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Clinicopathological Analysis of 2 Cases of Intracranial Mesenchymal Chondrosarcoma

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Abstract: *Objective* To analyze the clinical imaging data, pathological manifestations, molecular genetic characteristics and treatment of intracranial mesenchymal chondrosarcoma (MC), and to explore its diagnosis, differential diagnosis basis and clinical treatment plan. *Methods* The clinicopathological features, imaging data and immunophenotype of 2 cases of intracranial MC were retrospectively analyzed, and related literatures were reviewed. Results Both patients were admitted to hospital because of headache and limited vision. Imaging examination showed intracranial and extracerebral lesions (possible meningioma?). Microscopically, the tumor showed bidirectional differentiation and consisted of small round undifferentiated mesenchymal cells with basically the same size and scattered islands of relatively mature hyaline cartilage. Hemangiopericytoma conformation was seen in some areas. Immunophenotype: small round cells CD99 and vimentin (+), Ki-67 proliferation index 15% to 30%, PCK, Syn and NSE (-), chondrocytes S-100 (+), local expression of cartilage matrix collagen II. *Conclusion* Primary intracranial MC is extremely rare and easy to be misdiagnosed. It needs to be compared with meningiomas, extraosseous Ewing's sarcoma, solitary fibrous tumor/hemangiopericytoma, soft tissue malignant lymphoma, small cell metastatic carcinoma and other types of chondrosarcoma. Phase identification.

Keywords: Intracranial Tumor, Mesenchymal Chondrosarcoma, Clinicopathological Features

1. Introduction

Mesenchymal chondrosarcoma (MC) is a malignant tumor originating from primitive mesenchymal tissue with chondrogenic potential. First described by Lightenstein and Bernstein in 1959, it is composed of more mature hyaline cartilage islands and undifferentiated small round cells under the microscope. MC can originate from bone and extra-osseous tissue, and occurs in about 1/3 of all cases, mainly in the head and neck, lower extremities, and occasionally intracranial. Intracranial MC is difficult to diagnose preoperatively due to its rare and lack of specific clinical manifestations and imaging features, and it still needs to be differentiated from various small round cell malignant tumors and cartilage-derived tumors after operation. This article retrospectively analyzed the clinical data, imaging features, pathological features, and immunophenotypes of 2 cases of MC, and reviewed the relevant literature, in order to further improve the understanding of this tumor.

2 Materials and Methods

2.1 Clinical Data

Case 1 Female, 16 years old, no obvious incentive, was admitted to hospital with bilateral frontal, parietal, and occipital headaches, decreased vision, and projectile vomiting 4 months ago. Physical examination: decreased vision, double vision. The temporal visual field of the right eye disappeared, and the visual acuity of the left eye was normal. One-legged standing test was positive. Head CT showed an intracranial and extracerebral lesion above the tentorium of the left occipital cerebellum, with a size of 7.7

cm × 6.9 cm × 5.0 cm (Figure 1). Sheet-like high-density calcification, with uneven enhancement of solid components after enhancement, clear lesion boundaries, and low-density edema shadows can be seen in the peripheral brain parenchyma. MRI showed an irregular mass-like mass in the left occipital lobe, with shallow separation at the edge of the lesion, and the border was still clear. The enhanced scan showed obvious uneven enhancement, and the surrounding brain parenchyma, pons, and fourth ventricle were obviously compressed. The posterior crus of the lateral ventricle was compressed and flattened and moved forward. The left occipital lobe was closely related to the straight sinus and sinus confluence, and formed an indentation (Figure 1). Intraoperative findings: the tumor was gray-red, with a complete capsule, abundant blood supply, and a slightly tough texture. The tumor base was located next to the tentorial transverse sinus, and calcification was visible.

Case 2 Male, 43 years old. 28 years after the operation for right frontal meningioma, he was admitted to the hospital for 1 month with recurring headache, immobility of the left upper extremity, and double vision. Physical examination: decreased visual acuity in both eyes, double vision, and decreased fine movement of the left upper extremity. Head CT showed that the right occipital falx was seen as a lump with slightly high-density shadow, and the enhanced scan showed obvious enhancement, and a large area of low-density edema was seen in the surrounding brain parenchyma, the lateral ventricle was compressed, the midline was deviated to the left, and the brain

Tumor recurrence is possible. MRI showed a type of circular space-occupying lesion at the top of the right side.

The boundary is clear, the size of the lesion is 6.7 cm × 5.0 cm × 6.0 cm (Figure 2), and the blood supply is abundant and rich, uniform T1 signal, dominated by isointensity, with punctate hypointensity in it, enhanced scan lesions showed uniform and obvious enhancement, adjacent brain tissue was compressed, and the midline structure was left deviated (Figure 2). Intraoperative findings: the tumor was gray-red, with a complete capsule and an abnormally rich blood supply. The base was located in the falx cerebrum.

