Radiology Case Reports 19 (2024) 825–830

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Case Report

Intracranial mesenchymal tumor with multiple extracranial metastases: A case report and literature review ☆

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ARTICLE INFO

Article history:
Received 10 September 2023
Revised 8 October 2023
Accepted 16 October 2023
Available online 25 November 2023

Keywords:
Intracranial mesenchymal tumor
Multiple extracranial metastasis
Highly aggressive
Surgical resection
Case report

ABSTRACT

This study presents a rare case of an older woman with an intracranial mesenchymal tumor in the right frontal and parietal lobes. Despite prompt surgical intervention, her condition rapidly deteriorated because of tumor dissemination, leading to her demise. We highlight the tumor's marked invasiveness and heterogeneity, coupled with a propensity for distant systemic metastasis, which negatively impacted the patient's prognosis. This particular clinical behavior had not been previously reported, making this a novel observation. Thus, through a comprehensive review of relevant literature, we aim to provide valuable insights for further understanding, diagnosing, and treating such tumors.

Introduction

Intracranial mesenchymal tumors represent a rare subset of central nervous system neoplasms that often pose diagnostic and therapeutic challenges in clinical practice. This study reports the case of an older female patient with an intracranial mesenchymal tumor that exhibited multifocal systemic metastasis. The patient presented with symptoms of left-sided limb weakness, dizziness, headache, and epileptic seizures. Preoperative imaging revealed tumor dissemination to multiple sites, including the lungs, liver, adrenal glands, and bones. Initially misdiagnosed with intracranial metastatic lesions, the patient underwent entire resection surgery; subsequent pathological examination confirmed the typical features of an intracranial mesenchymal tumor. Despite the surgical intervention, the patient's condition deteriorated rapidly, leading to her death 1 week after discharge.

Abbreviations: AFH, angiomatoid fibrous histiocytoma.

☆ Competing Interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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https://doi.org/10.1016/j.radcr.2023.10.043

Clinical presentation

Twelve days before admission, the patient (a 73-year-old woman) began to experience inflexibility in her left limb, which she had not noticed before this instance. Seven days later, the patient suddenly experienced convulsions in the left upper limb and face, which lasted for several minutes and then resolved spontaneously, as well as dizziness, nausea, and headache. She received treatment at a local hospital, including intracranial pressure reduction, neurotrophic therapy, and epilepsy control. However, since her condition did not improve significantly, she was referred to our hospital for further treatment. Since the onset of symptoms, the patient remained conscious, fluent in speech, and without fever, convulsions, or incontinence; however, she reported headache, dizziness, poor appetite, and poor sleep.

The patient was conscious, articulate, and fluent during the nervous system examination. All examinations were normal. The eyelids were not drooping, the pupil diameter was 3.0 mm, and the light reflection and eye movements were normal. The facial expression was symmetrical, the mouth angle was not skewed, and the tongue was in the middle of the mouth. The neck was soft, the breathing sounds were clear, and the heart rhythm was consistent with no heart murmur. The abdomen was soft, without tenderness and rebound pain, the liver and spleen were not palpable, and there was no edema in the limbs. The muscle strength of the right side was V, and the muscle strength of the left side was IV. Physiological reflexes were present, and ataxia tests were normal. The patient had a history of diabetes and hypertension for 20 years, and laboratory examination results showed no obvious abnormality.

Brain magnetic resonance imaging showed an irregular and massive abnormal signal in the brain parenchyma of the right frontoparietal lobe, and the area surrounding the lesion showed annular enhancement, with an approximate size of 2.8 × 2.3 cm (Fig. 1). Other imaging showed that the tumor had metastasized to the liver (Fig. 2A), adrenal glands (Fig. 2B), ilium (Fig. 2C), lungs (Fig. 2D) and ribs (Fig. 2E). The tumor was completely removed during surgery, but the pathological results identified an intracranial mesenchymal tumor instead of a metastatic tumor or glioma. Since the tumors of other organs were multiple and had multiple small lesions and because the results of the pathology investigations fit the characteristics of primary intracranial mesenchymal tumors, we considered the tumors of the liver, adrenal glands, iliac crest, lungs, and ribs as metastatic. The patient unexpectedly died of tumor progression within 1 week after discharge.

