

Dear editor-in-chief:

We have submitted our revised manuscript, and Please find our attached files and revised manuscript.

**Title:**

Primary intracranial Extraskkeletal Myxoid Chondrosarcoma: A Case Report and Literature Review.

**Authors:**

Zi-You Zhu, Yu-Bo Wang, Han-Yi Li, Xin-Min Wu.

We are very appreciative to you and the reviewers, thank you very much for giving us helpful comments and suggestions which enabled us to improve the quality of our manuscript, and making efforts on our manuscript titled “Primary intracranial Extraskkeletal Myxoid Chondrosarcoma: A Case Report and Literature Review” (Manuscript ID: 73631). And we request that you kindly consider our revised manuscript for publication in World Journal of Clinical Cases as a case report.

We have followed the constructive comments and suggestions of reviewers and editors, and have our manuscript revised. The revised manuscript has been uploaded as Supplementary Material. The revised parts in the manuscript are displayed in blue text. We have addressed all the concerns and comments from the reviewers in the following paragraphs.

The following part is the responses for the questions and suggestions

of the reviewers:

**For Reviewer 1:**

1. Dear author, Greeting, you have reported a very rare and unique case  
It is well written and is very useful to other colleagues around the world

Response:

We thank the reviewer for his/her positive feedback and recognition  
to our manuscript.

**For Reviewer 2:**

1. We strongly suggest an overall grammar check for the language, that  
could be consistently improved. Some minor revision are listed by line:  
pag 3 line 27: check the spell for typos ( ...follow-up is also necessary for  
paatients). pag 4 line 2 - 3: grammar check of the sentence (i.e.  
"recurrence rate" instead of recurrent rate) pag 4 line 7: check "recurrent  
rate" pag 5 line 23: check "quited"

Response:

Thank you very much for this important and helpful suggestion which  
enabled us to improve the quality of our manuscript. We have read the  
manuscript carefully and made modifications and lingual embellishment  
by a native-English speaker for grammar, sentence structure, word usage,  
spelling, capitalization, punctuation, format, and general read ability.

2. We suggest to discuss about the indications of preoperative biopsy  
and the decision for upfront surgery. Preop biopsy is mandatory for

extra-axial deep masses, according to present guidelines (ESMO). Which are the indications for a intracranial mass?

Response:

We thank reviewer for this important comment. And we added the discussion of the indication of preoperative biopsy of STS and intracranial neoplasm, and we also discussed the decision of upfront surgery:" Soft tissue sarcoma (STS) is a rare mesenchymal neoplasm that, nevertheless, contains more than 70 subtypes, and the management and prognosis of patients can vary significantly between different subtypes. Only relying on preoperative radiographic exams and empirical diagnosis sometimes causes misdiagnosis. Pathological examination is the gold standard of diagnosis of STS and is an indispensable method that accurately indicates the pathological natures of intracranial lesions, such as neoplastic or nonneoplastic, benign or malignant, degree of malignancy, progression, pathological subtype and molecular features, and is also the core method that provides crucial and valuable guidance for surgeons, radiologists and oncologists to make proper and beneficial treatments of STS. Thus, accurate diagnosis with the basis of pathological examination is critical for the management of STS and should be diagnosed by expert pathologists due to the various and complicated pathological features of STS. Meanwhile, management should be discussed and performed by a multidisciplinary tumor board (MTB) once the lesion is preoperatively

suspected to be STS. Thus, all of the deep and superficial lesions in soft tissue that have diameters over 5 cm should undergo preoperative biopsy and pathological examination, and biopsy is also considered mandatory before treatment. With regard to intracranial lesions, especially to suspected malignancies, stereotactic frame-based or frameless brain biopsy is recommended to increase the accuracy of preoperative diagnosis and provide guidance for appropriate treatments, including lesion resection, adjuvant radiotherapy and chemotherapy. With the guidance of CT, MRI and positron emission tomography (PET) technologies, stereotactic brain biopsy is considered to be a safe, less aggressive and effective means to obtain tissue from intracranial lesions and is generally suitable for patients with the following conditions: 1). Multiple intracranial lesions; 2). The lesion is in the deep locations of the brain, such as the brainstem, thalamus, callosum and basal ganglia, or functional cortical or subcortical areas; 3). The tumor cannot be totally removed by open microsurgery; 4). The general condition of patients is not tolerant to anesthesia, open craniotomy and microsurgery; 5). Patients who have risk factors such as advanced age, systematic disease, severe cardiac disease, etc.; 6). Based on radiological and clinical manifestations, the preoperative diagnosis of lesions is intricate, ambiguous and unclear. Therefore, if one intracranial lesion is an extra-axial neoplasm and suspected to be STS based on radiographic

