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Case Report

Multiple Surgical Treatments for Repeated Recurrence of Skull Base Mesenchymal Chondrosarcoma

Yuta Murakami,[1] Shinya Jinguji,[1] Yugo Kishida,[2] Masahiro Ichikawa,[1] Taku Sato,[1] Masazumi Fujii,[1] Jun Sakuma,[1] Fumi Murakami,[3] and Kiyoshi Saito[1]

We report a case of a young male who received multiple surgical treatments for repeated recurrence of skull base mesenchymal chondrosarcoma (MC). When the patient was 18 years old, we subtotally removed the skull base MC and he was treated with stereotactic radiosurgery for remnant tumors in the left cavernous sinus. After 30 months, we removed residual tumors that had regrown partially, via combined endonasal endoscopic and orbitozygomatic approaches. Over the next 65 months, the patient refused radical resection, and received six salvage surgeries, two stereotactic radiotherapies, and five stereotactic radiosurgeries for repeated recurrence. At 95 months after initial surgery, the tumors had extended to the skull base and nasal cavities. As a result, the left eye had been blinded and right visual acuity was deteriorated. We performed left anterior-middle cranial base resection, removal of nasal and intradural tumors, high flow bypass, en-bloc resection of the left cavernous sinus and clivus, and reconstruction using an abdominal flap. Even though the main tumors were removed with safety margins, tumors around the right optic nerve were removed by piecemeal to preserve right eye function. Six months after the radical resection, tumors in the right orbital apex recurred because we had been unable to remove the tumor with adequate safety margins. Skull base MC has a high tendency to recur locally, so these tumors should be radically removed with safety margins as early as possible to prevent recurrence.

Keywords: endonasal endoscopic surgery, mesenchymal chondrosarcoma, radical resection, skull base tumor, salvage surgery

Introduction

Chondrosarcoma is a rare disease that accounts for approximately 0.15% of all intracranial tumors and 6% of skull base tumors.[1)] There are five subtypes of chondrosarcomas: grades I–III, mesenchymal, and myxoid.[2)] The pathological classification of the subtype grades I–III is based on differences in differentiation: grade I (well differentiated), grade II (moderately differentiated), and grade III (poorly differentiated), whereas mesenchymal subtype tumors have primitive spindle cells, and myxoid type tumors are composed of strings of rounded cells in a more or less myxoid matrix.[2,3)] Prognosis is based on the pathological classification. The 5-year recurrent rate and of grades I, II, III, mesenchymal, and myxoid subtype have been reported to be 15%, 16%, 33%, 63% and 16%, respectively, and the 5-year survival rates are 90–95%, 81–90%, 43–75%, 46%, and 94%.[2,3)] In this classification, mesenchymal chondrosarcoma (MC) is the most aggressive and malignant subtype.[4)] Here, we report a case of a young male who received multiple surgeries for intractable skull base MC, and describe what we learned from this case.

Case Report

An 18-year-old healthy male presented with the left ophthalmalgia and lower quadrantanopsia. Magnetic resonance imaging (MRI) revealed a left cavernous sinus tumor which extended to the left mandibular sinus, sphenoid sinus, planum sphenoidale, orbit, temporal pole, and clivus (Figs. 1A and 1B). Thus, the subtotal tumor resection via the anterior craniofacial approach was performed (Figs. 1C and 1D), and a pathological diagnosis of MC was made (Figs. 2A–2D). After the surgery, stereotactic radiosurgery (SRS) was performed for the residual tumor in the left cavernous sinus, and tumor growth was suppressed. However, 30 months after the initial surgery, the residual tumors in the left cavernous sinus showed signs of regrowth (Figs. 1E and 1F). Therefore, the residual tumors were subtotally removed via combined endonasal endoscopic, and orbitozygomatic approaches, and stereotactic radiotherapy (SRT) to the left orbit and left subtemporal fossa was performed. Pathological examination revealed that the tumor has a similar histology to that of the previously resected tumors, and the MIB-1 score of this tumor was 10% (Fig. 2E). Between 41 and 74 months after initial surgery, the patient underwent three surgical treatments, one SRT, and one SRS for local recurrent sites (Fig. 3). Narrowing of left visual field occurred, whereas right eye function was preserved. The pathological findings were similar to those of the previous recurrent tumors, and the MIB-1 score of this tumor increased to 20–25% (Figs. 2E and 3).

