A Case of Occipital Malignant Peripheral Nerve Sheath Tumor with Neurofibromatosis Type 1

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Introduction: The prognosis of malignant peripheral nerve sheath tumor (MPNST) with neurofibromatosis type 1 (NF-1) is worse than that of a solitary MPNST, because of the tumor size and location difficult to resect completely. We experienced a case of MPNST in the occipital region with NF-1.
Case report: A 59-year-old woman presented with NF-1 and an MPNST of the occipital region. We performed wide excision involving the occipital bone, and reconstructed with a titanium plate and a free latissimus dorsi muscle flap. Despite three operations and postoperative radiotherapy, the tumor locally recurred after each surgery; further complicated by lung and mediastinal metastasis. Adjuvant therapy was insufficient to control local recurrence, which was observed intracranially, resulting in sagittal sinus invasion. Thirty months after the initial surgery, the patient died of respiratory failure due to lung metastasis.
Conclusion: MPNST with NF-1 has poorer prognosis than that of a solitary lesion. Recently, it is reported in several literature that combination therapy with surgery and radiotherapy improve survival rates. But as we presented, when the complete local resection with free margin could not achieved due to the size and anatomical location of the tumor, the effectiveness of radiotherapy is not sufficient to control local recurrence.

Key words: malignant peripheral nerve sheath tumor, neurofibromatosis type 1, occipital, local recurrence, radiotherapy

INTRODUCTION

The incidence of von Recklinghausen disease (neurofibromatosis type 1, NF-1) with malignant peripheral nerve sheath tumors (MPNSTs) is reportedly 2%–29% [1–3], and the prognosis remains poor because of the high rate of local recurrence and distant metastasis [2–4]. Here, we present the case of MPNST arising in the occipital region of a patient with von Recklinghausen disease.

CASE REPORT

A 59-year-old woman visited our outpatient clinic because of a mass that had been growing on her occipital region for 3 years. She was diagnosed as neurofibromatosis type 1 (NF-1) because of a history of multiple neurofibromas occurring over her entire body from her teenage. A physical examination revealed a protruding tumor in the occipital region that was 75 mm in diameter (Fig. 1). Computed tomography demonstrated that the tumor was hypodense with an enhanced margin that invaded the cranium and caused thinning (Fig. 2). Total tumor excision was performed with a minimal surgical margin. The mass was a yellow, solid, globular tumor, 70 mm in diameter, and the cut surface was yellowish-brown. Microscopically, the tumor showed diffuse proliferation of atypical spindle-shaped cells arranged in fascicular or interlacing patterns with myxoedematous stroma (Fig. 3a). Tumor cells possessed enlarged, ovoid-shaped nuclei with occasional prominent nucleoli (Fig. 3b). Four mitotic figures were identified per 10 high-power fields. Tumor cells infiltrated between adipose tissues. Immunohistochemical staining showed that the tumor cells were negative for S-100 (Fig. 3c). Ki-67 (MIB1) labeling index was approximately 20% (Fig. 3d). The pathological diagnosis was MPNST.

Considering the diagnosis of MPNST, we performed additional excision, which included the cranial bone. We resected the tumor with a lateral surgical margin width of 20 mm and the occipital bone beneath the tumor. The defect was reconstructed with titanium mesh and a free latissimus dorsi muscle flap of the left (Fig. 4, 5). Neither postoperative radiotherapy nor chemotherapy were performed.

Eleven months after initial surgery, a tumor was noticed protruding from the right peripheral margin of the latissimus dorsi flap. Computed tomography demonstrated a dense soft-tissue mass, 30 mm in diameter, which had infiltrated the cortical bone underlying the mass. Therefore, we performed additional excision of the tumor along with that of the affected bone. The defect was covered with an artificial dermis graft, and after granulation, a split-thickness skin graft was performed.