Operative details

The patient was placed in a left lateral position while the right side was marked for frontal and parietal U-shaped skin incisions. After disinfection and laying the surgical towel, an approximately 20 cm-long incision revealed the frontal bone. The frontal bone flap (approximately 6 × 5 cm) was milled off

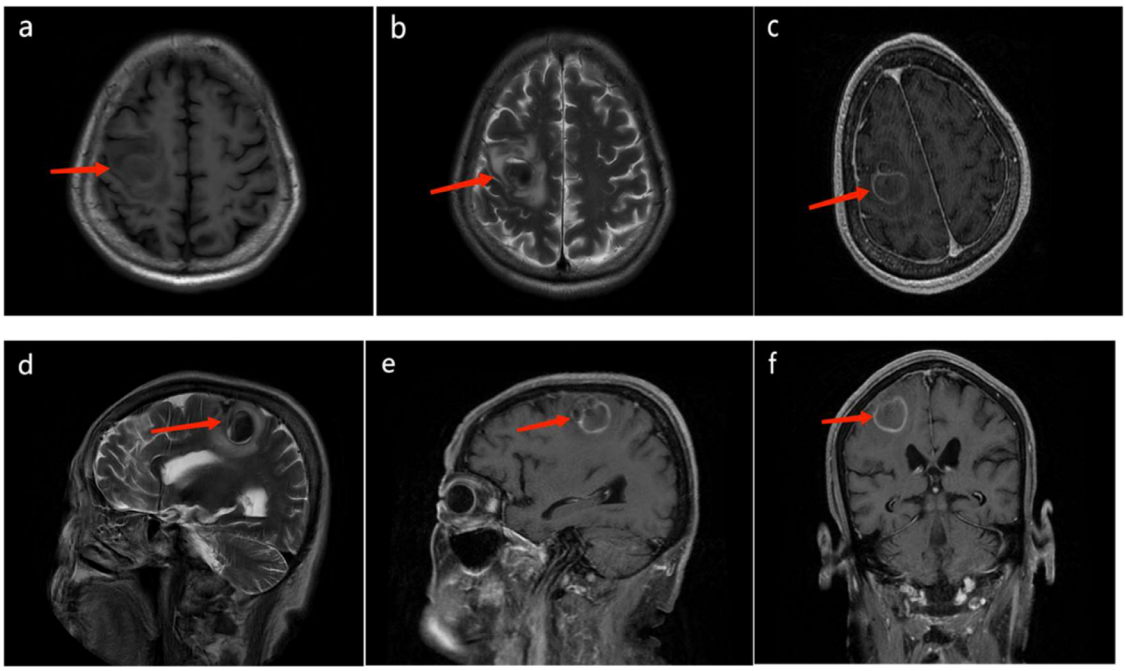

Fig. 1 – (A) The horizontal bit T1-weighted imaging presented a mixed isolow signal. (B) Horizontal T2-weighted imaging showed mixed high and low signals. (C) After intravenous injection of a contrast agent (Gd-DTPA), the focus showed noticeable ring-like enhancement, with a size range of approximately 2.8 x 2.3 cm. The boundary was clear, and finger cuff-like edema could be seen around the focus. (D) Sagittal T2-weighted imaging showed mixed high and low signals. (E) Sagittal images showed that the tumor was enhanced. (F) Coronal position showed that the tumor was located in the frontal lobe and temporal lobe and was enhanced.