[1]Department of Neurosurgery, Fukushima Medical University, Fukushima, Fukushima, Japan
[2]Department of Neurosurgery, Nagoya Daini Red Cross Hospital, Nagoya, Aichi, Japan
[3]Department of Diagnostic Pathology, Fukushima Medical University, Fukushima, Fukushima, Japan

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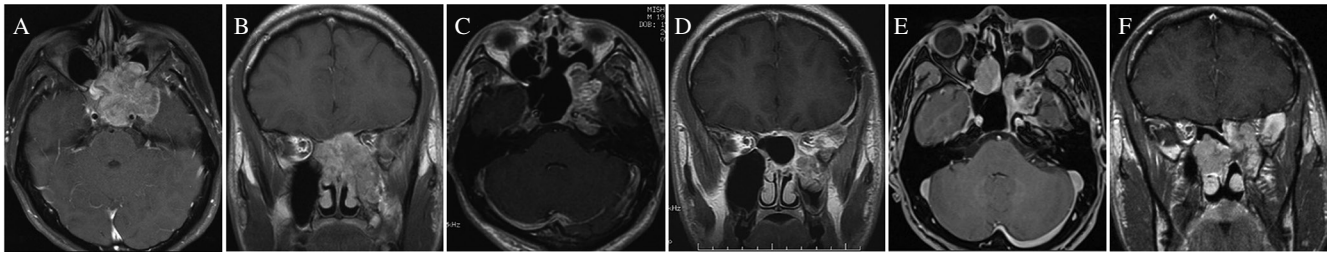

Fig. 1 Preoperative (A, B) and postoperative (C, D) gadolinium-enhanced T1-weighted MRI at initial surgery, demonstrating left cavernous sinus tumors, which extended to the left mandibular sinus, sphenoid sinus, planum sphenoidale, orbit, temporal pole, and clivus, was subtotally removed. Recurrent tumors were found 30 months after initial surgery (E, F).

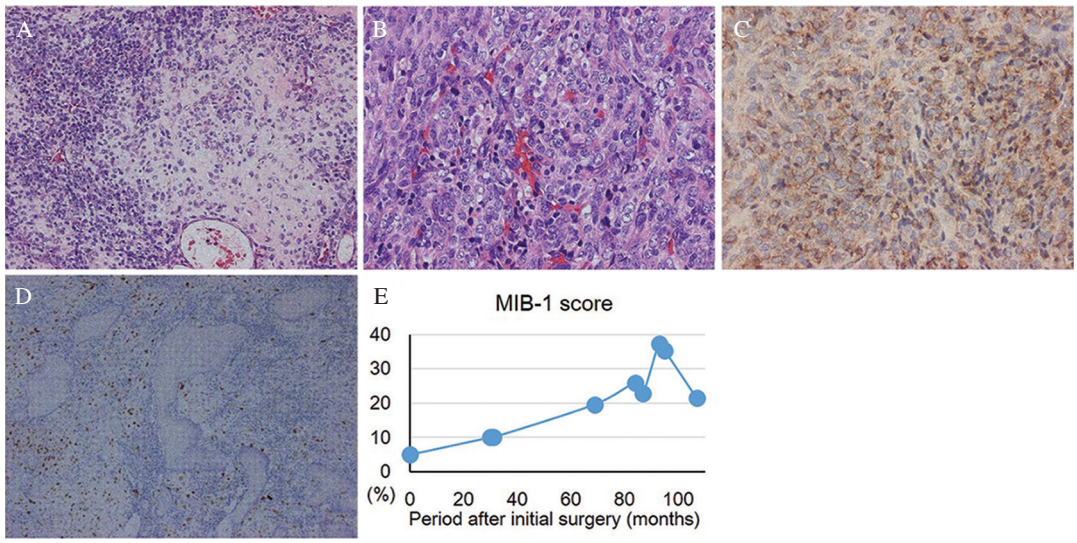

Fig. 2 Pathological photomicrograph of surgical specimen showing MC. Hematoxylin and eosin staining shown that undifferentiated oval tumor cells spread diffusely and were arranged in a hemangiopericytomatous pattern around the vascular cleft, but had a tendency to differentiate to chondrocytes (A and B, ×100 and ×200, respectively). Immunochemical staining of mesenchymal cells positive for CD99 (C, ×200). Immunochemical staining of the chondroid area positive for S-100 protein (D, ×200). Summarized course of MIB-1 score (E).