Histologically, local recurrence of MPNST was diagnosed. Eight months after the second surgery, local recurrence occurred again. This time, the tumor extended into the intracranial space. We performed a wide excision around the tumor and cranial bone, and

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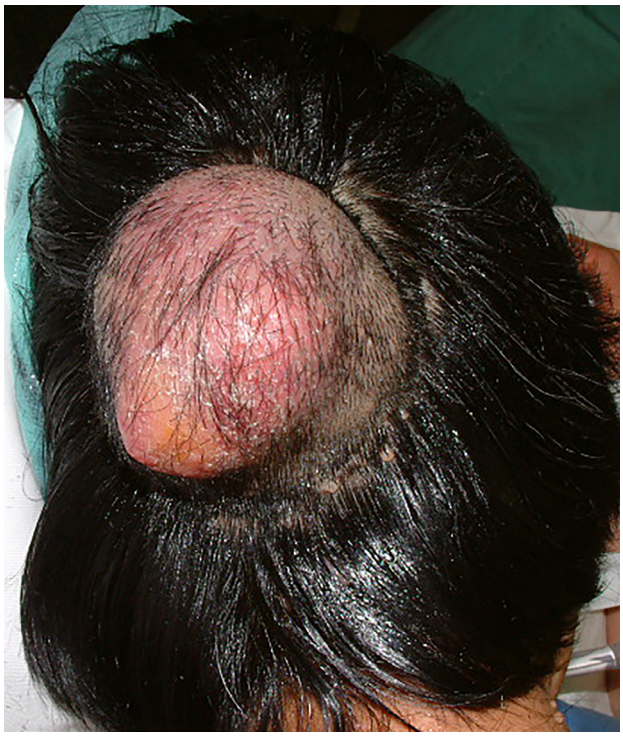

Fig. 1 Photograph at the excisional biopsy. There is a protruding tumor in the occipital region, 75 mm in diameter.

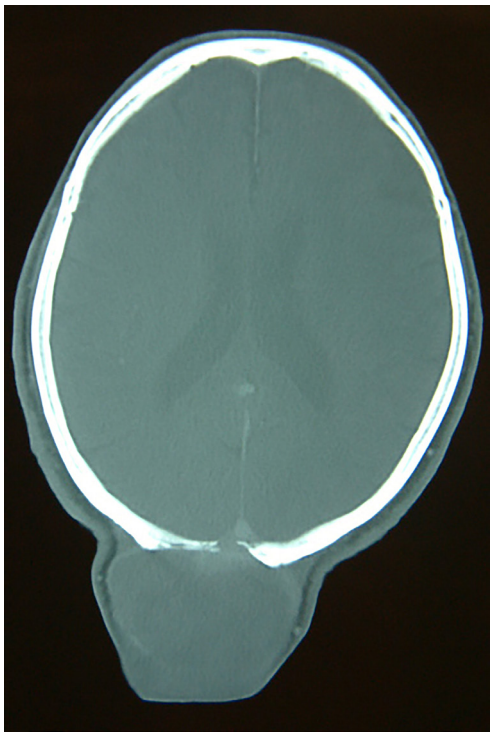

Fig. 2 Computed tomography scan of the head showing a tumor in the occipital region; hypodense and invaded the cranium and caused thinning.

