9). Thus, it is possible to consider that the S-100 protein expression could reflect the degree of Schwann cells. Malignant schwannomas, at times, reveal a progressive anaplasia, although the tumors remained encapsulated (9), but in our case, there was no significant pathological differences between the tumors at first and second recurrence. The cellular schwannoma which makes up about 10% of schwannomas has a higher than usual recurrence rate, especially if they occur in the cerebellopontine angle. But It is composed entirely of well differentiated Schwann cell and is well stained by S-100 protein. The cellular variant is not malignant (9, 10, 12). To differentiate low and high-grade malignant schwannomas from a cellular schwannoma, the required mitotic count varies from a rare or isolated mitosis to mitoses numbering more than 5 per 10 high-power fields. In present case, the microscopic findings of the initial tumor specimen are certainly that of a typical schwannoma, with hyalinized vessels and S-100 immunoreactive schwannoma cells. The histologic features of the recurrent tumor are that of a hypercellular, proliferative spindle cell tumor, best termed malignant peripheral nerve sheath tumor.

In conclusion, our case might serve a rare example of malignant transformation of a typical VS following microsurgery. VS, essentially a benign tumor, appears to have a rare capacity to develop into malignant schwannoma. In this regard, we should take into account a potential risk of tumor progression, and malignant change in VS especially in a patient with a very short-term and repeated recurrence.

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