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Clinical report

Giant malignant peripheral nerve sheath tumors of the occipital scalp

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Background: Malignant peripheral nerve sheath tumors (MPNST) are rare neoplasms, usually arising from peripheral nerves or showing a nerve sheath differentiation. Primary MPNSTs of the scalp is exceptionally rare, and only sporadic cases have been reported recently.
Objectives: Report a rare case of giant malignant peripheral nerve sheath tumor (MPNST) beneath occipital scalp, and discuss how to treat with this kind of tumor.
Methods: Descriptive study of a rare case of giant peripheral nerve sheath tumors of occipital scalp without adjuvant treatment with nine months follow up.
Results: In a 52-year-old man with MPNSTs beneath occipital scalp, the tumor was treated with complete surgical resection. Histological examination proved that the lesion was a scalp MPNST. The patient was followed up asymptomatic for the following nine months after surgical resection without adjuvant radiotherapy.
Conclusion: MPNSTs beneath the occipital scalp should be treated individually, for those well-circumscribed MPNSTs without bone destruction or brain invasion (low-grade tumors), complete surgical resection with clear margins (if possible) is recommended. Otherwise, adjuvant postoperative radiotherapy is necessary.

Keywords: Malignant peripheral nerve sheath tumor, occipital scalp, S-100, surgical resection, radiotherapy

Malignant peripheral nerve sheath tumors (MPNSTs) are malignant tumors. They arise from a peripheral nerve or show a nerve sheath differentiation, with the exception of tumors originating from the epineurium or the peripheral nerve vasculature [1]. These tumors are treated as a subcategory of soft tissue sarcomas, in which they comprise three to ten percents of all such tumors [2]. MPNSTs are rare tumors with an incidence of approximately 0.001% in the general population [3]. Most of MPNSTs are located on trunk and extremities. The head and neck are unusual sites for their development [4].

Primary scalp MPNST is exceptionally rare, and only sporadic cases have been reported recently [1, 2, 4, 5]. In this report, we present a case of primary MPNST of the occipital scalp region.

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Case report

A 52-year-old man presented with a gradually increasing spongy mass beneath the occipital scalp since seven years ago. There was no associated infection, local pain, or trauma at this site. The mass was the size of a peanut at first and gradually increased. The patient underwent surgical resection twice, four and six years ago, respectively, when the mass was the size of an egg, and postoperative pathology indicated neurofibroma. After the last surgery, the mass recurred again and gradually increased in size for three years, and experienced a rapid growth over the recent six months. No associated symptoms of headache, dizziness, seizure, vomiting, hearing, or visual impairment were observed. There was no significant history related to neurofibromatosis.

Physical examination revealed a giant hemispherical, relatively spongy, well-margin, non-pulsatile, and painless mass that grossly measured 14x7cm in the occipital region, which was relatively removable to the underlying bone. There was no thrill

on palpation or bruit on auscultation. On general examination, there was no lymphadenopathy, subcutaneous nodule, or signs of neurofibromatosis. **Figure 1** shows magnetic resonance imaging (MRI) of the mass beneath the occipital scalp. We note that the mass was well confined beneath occipital scalp without bone destruction and brain invasion.

The patient underwent a third operation and the mass was resected completely. Reconstruction was made by inferior-based transposition flap, and the donor site was repaired by a full-thickness graft obtained from medial thigh. Since there was no bone destruction, brain invasion, or distant metastasis, no further craniectomy was required. The postoperative condition was uneventful, although an acute wound swelling was visible at the skin graft site. After appropriate hemostatics, dehydrants, antibiotics, and compressive dressings were managed, the incision was not tense and healed well without any leakage or infection. The patient was discharged seven days after operation, and has been followed up asymptomatically for the following nine months. There was no evidence of recurrence.