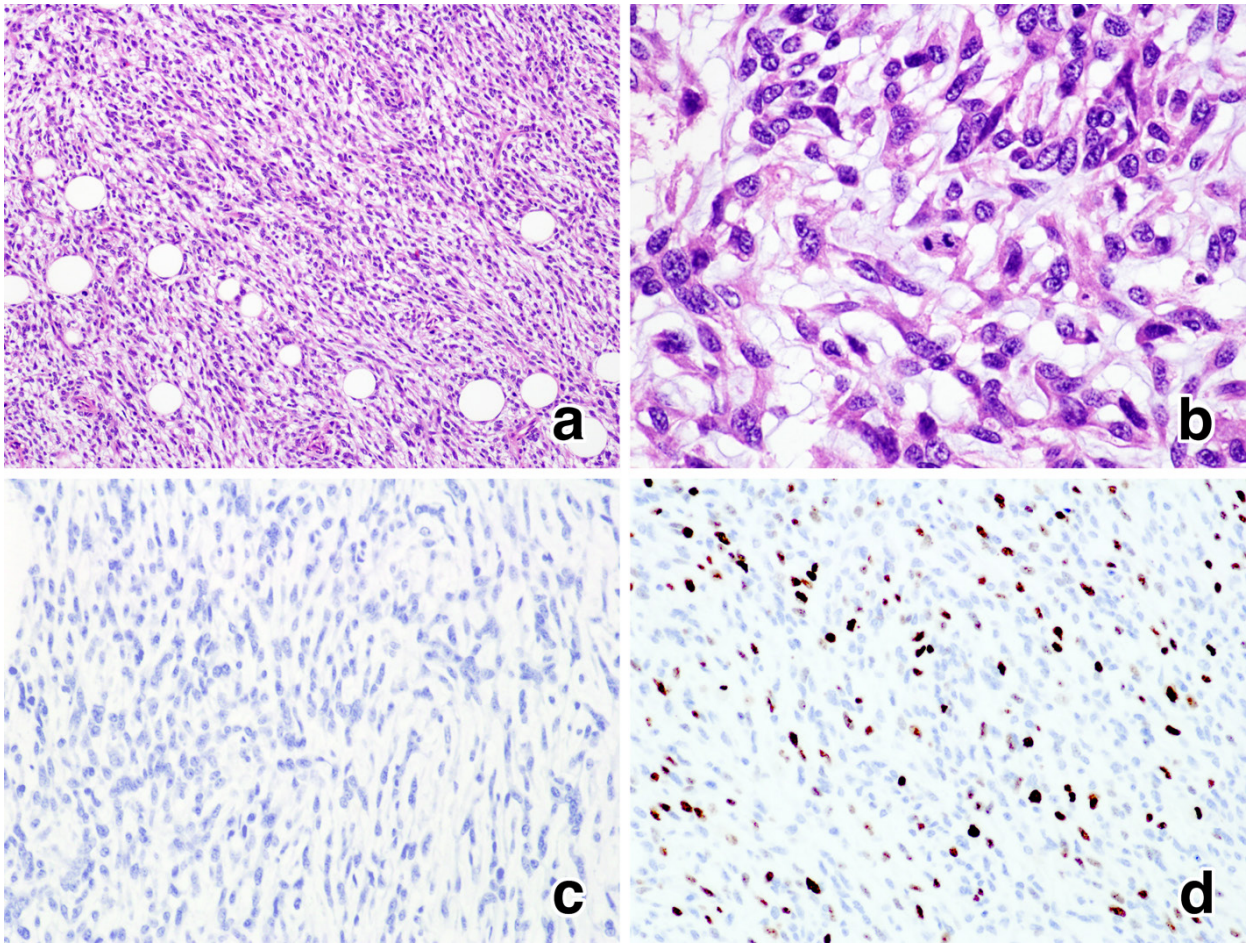

Fig. 3 Microscopic findings and the results of immunohistochemistry. (a) The tumor shows proliferation of atypical spindle-shaped cells arranged in fascicular or interlacing patterns (low-power view, H&E stain). (b) Tumor cells possessed enlarged, ovoid-shaped nuclei with occasional prominent nucleoli (high-power view, H&E stain). (c) Tumor cells are negative for S-100. (d) Ki-67 (MIB1) labeling index is approximately 20%.

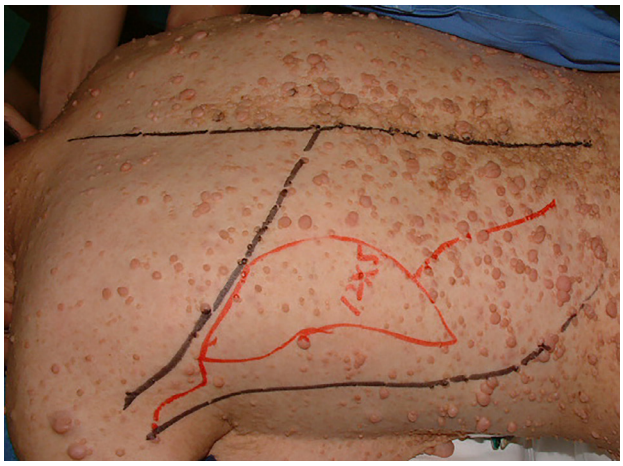

Fig. 4 Photograph at the initial surgery. A free latissimus dorsi muscle flap is designed.