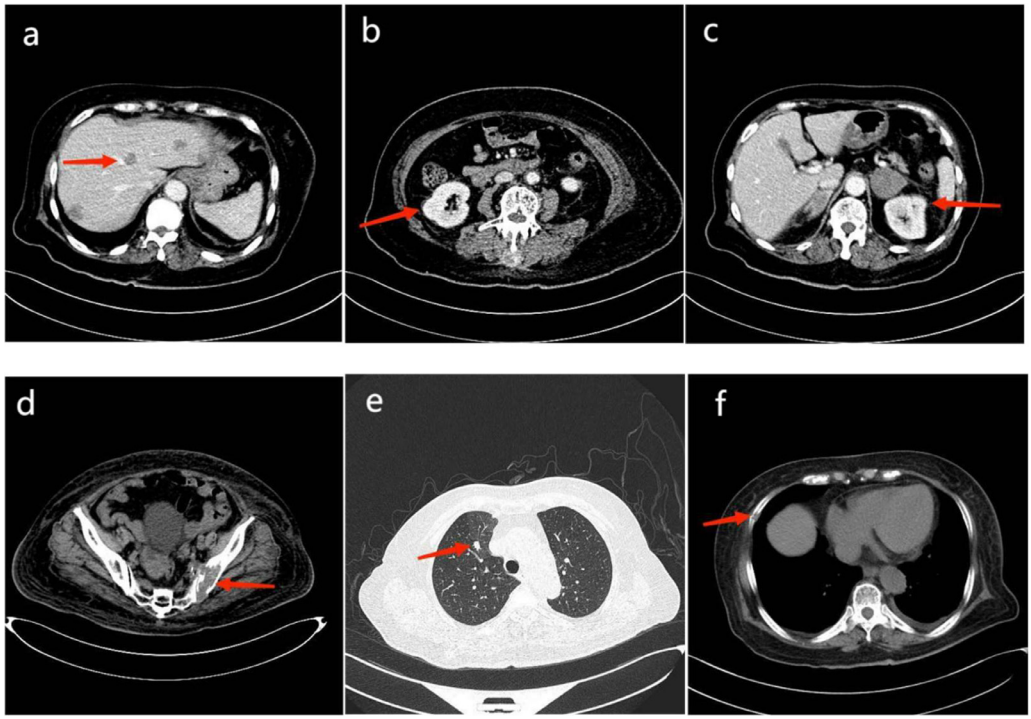

Fig. 2 – (A) Abdominal enhanced computed tomography revealed multiple slightly hypoattenuating lesions within the liver, with unclear borders and exhibiting mild ring enhancement after contrast administration. (B and C) Adrenal enhanced computed tomography demonstrated nodular high-density lesions, showing uneven mild enhancement. (D) A soft tissue density shadow was observed in the left iliac bone region, accompanied by adjacent bone destruction. Patchy high-density shadows were seen within both iliac bones. (E) A solid nodule was present in the apical segment of the right upper lung lobe, adjacent to a blood vessel. (F) Localized bone destruction was evident in the right sixth rib area.

with a milling cutter by drilling 4 times near the midline and at the top of the forehead (Fig. 3A). The dura mater was then cut with a cross, and the brain tissue was observed to be full. A purplish red tumor appeared at 3 cm beside the midline of the anterior central gyrus, and its boundary with the brain tissue was clear. The tumor broke through the brain's surface (Fig. 3B) and showed abundant blood supply, tough texture, and cystic solidity. The capsule contained dark red bloody fluid, with an approximate size of 4 × 3 × 3 cm. After operating along the tumor boundary, the entire tumor was removed successfully (Fig. 3C).

Histology and immunohistochemistry

After being fixed in formalin and embedded in paraffin, the tumor specimens were stained with hematoxylin and eosin (HE). Visual inspection revealed that the size of the resected intracranial space-occupying tissue was 18 × 16 × 10 mm, with a gray and grayish-yellow appearance and moderate texture. In addition, a broken gray-red tissue with a size of 15 × 7 × 5 mm was observed (Fig. 3D). Microscopic examination revealed that the tumor cells were closely arranged in solid sheets, and their shapes were primarily round, oval, and long-nucleated, with obvious nuclear atypia and giant cell tumors (Fig. 4A). The nuclei were vacuolar, and the nucleoli were evident and large. There were approximately 30 mitotic images in every 2 mm^2. No apparent necrosis was observed on the section. Immunohistochemical results showed that tumor cells were negative in keratin CK staining (Fig. 4B) and showed no positive reaction for glial fibrillary acidic protein (GFAP), dermal cell adhesion molecule EMA, S-100 protein, 0Lig-2, HMB45, Melan-A, SMA, desmin, actin, Bc1-2, CD99, and Sox-10 staining. However, the staining results were positive for vimentin (Fig. 4D) and CD34. The index of Ki-67 labeling in tumor cells was approximately 30% (Fig. 4C). Therefore, based on the data from the pathological morphology of the tumor and immunohistochemistry results of CK protein and vimentin, the pathologist believed that this tumor was an intracranial mesenchymal tumor.

Discussion

We present a rare case of intracranial mesenchymal tumor occurring in a 73-year-old woman. Although the patient promptly underwent surgical treatment, she succumbed to the tumor's rapid spread, characterized by its highly invasive nature and widespread metastasis to multiple sites in the body, which has not been previously described in the literature.