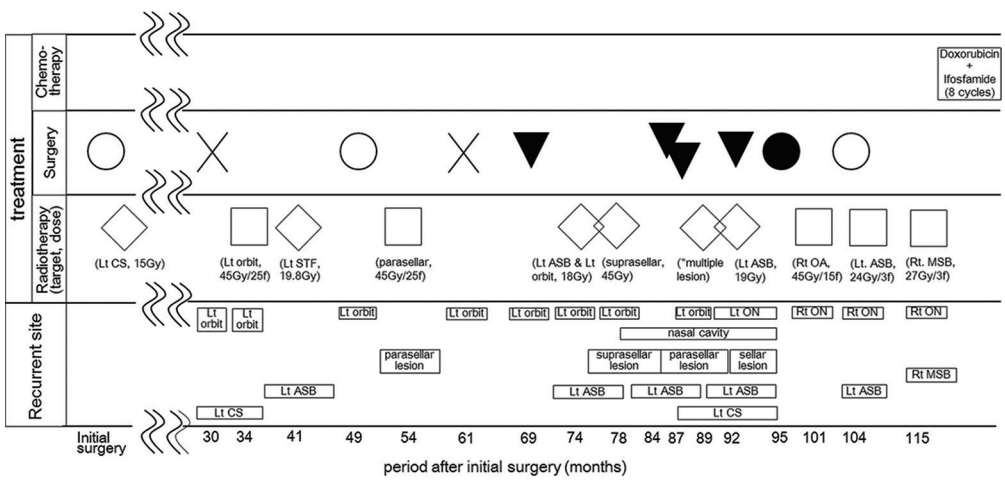

Fig. 3 Summarized clinical course and treatment. Horizontal axis shows number of months after initial surgery. Upper row shows surgical treatments and radiotherapies, and lower row shows tumor recurrent sites. White circle (○) indicates microsurgery, black circle (●) radical resection, cross (×) combined endonasal endoscopic and microsurgery, black inverted triangle (▾) endonasal endoscopic surgery, white square (□) stereotactic radiotherapy, and white diamond (◇) stereotactic radiosurgery. ASB: anterior skull base, CS: cavernous sinus, Lt: left, MSB: middle skull base, OA: optic apex, ON: optic nerve, Rt: right, STF: subtemporal fossa, * = Rt sellae 15 Gy, Rt CS 15 Gy, olfactory glove 18 Gy, Rt ethmoid sinus 20 Gy, Lt CS 16 Gy.

Between 75 and 84 months after initial surgery, two SRS were performed (Fig. 3). His tumor had become repeatedly relapsed over a short period of time and the MIB-1 score of the tumors increased over time (Fig. 2E). At 84 months after the initial surgery, we strongly recommended a radical resection including the left eye because the patient had lost left visual acuity. However, he refused our suggestion and chose to undergo other treatments to avoid removal of the left intraorbital contents, which resulting in facial deformation. From 85 to 92 months after initial surgery, three endoscopic endonasal surgeries and two SRS were performed due to repeated tumor recurrence mainly in the nasal and paranasal cavities (Figs. 4A–4F). As the number of operations increased, recurrent tumors became more hemorrhagic, although the pathological findings were similar to those of previous recurrent tumor, though the MIB-1 score of this tumor increased to 35% (Figs. 2E). At 95 months after the initial surgery, the recurrent tumors extended to the anterior and middle skull base, left orbit, posterior space of the right orbit, and the nasal cavities (Figs. 4G and 4H). The patient left eye was blind at this point, and his right visual acuity was deteriorated. This was the last chance to perform radical tumor resection to preserve right eye function was suspected, because one of the recurrent tumors was located close to the right optic nerve. Finally, the patient agreed to undergo radical tumor resection. Left anterior and middle cranial base resection, removal of the nasal and intradural tumors, high flow bypass, en-bloc resection of the left cavernous sinus and clivus, and reconstruction with an abdominal flap were performed. Before this surgery, it was hypothesized that it would be possible to remove most of the tumors with safety margins, including the tumors near the right optic nerve. However, the tumors had adhered to the patient's right optic nerve, so the tumors were removed piece by piece to preserve his right eye function. The pathological findings were also similar to those of the previous recurrent tumors, and the MIB-1 score was 35% (Fig. 2E). The patient's right visual acuity restored and returned to work (Figs. 4I and 4J). However, 6 months after this surgery, a small recurrent tumor in the right orbital apex was found, and treated using SRT. Nine months after the last radical resection (at 104 months after initial surgery), a recurrent tumor in the frontal skull base was found, and treated using SRT after subsequently removed. The patient was once again discharged without right visual deterioration and returned to work. Finally, at 19 months after the last radical resection (115 months after initial surgery), the patient had become blind because of recurrent tumors in the right optic nerve as well as in the right middle skull base. His tumor had progressed to an inoperable stage, whereas his Karnofsky performance status (KPS) score had remained constant at 60. He underwent SRT, and systemic chemotherapy was administered, with a regimen of both doxorubicin 75 mg/m^2 and ifosfamide 9000 mg/m^2 on day 1 through 3 ever 4 weeks.[5,6] At 29 months after the last radical resection (125 months after initial surgery), eight cycles of systemic chemotherapy had been completed. Although his tumors were radiologically and clinically controlled without any complications, his KPS score changed 60 to 50. During the clinical course, repeated radiotherapies to the same recurrent sites (left cavernous sinus, left anterior skull base, and left orbit) were treated outside the previous irradiation field.

