Case Report

Rare case report and literature review of intracranial mesenchymal chondrosarcoma

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Abstract: Intracranial mesenchymal chondrosarcoma (IMC) is a rare primary malignant tumor in the skull, but mostly originates from the abnormal residual chondrocytes in the embryonic period, which grow slowly, and primarily occurs at the junction of the cartilage of the skull base. IMC is difficult to diagnose by preoperative imaging and is easily misdiagnosed. It needs to be differentiated from meningiomas, gliomas, hemangioma, fibroids, etc.; this article introduces a case of primary IMC in a 38-year-old female teacher, and reviews the literature on the diagnosis and treatment of symptoms. The patient suffered from persistent severe headaches without nausea and vomiting. There was no obvious abnormality in the physical examination. Magnetic resonance imaging (MRI) of the head showed a circular space-occupying lesion on the right frontal bone and forehead; the mass was approximately 5.9 cm × 5.2 cm × 5.5 cm, and there was a large edema band surrounding it. The space-occupying effect was obvious; bilateral ventricles were compressed, and on the right side, the midline structure was shifted to the left. The patient was initially diagnosed with simple meningioma. After admission, the right frontal lobe meningioma was resected under general anesthesia, and the tumor tissue was completely removed in blocks. The postoperative pathology report stated: malignant tumor of the right frontal lobe; consider mesenchymal chondrosarcoma. Following a difficult pathological consultation at the Provincial Medical Association, the tumor was found to be consistent with mesenchymal chondrosarcoma. Intracranial chondrosarcoma is a very rare malignant tumor. Other intracranial masses, such as meningioma and glioma, should be distinguished through differential diagnosis. At present, more attention is paid to surgical intervention and combined radiotherapy and chemotherapy for the treatment of IMC, which should also be the future treatment option.

Keywords: Intracranial; chondrosarcoma; radiotherapy combined with chemotherapy; metastatic tumor; case report

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Introduction

Intracranial mesenchymal chondrosarcoma (IMC) is a rare malignant tumor of the central nervous system, which accounts for less than 0.16% of all intracranial tumors. The pathogenesis of IMC has not yet been elucidated. There are no clear treatment guidelines, and there are very few intracranial chondrosarcomas. Therefore, it is more important to differentiate from meningioma and glioma. The three diseases can generally be initially identified using CT, MRI, and enhanced CT and MRI. Meningioma is a benign tumor that originates in the meninges, grows slowly, and can usually be surgically removed and cured. Glioma is actually a malignant tumor that originates from glial cells in the brain and has varying degrees of malignancy. IMC is a rare malignant tumor that can occur in the cartilage at the base of the skull and can begin as a chondrosarcoma or be formed by the malignant transformation of chondrosarcoma,

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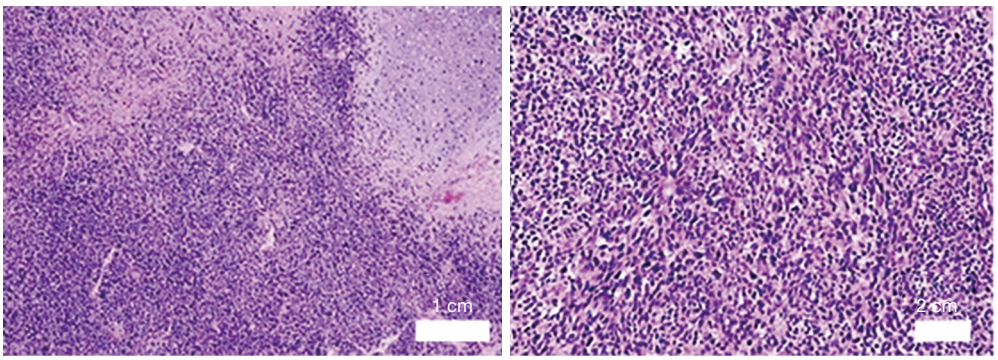

Figure 1 hematoxylin-eosin staining of intracranial chondrosarcoma (left ×100, right ×200).

with poor prognosis and highly susceptible to local recurrence and distant metastasis. The gold standard for the identification of these three diseases is pathological examination and immunohistochemistry. This article introduces the onset and treatment process of a 38-year-old female teacher with IMC. In this case the patient was treated with postoperative radiation therapy after resection of the intracranial occupying lesion; however, we found that the patient had an occupancy in the frontal sinus that was also altered before and after radiation therapy, which led us to wonder whether this was also a lesion or even a primary lesion. The posterior wall of the frontal sinus is thin and adjacent to the meninges and frontal lobe of the brain, so it is not known whether the lesion invaded the skull from the posterior wall. We also need further consultation with an ENT-head and neck specialist to clarify the etiology. Combined with relevant literature reports, it discusses the histopathological characteristics, imaging findings, magnetic resonance imaging (MRI) presentation after radiotherapy and the subsequent combined chemotherapy treatment methods, as well as research into further treatment methods. We hope that through the clinical manifestations of this disease and the effects of treatment, we can obtain a deeper understanding of the disease and provide appropriate management methods for patients, so as to facilitate differential diagnosis among young people and adults with intracranial lesions.