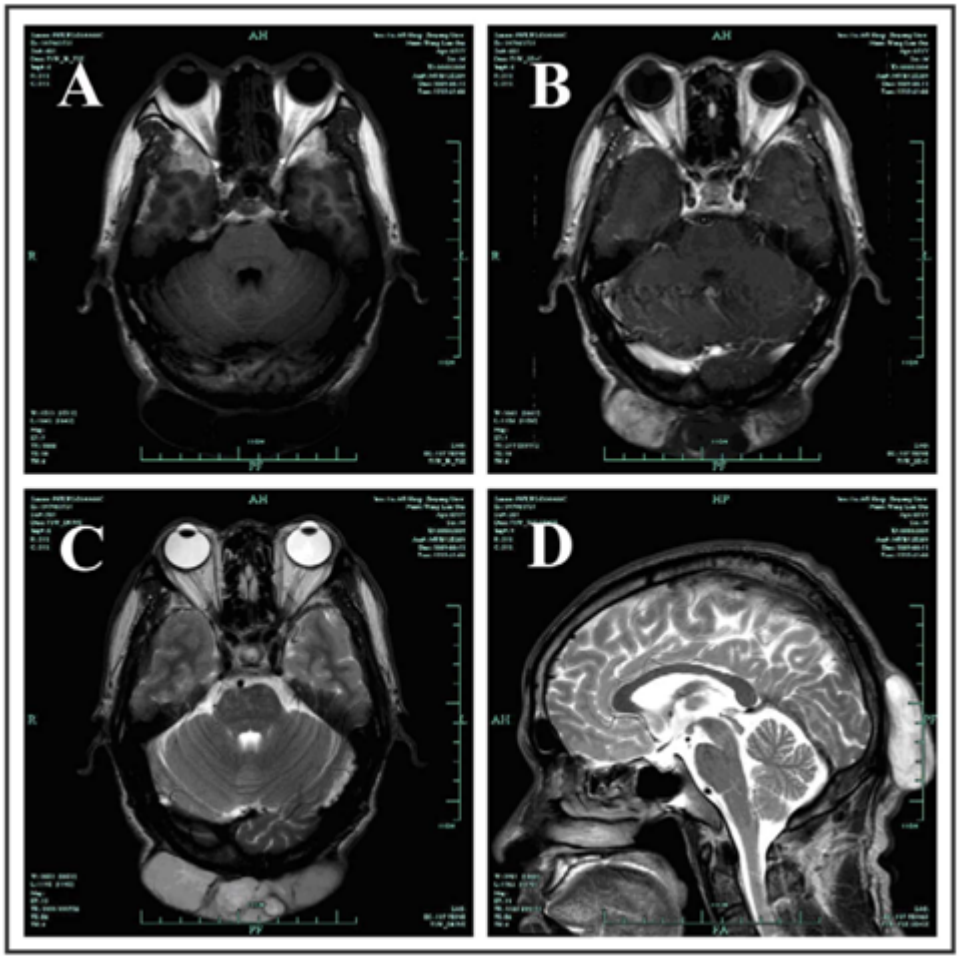

Figure 1. MRI showing that the mass is clear and multilocular measuring 11.1x6.7x2.4cm beneath the occipital scalp. **A:** Longitudinal relaxation time T1-weighted image showing the mass is hypointensity. **B:** The bilateral parts of the mass on the T1-weighted images are enhanced asymmetrically by gadolinium diethylenetriamine pentaacetic acid (Gd-DTPA), while central cystic part is not enhanced. **C** and **D:** axial and sagittal T2-weighted image showing the mass is high intensity, respectively.

Grossly, the specimen showed a grayish, relatively soft, giant hemispherical tissue, which seems to be encapsulated and measured 11 4.5 3cm. **Figure 2** shows microscopic images of tumor cells observed using H-E staining or immunohistochemical staining. We note that the tumor cells were pleomorphic obviously with oval, round, spindle to wavy nuclei in a fascicular pattern (**A**). Mitotic activity (50/10 high-power fields) and invasive growth were visible (**B**). Immunohistochemical testing showed scattered S-100 protein staining (**C)**, whereas cytokeratin (CK) (**D**), epithelial membrane antigen (EMA), glial fibrillary acidic protein (GFAP), CD34, Desmin and HMB45 were all negative. There was over expression of Ki-67 (mean 20%). Based on these findings, a diagnosis of an MPNST beneath the occipital scalp was made. Follow-up is ongoing regularly.

Discussion

MPNST is a rare malignant soft tissue tumor that may derive from components of nerve sheath such as perineural fibroblasts or Schwann cells [2, 6]. Many terminologies, such as malignant schwannoma, neurofibrosarcoma, malignant neurilemoma, and neurogenic sarcoma have been used to describe the entity. MPNSTs usually occur in the third to sixth decades of life, and the mean age of incidence of MPNST is 42 years [7]. Most of MPNSTs occur in the trunk and proximal limbs [4]. They typically affect the medium and large nerves (sciatic nerve, brachial plexus, and sacral plexus), as well as the mediastinum, retroperitoneum, and viscera [8, 9]. While primary scalp MPNSTs are extremely rare, only four cases have been reported since 2000 as shown in **Table 1** [1, 2, 4, 5].