Discussion

We reported a case of a young male with skull base MC who underwent multiple surgical and radiation therapies for repeated localized tumor recurrence. Over a period of approximately 10 years, he underwent 10 surgeries and 11 radiotherapies. This case suggested two important clinical instructions. First, because the frequency of localized recurrence is higher than metastasis in skull base MC, radical resection of these tumors in the early stages, when there is

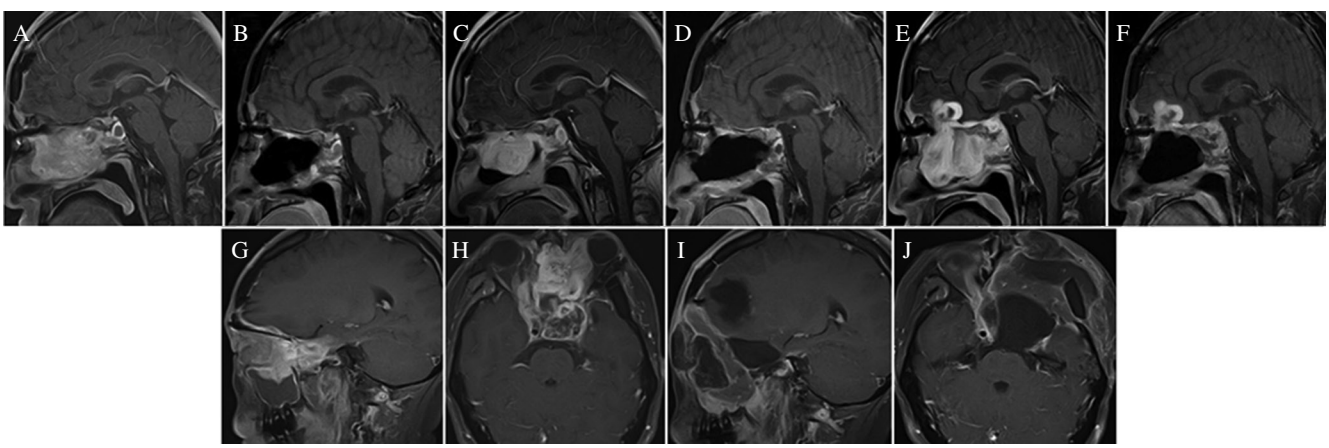

Fig. 4 Gadolinium-enhanced T1-weighted MRI at 84 (A), 87 (C), and 92 months (E) after initial surgery demonstrating recurrent tumors extended to the left anterior skull base, nasal cavity, and parasellar lesion. Each recurrent tumor was subtotally removed by endonasal endoscopic salvage surgery at 84 (B) and 87 (D) months after initial surgery. We could not remove all tumors at 92 months after initial surgery (F). Gadolinium-enhanced T1-weighted MRI before (G, H) and after (I, J) radical resection at 95 months after initial surgery demonstrating that the tumors were removed gross totally.

less extension to the surrounding tissues, is important for the patient's survival. Second, salvage surgeries by endonasal endoscopy and radiotherapy for intractable skull base MC may preserve neurological function and maintain the patient's quality of life.