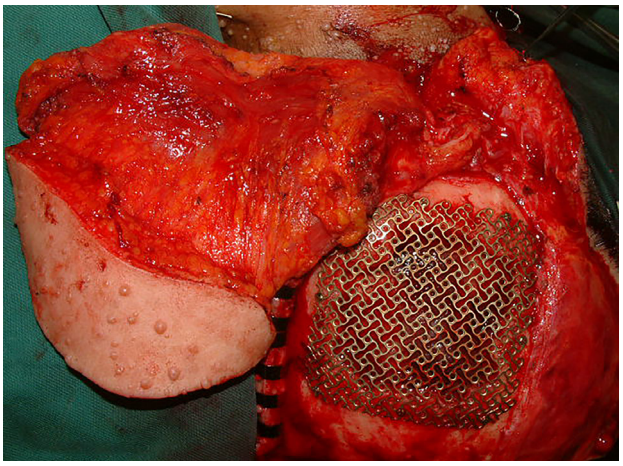

Fig.5 Intraoperative photograph. A titanium plate covering the occipital bone defect and a free latissimus dorsi muscle flap are visible.

reconstructed the defect with titanium mesh and a free latissimus dorsi muscle flap of the right. In addition, postoperative treatment included 60 Gy of radiotherapy. Fourteen months after the excisional biopsy, lung metastasis (S5) was revealed. Thoracoscopic lung tumorectomy was performed by a thoracic surgeon. Furthermore, 9 months after lung surgery, mediastinal metastasis was discovered, which was managed by partial resection of the left lower lobe of the lung and diaphragm. A histopathological diagnosis of both specimens indicated distant metastasis of the MPNST.

In spite of administering adjuvant therapy, local recurrence was observed again intracranially 3 months after radiotherapy (Fig. 6a). Magnetic resonance imaging revealed sagittal sinus invasion of the tumor and the subsequent tumor embolism (Fig. 6b). Resection of the lesion was not planned and 30 months after the excisional biopsy (16 month after lung metastasis), the patient died of respiratory failure due to lung metastasis.

DISCUSSION

MPNST, previously known as malignant schwannoma, neurofibrosarcoma, neurogenic sarcoma, and malignant neurilemmoma, is a rare neoplasm that originates from nerve sheath cells, including Schwann cells, as well as neural and perineural fibroblasts [5]. It is very aggressive neoplasm with high rate of local recurrence and distal metastasis [2–4]. The most common locations are the trunk and extremities. Occurreence in the head and neck is about 9%–19% [2, 3, 6, 7]. The prevalence of MPNST among the general population is about 1 case per 100,000 persons [2]. Otherwise, the incidence of MPNST with von Recklinghausen disease (NF-1) is reportedly 2%–29% [1–3]. Therefore, the lifetime risk of MPNST is approximately 4,600-fold greater in a NF-1 patient than the general population [2, 8]. For patients with NF-1, the 5-year survival rate is reportedly 15%–23% [2, 4, 7]. In contrast, among patients with a solitary MPNST, the 5-year survival rate is reportedly 47%–53% [2, 4]. Therefore, the presence of NF-1 is an independent poor prognosis factor of MPNST [2, 4, 7, 9].

Some studies have suggested that the prognosis is worse in patients with NF-1, because this group has a tendency toward larger lesions, multifocality, poorer differentiation, central distribution of the location, and higher rates of local recurrence and metastasis [2–4, 10]. The rate of local recurrence for patients with a solitary MPNST is 38%–58% and 45%–78% among those with NF-1. Meanwhile, the rate of distant metastasis is 16%–52% for patients with a solitary MPNST and 39%–84% among those with NF-1 [2, 4, 7]. These percentages are the highest of any sarcoma [11, 12].