Intracranial mesenchymal tumor is a rare central nervous system tumor that has previously been described as intracra-

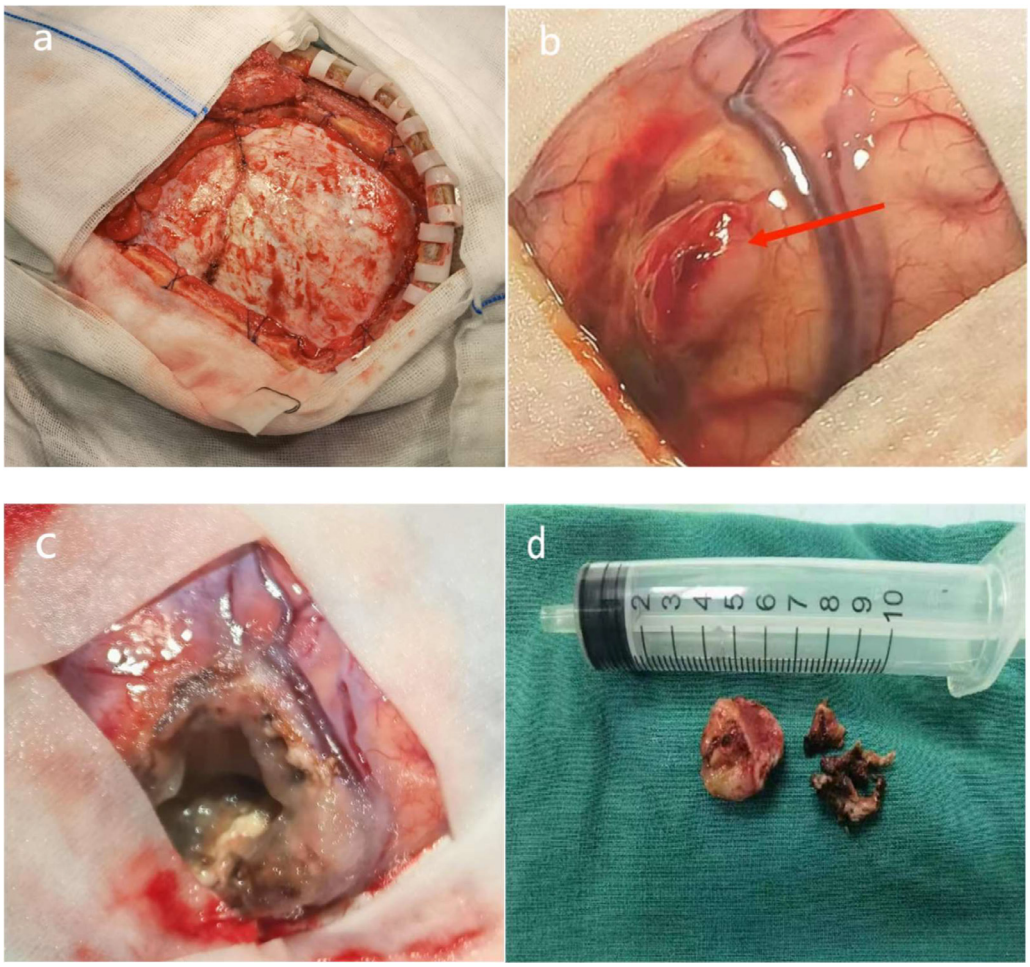

Fig. 3 – (A) The bone flap was opened during the operation. (B) After the dura mater was uncovered, the tumor was located in the frontal and temporal lobes. (C) The tumor was removed entirely. (D) The tumor after resection; its section was reddish brown.

nial vascular tumor-like fibrous histiocytoma, exhibiting immunophenotypic and molecular features similar to an angiomatoid fibrous histiocytoma (AFH) [1]. Although primarily originating from the deep dermis and subcutaneous tissues of the extremities, reports of this tumor in the intracranial region have also been documented, particularly in children or young individuals. These tumors have a relatively low mitotic activity and proliferation index and typically occur in the dura mater, with EWSR1-CREB being the primary gene fusion type [2,3].