MC is a rare malignant neoplasm which is derived from primitive cartilage mesenchyme and constitutes a very small subset of intracranial neoplasms.[7] To the best of our knowledge, there have been no studies describing the prognosis of skull base MC. The prognosis of intracranial MC is poor, and the 5-year survival rate has been reported to range from 42% to 74%, whereas the 10-year survival rate has been reported to range from 28% to 67%.[3,8–11] It is suspected that complete removal of intracranial MC, especially located in the skull base, is difficult from the perspective of preservation of neurological functions.[12] However, a previous study reported intracranial MC patients who had two recurrences and survived 18 years,[13] indicating that tumor recurrence does not always mean a poor prognosis.[14] Although the 5-year recurrence rate is high at 63%,[15] remote metastatic cases have been rarely reported.[8,16,17]

MC usually does not metastasize until a very late stage,[18] and it has a high tendency of repeated local recurrence.[15] Our treatment strategy for skull base MC is radical resection of the tumor with safety margins in the first surgery or the early stage. Hence, it is speculated that the prognosis of skull base MC could be improved radical resection of a tumor with safety margins is performed at early stage. It has been reported that a series of intraorbital MC patients had good outcomes after radical removal of their tumors.[19] However, the most difficult problem is the decision to determine the appropriate timing of total removal with minimal neurological deficit. Even if radical resection is not performed in the first surgery, the patient's outcome could improve if the tumors were removed with safety margins in the multiple surgeries.[19] In the current case, if we had removed his tumor with safety margins less than 84 months after initial surgery, the tumor might not have recurred.

If we could not perform radical tumor resection, treatment outcome could improve when combined with the appropriate adjuvant therapies.[20] Repeated salvage surgeries for skull base MC patients may be effective as palliative surgical therapy while maintaining their neurological functions.[21] In addition, endonasal endoscopic surgery for skull base chondrosarcoma is useful because it is less invasive and its anatomical nature which is located at the paramedian skull base, displacing adjacent cranial nerves laterally.[22,23] Furthermore, adjuvant radiotherapy for intracranial MC can also prolong survival rate.[23–25] In the present case, when the patient refused radical surgery, salvage surgeries were performed. The tumors repeatedly recurred and mainly invaded not the intracranial side, but the nasal cavity. Thus, we selected the endoscopic endonasal approach with SRS for the recurrent tumor as a minimally invasive therapy. Our patient was discharged for short days after each of his four endonasal endoscopic surgeries, and was able to return to work after each hospital discharge. Maximum safe resection with radiotherapy could improve the survival rate of intracranial MC patients.[20,21,26] The reported progression-free tumor control rates for SRS for skull base chondrosarcomas including all subtypes are 91%, 72%, 72%, and 54% at 1, 3, 5, and 10 years, respectively, whereas the overall patient survival rate for the same period after SRS are 95%, 76%, 70%, and 56%, respectively.[27,28] It has been reported that radiosensitivity of intracranial MC could increase in patients with more than subtotal resection of tumors.[26] In terms of radiotherapies, endoscopic endonasal surgeries are effective for skull base MC as a palliative surgical approach, which invaded for nasal and paranasal cavities, to improve patient's survival time without neurological deterioration. In the present case, although the tumors recurred rapidly and repeatedly in this phase, if the patient had not undergone salvage therapies, it is likely he would have died due to his MC. In a recent report, a high-precision radiotherapy series reported that doses ranging from 66–76 Gy provide in skull base chondrosarcomas patients, including all subtypes, resulting in a 5-year progression-free survival and survival of 100% without cranial nerve deficit or brainstem damage. Furthermore, the 5-year control rate after proton therapy for chondrosarcoma is also reported to be in the range of 85–95%.[28]

Conclusion

Skull base MC is intractable and difficult to cure unless the tumors are completely removed with safety margins. Hence, we concluded that it is important to select an appropriate time to perform radical resection at an early stage with minimum neurological deterioration to prevent recurrence.

If a situation occurs where radical resection cannot be performed, less invasive salvage surgery, such as endonasal endoscopic surgery, combined with radiotherapy would be one of the better clinical options to preserve neurological function and improve prognosis.

Conflicts of Interest Disclosure

There are not any conflicts of interest or financial disclosures for all authors.

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Corresponding author:
Yuta Murakami, MD, PhD, Department of Neurosurgery, Fukushima Medical University, 1 Hikarigaoka, Fukushima, Fukushima 960-1295, Japan.
✉ y-mura@fmu.ac.jp