Aggressive surgical intervention significantly improves disease-free survival [3]. Many studies have indicated that complete surgical resection of MPNST is the mainstay of treatment and most important prognostic factor [13, 14]. As described in the present report, wide and radical excision is key for primary resection.

Reconstructive surgery of the defect is important, especially for lesions of the head and neck. For the present case, we successfully performed wide excision with a tumor-free margin and reconstruction of the hard and soft tissues using titanium mesh and a free latissimus dorsi muscle flap, respectively. Hard-tissue reconstruction is indispensable for very large defects after calvarial surgery. The options for hard-tissue reconstruction include the use of titanium mesh, hydroxyapatite artificial bone materials, and autologous bone grafts (e.g., costal graft). We chose titanium mesh because of the flexibility of the material to adapt for the intraoperative change of the removal area, and avoided custom-made artificial bone material, which limits the range of reconstruction by preoperative planning. A free flap constructed from the latissimus dorsi muscle is often used for reconstruction of defects of the scalp and calvarium, because of the large size of these defects and ease of harvesting [15–18].

Neither adjuvant chemotherapy nor radiotherapy has been shown to consistently influence survival rates [2, 3, 10]. In a 1986 review of 120 cases of MPNST, Ducatman *et al.* [2] reported that adjuvant chemotherapy or radiotherapy did not seem to improve survival. However, adjuvant chemotherapy is required for patients with local recurrence and metastasis. Doxorubicin and/or ifosfamide-based chemotherapy have been used for adult soft-tissue sarcomas, although such regimens have not shown significant effectiveness for MPNSTs [19].