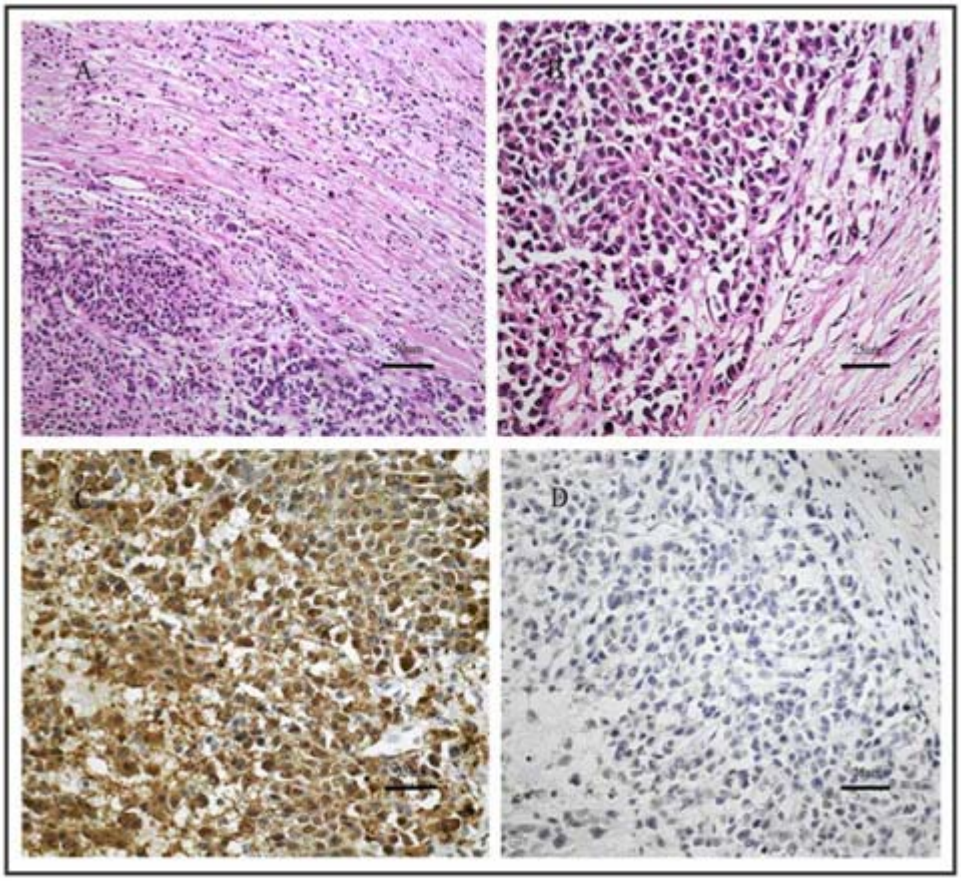

Figure 2. **A:** The tumor cells are pleomorphic obviously with oval, round, spindle to wavy nuclei in a fascicular pattern (H-E staining, original magnification x200). **B:** Mitotic activity (50/10/HPF) and invasive growth are visible (H-E staining, original magnification x400). **C:** S-100 protein is scattered positive (immunohistochemical staining, original magnification x400). **D:** CK, EMA, GFAP, CD34, Desmin and HMB45 are negative (immunohistochemical staining, original magnification, x400)

Table 1. Clinical features of MPNSTs beneath scalp reported between 2000 and 2010

Reference	Case age (year)/Sex	Tumor			History of NF	Meta stasis	Treatment	Follow-up
		Site	Size (cm)	Margin				
Kumar et al. [1]	36/ Male	Occipital	6 7	Well-circumscribed bone destruction and brain invasion	Yes >30 yrs	No	SR+RT	Asymptomatic (28 months)
Fukushima et al. [5]	38/ Male	Parieto-occipital	21 19 9	Well-circumscribed no bone destruction and brain Invasion	Yes >3 yrs	No	SR	Multiple Metastases and Died (4 months)
Garg et al. [2]	50/ Male	Occipital	21 17	Well-circumscribed bone destruction, new bone formation and brain invasion	Yes >8 yrs	No	SR+RT	Not mentioned
Demir et al. [4]	80/ Male	Parietal	1.5 2	Well-circumscribed no bone destruction and brain invasion	No >2 yrs	No	SR+RT	Asymptomatic (6 months)
Current case	5/ 52/ Male	Occipital	14 7	Well-circumscribed no bone destruction and brain invasion	Yes >7 yrs	No	SR	Asymptomatic (9 months)

NF=neurofibromatosis, SR=surgical resection, RT=radiotherapy

MPNSTs may arise *de novo* or from malignant transformation of neurofibroma [2]. About two-third of MPNSTs arise in association with benign neurofibroma. Nearly half of these tumors are genetically predisposed with neurofibromatosis-1 (NF-1) [10]. Conversely, malignant transformation of schwannoma is extremely rare [11, 12]. In cases where they are associated with neurofibroma, they usually describe a long history of a mass with a recent rapid enlargement, which always means malignant transformation occur [13]. Our patient had a gradually bigger mass for seven years. This shows rapid enlargement in last six months, and postoperative pathology by previous two surgical resections indicating neurofibroma. It is reasonable to deduce that a malignant transformation had occurred in the previous relatively benign neurofibroma.