We present the following article in accordance with the CARE reporting checklist (available at https://dx.doi.org/10.21037/apm-21-2290).

Case presentation

A 38-year-old female patient suffered from persistent pain in the forehead in July 2020. After taking "pain relievers" by herself, her symptoms were less relieved, but her headache was subsequently aggravated. There were no symptoms of nausea, vomiting, syncope, no limbs, language, or symptoms. Sensory dysfunction, unconsciousness, and neurological examinations were not positive. The patient's personal and family history were unremarkable. She underwent brain computed tomography (CT) at her local hospital, which showed right frontal lobe space-occupying lesions; meningiomas were considered, and surgical treatment was recommended. Later, the patient went to a tertiary hospital. A head MRI showed the following: T1 showed mixed low signal; T2 showed mixed high signal; FLAIR (FLuid Attenuated Inversion Recovery) showed mixed high signal; DWI (diffusion weighted imaging) showed low or equal slightly high signal; and ADC (apparent diffusion coefficient) showed high, equal low signal. Scanning after the injection of glucosamine zapentate meglumine showed obvious uneven enhancement. The MRI diagnosis was as follows: right frontal space-occupying lesions; considering the high possibility of meningioma, solitary fibroma, and other lesions are not excluded.

Subsequently, on July 31, 2020, the patient underwent "right frontal lobe tumor resection" under general anesthesia. The postoperative pathological examination showed a (right frontal lobe) malignant tumor; mesenchymal chondrosarcoma was considered, and provincial consultation was recommended (*Figure 1*, left), the pathological section was seen under low magnification to be composed of large undifferentiated small cells with small, round or short spindle-shaped cells and little cytoplasm. The nuclei were round or ovoid, deeply stained, and the nucleoli were inconspicuous. A few small islands of hyaline cartilage were seen in between, and the

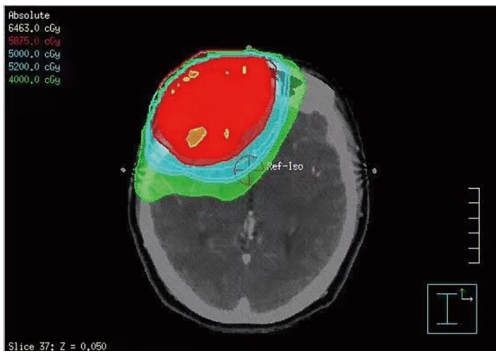

Figure 2 The radiation dose distribution to the lesion.

cartilage differentiation was relatively mature (*Figure 1*, right). The immune examination results were as follows: CD34 (vascular+), CD56(+), CD99(+), CK (AE1/AE3) (–), Desmin(–), EMA(–), GFAP(–), Ki67 (the hot spot was approximately 30%+), Myogenin(–), Olig-2(+), S-100(–), STAT6(–), SYN(–), Vimentin(–), and SMA(–). Following consultation at the Provincial Medical Association Difficult Pathology Consultation Center on August 19, 2020, the patient was deemed to have a (right frontal lobe) malignant tumor, consistent with mesenchymal chondrosarcoma. Postoperatively, the patient suffered intermittent headaches and bilateral eye swelling. The postoperative changes were temporarily considered, and she was readmitted to hospital on August 27, 2020. After admission, her head was re-examined with 3.0T plain MRI + enhancement , which showed that the right frontal lobe was spotted sheet-shaped short T1 and long T2 signal shadows, FLAIR showed high signal, DWI showed high signal, the enhanced scan was locally slightly enhanced. Also, it was surrounded by an edema band, the right lateral ventricular anterior horn was slightly compressed, and the midline structure was in the middle. The patient's right frontal lobe chondrosarcoma had a low degree of malignancy after surgery, and may have had low sensitivity to radiotherapy and chemotherapy. However, the patient suffered intermittent headaches and bilateral eye swelling, and the chief physician of the radiotherapy department carefully examined the patient's head MRI. Although the imaging reports there is no special reminder, but it was found that the patient had obvious enhancement signals in the frontal sinus. Considering that there were also lesions in the frontal sinus, residual lesions after surgery could not be ruled out. In summary, the patient was indicated for radiotherapy, and after excluding contraindications, she received head radiotherapy on 2020-09-07. The prescribed doses were as follows: PGTV (planning gross target tumor volume): 64 Gy; PTV 1 (planning target volume 1): 60 Gy; and PTV 2: 54 Gy (*Figure 2*), for a total of 30 times (5 times/week, treatment from Monday to Friday). The entire course of radiotherapy was tolerated; the patient's pain and swelling symptoms were significantly relieved, and she was discharged. Daily life can be self-care. Following radiotherapy, her head MRI (3.0T) was rechecked several times postoperatively, and indicated that the slices (2020-08-27) of contrasting surgical area had less absorption of bleeding foci than before, and the remaining tissues were not significantly changed compared with the previous scan. However, the foci at the frontal sinus were obviously reduced (*Figure 3*); therefore, it was not ruled out that the frontal sinus may also have primary foci, which later progressed to the frontal lobe of the brain.