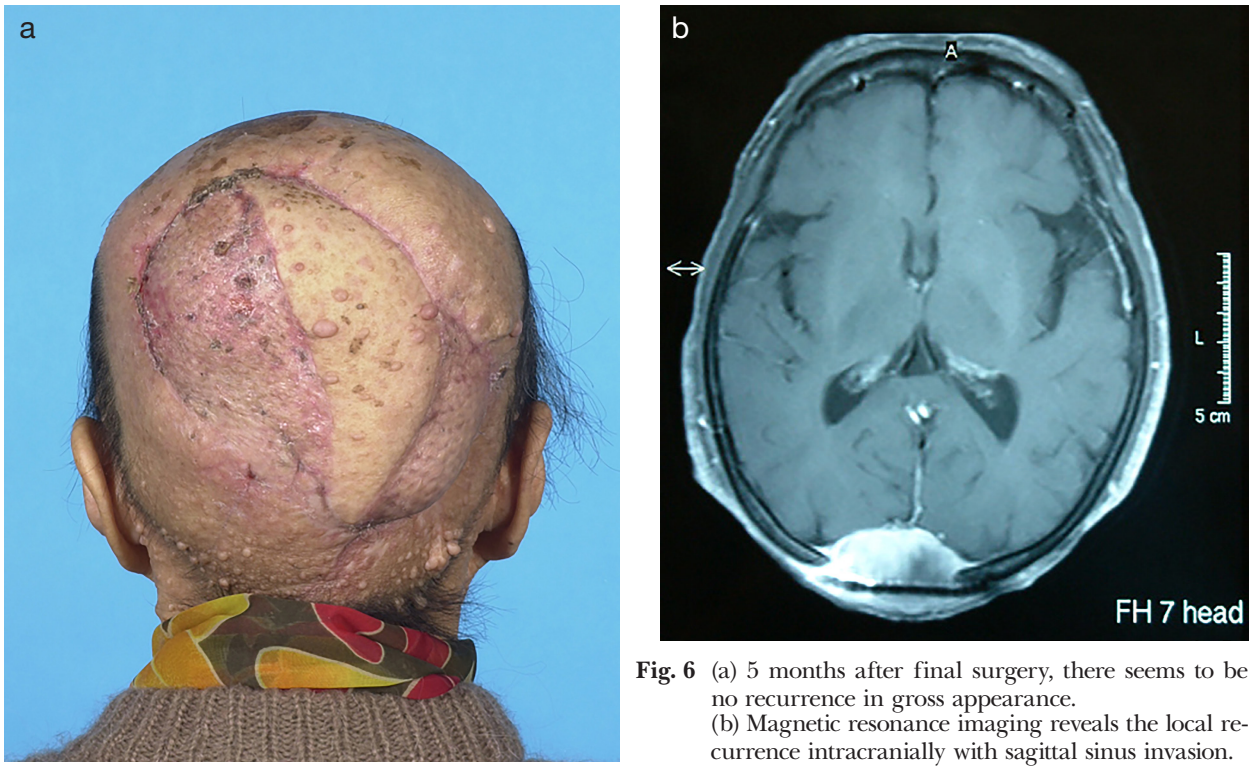

Fig. 6 (a) 5 months after final surgery, there seems to be no recurrence in gross appearance.
(b) Magnetic resonance imaging reveals the local recurrence intracranially with sagittal sinus invasion.

Some recent case reports described the efficacy of new chemotherapeutic regimens [20–22]. Steins *et al.* [21] reported the effectiveness of carboplatin and etoposide combination chemotherapy for treatment of two cases with tumors refractory to doxorubicin and ifosfamide. Kinebuchi *et al.* [20] used carboplatin and etoposide combination chemotherapy for treatment of a case with lung metastasis, which decreased lesion size. Gallo *et al.* [22] reported the successful use of ifosfamide, vincristine, and doxorubicin combined chemotherapy, and several authors recently reported that the combination of surgery and radiotherapy decreased the rate of local recurrence of MPNST and improved survival rates [3, 11, 14, 23–25]. Basso-Ricci *et al.* [23] demonstrated that 56% of 14 patients with MPNSTs were disease-free for 3 years after combined surgery and radiotherapy. This percentage is higher than that of cases treated by surgery only [2]. The recommended dose of radiotherapy continues to change over the years, and it varies according to the presence of microscopic residual disease or a gross tumor from 45 Gy to approximately 65–70 Gy [14]. Other authors have reported that despite a negative surgical margin and even with radiotherapy, local recurrence was noted in up to 50% MPNSTs [25–27]. Dimitrakopoulos *et al.* [27] reported a case of MPNST in the temporalis muscle that was resected with a 20-mm surgical margin. Pathologically, the margin was confirmed as negative; however, despite 66 Gy of postoperative radiotherapy, local recurrences ensued twice (16 and 31 months, respectively, after initial treatment).

Our patient experienced recurrence thrice (11 months after initial surgery, and 8 months after second surgery, and 5 months after final surgery) despite the use of combined therapy with a 20-mm wide resection and radiotherapy at a dose of 60 Gy. We were unable to completely resect the recurrent tumor because it was located in the median occipital cranial space, resulting in sagittal sinus invasion with subsequent tumor embolism. The most widely accepted treatment is radical excision with a free margin as possible [2, 3], although this is sometimes difficult to achieve because of the large size or anatomically difficult locations of the tumors, such as the head and neck area [8, 26], which explains the poor prognosis of MPNSTs of the head and neck [2, 6, 8, 27].

CONCLUSION

An MPNST with NF-1 is associated with a poorer prognosis than that of a solitary lesion. We experienced a case of MPNST in the occipital region with von Recklinghausen disease (NF-1). Recently it is reported in several literature that combination therapy with surgery and radiotherapy improve survival rates. But when the complete local resection with free margin could not achieved due to the size and anatomical location of the tumor, as the case we presented in this report, the effectiveness of combined radiotherapy is not sufficient to control local recurrence.

CONFLICT OF INTEREST

All authors declare no conflict of interest.

ETHICAL STANDARDS

All procedures performed in this article were in accordance with the ethical standards of the institutional ethical board of Tokai University School of Medicine and with the 1964 Declaration of Helsinki and its later amendments.

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