This kind of tumor was only recently identified. In 2017, Kao et al. [4] proposed a new tumor entity with typical histological features inconsistent with AFH, reporting a series of mucinous mesenchymal tumors characterized by morphological and immunophenotypic features and demonstrating a significant predilection for intracranial ventricles in young patients, which suggested the existence of a novel pathological entity. In 2020, Komatsu et al. [5] described an atypical case that lacked typical histological markers such as pseudovascular spaces, lymphocytic cups, and fibrous pseudocapsule, suggesting a variant of mucinous AFH. Finally, in 2021, the World Health Organization designated this tumor as an intracranial mesenchymal tumor, FET-CREB fusion-positive. Essential diagnostic criteria were proposed: originating in the intracranial region; displaying variable morphology such as spindle cells, mucin-rich stroma, and vascular-like lumens; epithelial cells located in a mucin-sparse collagenous stroma; and FET-CREB gene fusion. Two additional entities were identified: primary intracranial sarcoma with DICER1 mutation and capicua transcriptional repressor-rearranged sarcoma, categorized as nonmeningeal mesenchymal tumors. Diagnosing nonmeningeal mesenchymal tumors based on morphology alone is challenging in clinical practice, as they often exhibit diverse morphological features. However, molecular techniques can be used to diagnose more accurately [6].

In previous case reports, most descriptions of intracranial mesenchymal tumors focused on their molecular features, with limited information on their clinical presentation [7]. Ochalski et al. [8] reported a case with multiple local recurrences and eventual death, but distant metastasis was not mentioned. Domingo et al. [9] presented a case of an EWSR1-CREB mutated intracranial tumor with evidence of invasiveness and rapid tumor growth on imaging. White et al. [10] reported another case where the tumor exhibited invasive