According to the preoperative diagnosis of neurosurgeons, the patient was considered to have intracranial lesions. After comparison, neurosurgeons are concerned about was also to observe the recovery of intracranial lesions. For further postoperative preventive treatment, the patient went to the oncology center. After consultation with professional imaging experts, and considering the combined treatment of surgery and postoperative radiotherapy, the tumor center administered three cycles of chemotherapy (Vincristine + Epirubicin + Cyclophosphamide and Ifosfamide + Etoposide). There was no significant progression at 1 year postoperatively. At present, the course of postoperative radiotherapy and chemotherapy has been completed, and the patient has no specific discomfort or tolerance, and thus, a regular review was ordered. Radiation experts believe that the intracranial lesions and the enhanced signal at the frontal sinus have changed. The patient should be further examined to clarify the nature of the enhanced signal at the frontal sinus. The patient and her family were informed and agreed to all of the above treatment plans. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal

Discussion

At present, the origin of intracranial chondrosarcoma remains unclear. First reported by Dahlin and Henderson (1) in

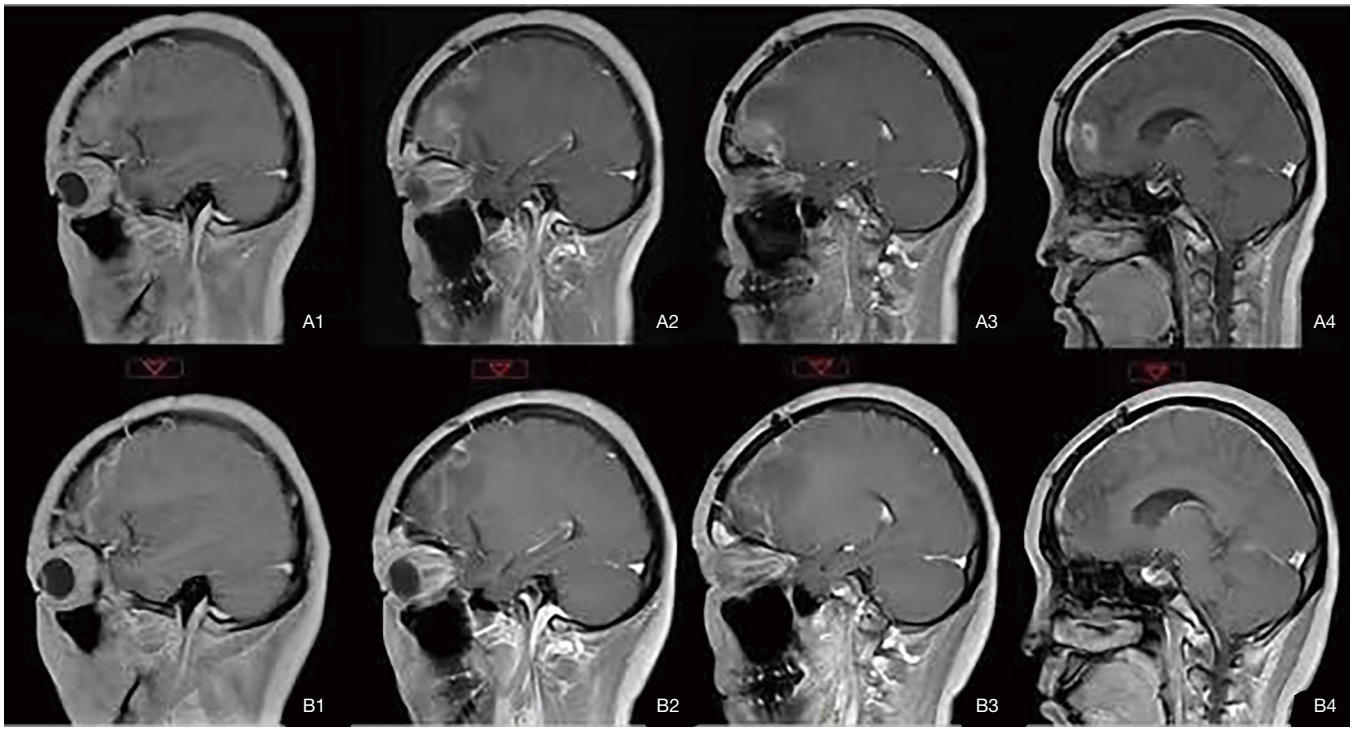

Figure 3 Magnetic resonance imaging of the brain, T1-weighted image. Sagittal section, before (A1-A4) and after (B1-B4) radiotherapy.