features, clinical manifestations, history of disease, etc., preoperative biopsy is necessary." (Page 11, line 32). And we also discussed the decision of upfront surgery. In our reported case, because the lesion was located in the left cavernous sinus, and preoperative intracranial CTA (CT angiography) indicated that the tumor was very closed to the left internal carotid artery and part of the artery was embed in the tumor, and important cranial nerves such as oculomotor nerve also situated in cavernous sinus and closed to the tumor, that our surgeons evaluated the risks of operating stereotactic brain biopsy were high: In our present case, because the lesion was located in the left cavernous sinus and adjoined the internal carotid artery and cranial nerves, the risks of operating stereotactic brain biopsy in this area were evaluated to be high by surgeons. Thus, we performed open craniotomy and tumor resection on the patient and obtained the whole lesion tissue for further pathological exams.(Page 12, line 34).

3. We suggest to point out that the histopathological diagnosis was done by an expert pathologist. Present guidelines state that diagnosis of STS have to be done by expert pathologists - or confirmed by pathological revision of the specimen.

Response:

We thank reviewer for this important and helpful comment, and we pointed out that the histopathological diagnosis was made by the

pathological experts of the pathology department: the Director of Pathology Department of The First Hospital affiliated with Jilin University and her colleagues discussed the pathological features of this lesion and finally diagnosed it as primary intracranial EMC. (Page 7, line 7)

4. We suggest to discuss about the importance of a multidisciplinary management of STS - and overall, of ultra-rare tumours.

Response:

We thank the reviewer for this important and helpful comment, and we added the discussion of multidisciplinary management of STS: Currently, the standard and crucial treatment modality for soft tissue sarcoma is multidisciplinary treatment (MDT), including surgery, adjuvant radiotherapy and systematic chemotherapy. Surgery is considered to be the basic and standard treatment for local lesions of STS. Wide tumor resection with negative margins is recommended on the contrast that positive margins can cause increasing recurrence and metastasis rates and impact the progression-free survival (PFS) and distant metastasis-free survival (DMFS) of patients. Adjuvant radiotherapy is recommended to improve local control and reduce the recurrence of STS. EMSO suggests that postoperative radiotherapy should be applied in patients who have a deep tumor, a tumor size over 5 cm or a high degree of malignancy (grades 2-3). In advanced disease, stereotactic radiotherapy or stereotactic surgery is adoptable for

patients who lose the chance for surgery or are in poor condition and cannot tolerate the operation. Given the occurrence of distant metastasis of STS, systematic chemotherapy is also recommended, although the efficacy is still debatable, and the primary first-line chemotherapeutic agents are anthracyclines such as doxorubicin, ifosfamide and gemcitabine. Other novel treatments, such as targeted therapy, immunotherapy, and antiangiogenic agents, such as pazopanib, are promising, and further research is needed. (Page 13, line4)

5. Was this case discussed in a multidisciplinary tumour board?

Response:

We thank the reviewer for this important and helpful comment. Due to the rarity of the primary intracranial extraskeletal myxoid chondrosarcoma and the atypical features of preoperative radiographic exams, the preoperative diagnosis of the intracranial neoplasm in present case is ambiguous. Two of our surgeons gave different empirical diagnosis: meningioma or hemangioma? But given the risk of preoperative biopsy was high for the reason that the tumor was very closed to internal carotid artery and important cranial nerves, thus we performed operation on patient and completely removed the tumor and sent the sample to the pathology department for further exams. After the outcomes of pathological exams came out, we had consultations and discussions in multidisciplinary tumor board consisted of neurosurgeons,

pathologists, oncologists and radiologists for further treatments.

**For editor:**

We provided the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement. We also provided the original figure documents and arrange the figures using PowerPoint. We added the Author Contribution part in the manuscript as request, and provided the editable tables using Word. We read the article carefully and made modifications and embellishment by a native-English speaker for grammar, sentence structure, word usage, spelling, capitalization, punctuation, format, and general read ability.

Once again, we are very appreciative and grateful for the helpful and constructive comments and suggestions which enabled us to improve and refine the quality of our manuscript from you and the Reviewers. Thank you very much in advance for your kind consideration of our revised manuscript for publication in World Journal of Clinical Cases.

Sincerely yours

Zi-You Zhu

02-04-2022