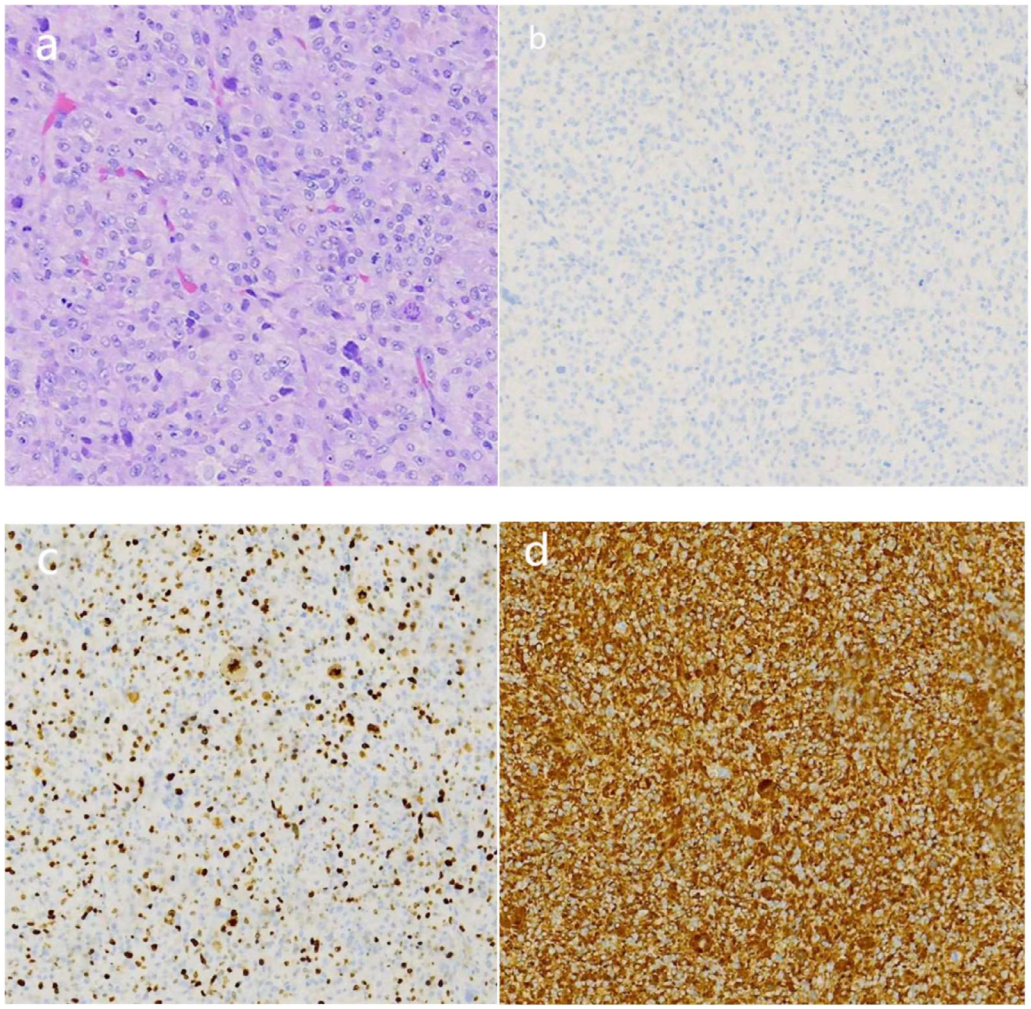

Fig. 4 – (A) Under 10 x magnification in HE staining, cells were densely arranged, exhibiting round, oval, and elongated nuclear shapes with significant variations in size and morphology. Giant cells were also visible. (B) Immunohistochemical staining showed negative expression of cytokeratin in cells. (C) Cells demonstrated apparent proliferative activity, with a Ki-67 index reaching 30%. (D) Immunohistochemical staining revealed a positive expression of vimentin in cells.

behavior, with complete initial tumor resection followed by local recurrence 6 months later. Sciot et al. [11] described the case of a 17-year-old girl with a 2.5 cm recurrent lesion discovered 20 months after complete tumor resection. There have been very few reports of local recurrence without distant metastasis.

The differential diagnosis of intracranial mesenchymal tumors includes vascular malformations, neurofibromas, solitary fibrous tumors, and meningiomas. A definitive diagnosis requires a combination of clinical, histological, and immunohistochemical findings. Typical histopathological diagnostic features of intracranial mesenchymal tumor are thick fibrous pseudocapsules, spindle, oval, or pleomorphic cells arranged in nests, pseudovascular spaces, and lymphocytic cuff-like infiltration. Specific gene fusions in intracranial mesenchymal tumor can be markers for clinical and pathological diagnosis [12]. The disease may be misdiagnosed or unidentified if diagnostic criteria are limited to pathological features and genetic, molecular, and immunohistochemistry characteristics are not considered. Preoperative imaging examinations may also misdiagnose mesenchymal tumors as meningiomas [13,14]. Some cases may be misdiagnosed in preoperative imaging examinations or intraoperative frozen sections, and many doctors may not consider the correct diagnosis, even if the imaging features of the lesion were discussed in detail before surgery [2]. In this case, because of the tumors found in multiple sites, we initially misdiagnosed it as intracranial metastasis, but the final result indicated an intracranial mesenchymal tumor. Therefore, it is crucial to increase awareness of the existence and characteristics of these tumors.

Due to the clinical and biological variability in the presentation of intracranial mesenchymal tumor, regular follow-up and assessment are essential. Currently, no standardized treatment protocols exist for intracranial mesenchymal tumors, and treatment selection is usually based on the patient's age, tumor size, location, invasiveness, and overall condition. Surgical resection, radiation therapy, and chemotherapy are currently used to treat intracranial mesenchymal tumors. Still,

the prognosis remains uncertain, highlighting the need for further research to enhance understanding and treatment of this disease.

Conclusion

This case is the first and only one to describe the highly invasive nature of intracranial mesenchymal tumors and their ability to metastasize to multiple sites in the body, resulting in a poor prognosis. We have provided clinical and pathological evidence of the tumor's behavior, offering further insights for neurosurgeons and pathologists.

Author contributions

Guo An Shen: Primarily responsible for initiating the research theme, conducting formal analysis, and taking the lead in writing and reviewing the initial draft. **Yan Zhao Li:** Managed patient clinical diagnosis and treatment, curated clinical data, and participated in writing the initial draft. **Gang Ren:** Oversaw patient clinical diagnosis and treatment and collected radiological data. **Mu Chun Wang:** Engaged in data collection and analysis and validated the conclusions. **Yi Man:** Assisted in clinical data collection. **Jing Bin Zhou:** Provided the primary resources for research and supervised the research progression. **Pi Tong Sun:** Played a significant role in reviewing the manuscript. **Wei Peng Lu:** Directed the collection and analysis of pathological data. **Xu Xin Zhang:** Initiated the research theme, supervised the research process, and managed the project, and final approval of the version to be submitted.

Patient consent

The next of kin has consented to publishing the case report in the journal.

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