1962, IMC is a rare malignant tumor of the central nervous system that usually occurs in young people, accounting for approximately 0.15% of intracranial tumors (2,3). Embryonic cartilage is located in the skull and dura, and is derived from meningeal fibroblasts or pluripotent mesenchymal cells in the dura or arachnoid. Radiological examinations, including CT, MRI, and angiography, are essential for any intracranial disease. For patients with intracranial chondrosarcoma, CT scans usually show mild high-density or iso-density lesions with uneven enhancement and frequent calcification. The vast majority of primary intracranial chondrosarcoma originates from the base of the skull (4,5); however, our patient's lesion was located in the right frontal lobe and was higher. The prognosis of intracranial chondrosarcoma is poor and the possibility of local recurrence is high (2). It has been reported that compared with surgery combined with postoperative adjuvant radiotherapy, surgery alone seems to be an ineffective treatment strategy (2), and therefore, surgery combined with postoperative radiotherapy can obtain the best survival time (6). Bloch *et al.* (2) found that the 5-year mortality rate of patients with chondrosarcoma treated with surgery alone was 26%, while the implementation of postoperative adjuvant radiotherapy significantly reduced the mortality rate to 4%. These numbers are not surprising, and numerous recent studies have pointed out without reservation that delicate surgical resection combined with postoperative radiotherapy can provide these patients with the best long-term prognosis. In 2002, Neff *et al.* (6) asserted that postoperative radiotherapy might be beneficial to these patients. A study of this type by Isaacson *et al.* (7) also clearly pointed out in 2007 that radiotherapy is an important adjuvant therapy for the treatment of chondrosarcoma. The prognosis of patients with intracranial chondrosarcoma is strongly influenced by several important factors, including postoperative adjuvant radiotherapy, pathological type, previous treatment (surgery or radiotherapy), degree of tumor resection, and chemotherapy application. Although, many people believe that local recurrence is the most important predictor of mortality in these patients. However, the lesion of our patient's frontal sinus was significantly reduced after radiotherapy. Considering the incomplete resection of the tumor, it can be said that the patient has non-primary intracranial chondrosarcoma, and there is a significant risk of possible recurrence for its prognosis. The patient is now followed up for 1 year after surgery and no significant tumor recurrence or progression is seen, but regular review is also

instructed to achieve early detection, diagnosis and treatment to improve the quality of survival. Currently, there is no clear diagnostic guideline for IMC, except for conventional surgical resection, post-operative radiotherapy is still the preferred treatment option; however, since it is an intracranial tumor, new therapeutic directions for this type of tumor can be sought through immunohistochemistry, screening for sensitive gene expression, or through research on molecular expression and pathways, such as nano- and targeted novel therapies, providing new hope for this rare disease.

Conclusions

Intracranial chondrosarcoma is an extremely rare tumor that is prone to local invasion and distant metastasis. Intracranial chondrosarcoma can be fatal, invading the brain and increasing intracranial pressure by blocking the passage of cerebrospinal fluid. In patients with intracranial chondrosarcoma, diplopia caused by intracranial nerve compression (III, IV, and VI), visual field defects, and headaches are the most common symptoms (8-11). Iyer *et al.* found that by performing stereotactic radiosurgery earlier after diagnosis, and through multimodal management including surgical resection, tumor control is more likely to be achieved (12). Differential diagnosis of this disease is very difficult because of its rarity and atypical imaging signs. Our patient is relatively young; radiotherapy can locally improve some symptoms, and the lesions have not changed significantly after chemotherapy. Otolaryngology surgical intervention can also be considered to explore the pathology of the frontal sinus, and clarify the nature of the lesions, as well as to provide timely intervention and treatment. Provide ideas for further treatment. The current treatment strategy is radical resection, and close follow-up should be performed postoperatively. Although the long-term results may be disappointing, this treatment strategy should also provide patients with the greatest chance of long-term recurrence. Radiotherapy and chemotherapy can be considered to reduce the risk of recurrence; however, the residual disease is not reassuring. Thus, we reiterate and emphasize the importance of surgical intervention. In the future, the combination of microsurgical resection and radiotherapy should become the treatment option for intracranial chondrosarcoma.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/apm-21-2290). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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