The clinical presentation of MPNSTs beneath the occipital scalp is atypical except mass effect and sometime local inflammatory response, so that postoperative pathology seems to be crucial in diagnosis. The criteria for a pathologic diagnosis of MPNST include origin from a major nerve, the presence of Schwann cells, S-100 protein staining, coexisting neurofibromatosis, and nuclear palisading. Grossly, the tumor is well circumscribed. The cut surface is multilocular, grayish to whitish in color, with some scattered myxoid, cystic, or necrotic areas [14]. Microscopically, the tumor contains different degree of cellularity, mitosis, and necrosis. They characteristically show a fascicular pattern, oval to spindle-shaped nuclei, and scant cytoplasm [1].

Immunohistochemical studies play a decisive role in diagnosis. Among several immunohistochemical markers, S-100 and Ki-67 attract our attention. S-100 protein, a calcium-binding protein present in Schawann cells, stains two-third of MPNSTs [2]. Its expression may be related to the predominantly neoplastic cells in MPNSTs for their diverse differentiation [15]. Ki-67 expression figures prominently in differentiating between the diagnosis of benign peripheral nerve sheath tumor (BPNST) and MPNST, but it does not seem to correspond with the histological grade [5, 16]. Overall, MPNSTs could be classified as low-grade, intermediate-grade and high-grade based on these mentioned characteristics above [17]. However, up to now, definite criteria for MPNSTs classification remain unclear, and treatment strategy is still controversial [18]. Our case showed scattered S-100 positive with over-expression of Ki-67 (mean 20%), based on the gross and microscopic features. The most possible diagnosis of the present case should be low-grade MPNSTs.

The optimum treatment strategy for MPNSTs remains unclear. According to the recommendation by the International Consensus Group [19], current management of MPNSTs should be identical to that of any other soft tissue tumors. Angelov et al. [20] reported that disease-free survival and overall survival of MPNSTs were approximately 64 and 30% at five years, respectively. Compared with 72 to 78% reported in the soft tissue sarcomas, the MPNSTs subgroup has a relatively worse prognosis than soft tissue sarcoma. The prognosis of MPNSTs in the head and neck region seems to be poorer than that on trunk and extremities [21, 22]. Since MPNSTs behave in an aggressive fashion, and carry a poorer prognosis than other soft tissue sarcomas, the optimum treatment strategy towards MPNSTs should be described specifically based on clinical, histological, IHC, and molecular results.

Surgical resection (SR) is the first treatment strategy under various situations, while adjuvant postoperative radiotherapy (RT) was involved in Kumar et al. [1] and Garg et al. [2] (see **Table 1**). In fact, Kumar et al. [1] get a satisfactory follow-up and postoperative RT proved to be effective in local recurrence control. Since positive tumor margins are determined as the most important prognostic marker by the previous study [20], Demir et al. [4] did a second complete resection with safe margins and gave postoperative RT to the patient with an inadequate excision before. They also had a good follow-up. For the patient with multiple metastases and died after SR described by Fukushima et al. [5], the giant, ulcerated, hemorrhagic tumor and patient's clinical presentation indicated that it was a MPNST in the advanced stage and, SR may be just a palliative treatment. We only adopted SR for the present case of scalp MPNST, by considering the following factors: a) the tumor was well-circumscribed without bone destruction or brain invasion; b) the tumor margin was negative; c) the histological features and IHC stain results revealed that this case might be a low-grade MPNST. No adjuvant RT was performed and the patient was asymptomatic in the following nine months after surgery. It indicated that not all MPNSTs beneath the occipital scalp should be treated with SR and RT. Some could achieve a satisfactory prognosis just with SR treatment alone.

Many articles [1, 2, 4, 17, 18] have reported satisfactory results in primary, recurrent or metastatic MPNSTs by adapting SR and RT treatment strategy, and the benefits of adjuvant postoperative RT are approved by most authors. However, we should not neglect some adverse reports about RT. Ducatman et al. [22] made a clinicopathologic study of 120 cases and concluded that the prognosis of MPNSTs seems to be related with location, size, presence of NF-1 and extent of tumor resection. However, mitotic rate, adjuvant radiation, or chemotherapy did not correlate with survival time. In addition, there were cases described with malignant transformation after radiotherapy [23, 24]. Shin et al. [23] found a TP53 mutation in a recurrent schwannoma after Gamma Knife surgery, which did not exist in the original tumor. Therefore, there may be a correlation between radiotherapy and malignant transformation.

In conclusion, MPNSTs beneath the occipital scalp are extremely rare and have a poor prognosis. They should be treated individually, for those well-circumscribed MPNSTs without bone destruction or brain invasion (low-grade tumors), complete surgical resection with clear margins, if possible, is recommended. Otherwise, adjuvant postoperative radiotherapy is necessary. Because of short clinical follow-up and inadequate cases, a meaningful relationship between clinical behavior, histological grade, IHC, and treatment strategy is not possible.

The authors have no conflict of interest to report.

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