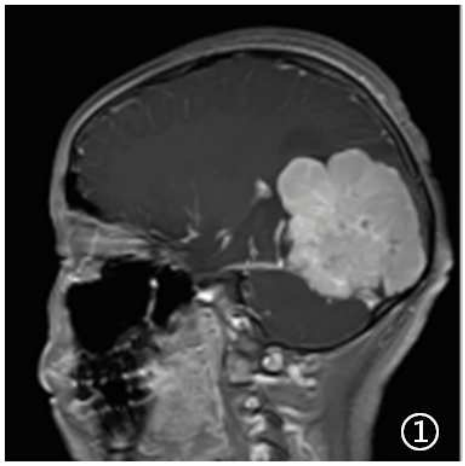

Figure 1. *CT and MRI images of case 1: The mass is located above the tentorium of the left occipital cerebellum, the size 7.7cm × 6.9cm × 5.0cm.*

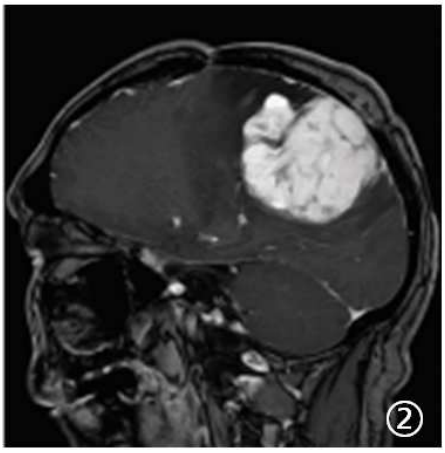

Figure 2. *CT and MRI images of the 2 cases: the mass is located in Right top, size 6.7cm × 5.0cm × 6.0cm.*

2.2. Methods

Specimens were fixed in 10% neutral formalin, embedded in paraffin, HE and immunohistochemistry EnVision two-step staining, light microscope observation. Antibodies used CD99, vimentin, Ki-67, PCK, Syn, NSE, S-100, collagen II were purchased In Fuzhou Maixin Company, the specific operation steps are carried out according to the kit instructions.

3. Results

3.1. Eye View E

xample 1: A pile of gray-red broken tissue, size 12.5cm × 11cm ×2.5cm, gray-red cut surface, soft. Example 2: A pile of gray-red shredded tissue, the size 6.5 cm × 5.5cm × 3.0 cm, the cut surface is gray-red and soft.

3.2. Microscopic Examination

2 cases showed of juvenile undifferentiated small round cells with patchy distribution under the microscope cells with scattered hyaline cartilage islands (Figure 3). Undifferentiated tumor cells are small round or short spindle-shaped (Figure 4), basically the same in shape and size, rare cytoplasm, hyperchromatic nuclei, densely arranged cells, and block-shaped, with abundant blood vessels in some areas resembling a hemangiopericytoma-like conformation, chondrocyte foci vary in size and shape, with mature differentiation and abundant hyaline cartilage matrix, and the small round or spindle tumor cells demarcation is not clear.

3.3. Immunophenotype

2 cases of small round cells CD99 (Figure 5) and vimentin (+), PCK, Syn and NSE (-), chondrocytes S-100 (+) (Figure 6), The cartilage matrix expresses collagen II in the local area, and the Ki-67 proliferation index is 15% ~30%.

3.4. Follow-Up

Case 1 died of complications on the 10th day after

operation, and case 2 Relapses again 7 months after operation, in poor condition.

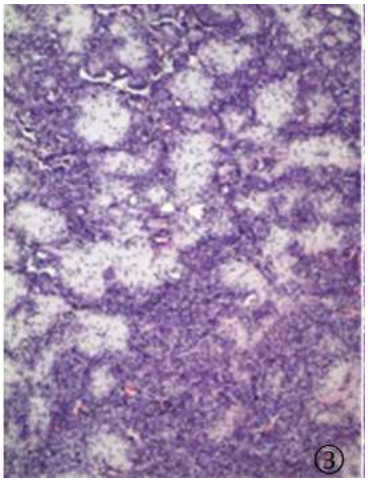

Figure 3. *The well-differentiated cartilage area and the undifferentiated mesenchymal cells are alternately distributed. The mesenchymal cells are small round, basically the same size, and are closely arranged in pieces; scattered cartilage islands are relatively mature.*

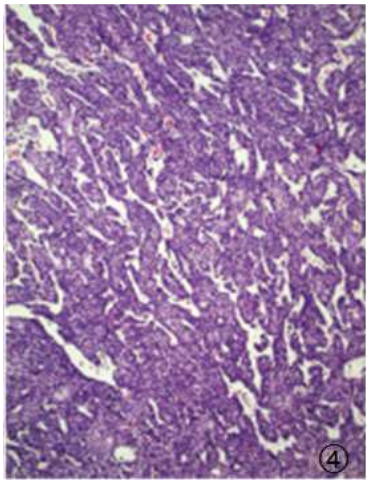

Figure 4. *The mesenchymal cells in some areas are round or short spindle-shaped, with extravascular appearance Skin tumor-like arrangement.*

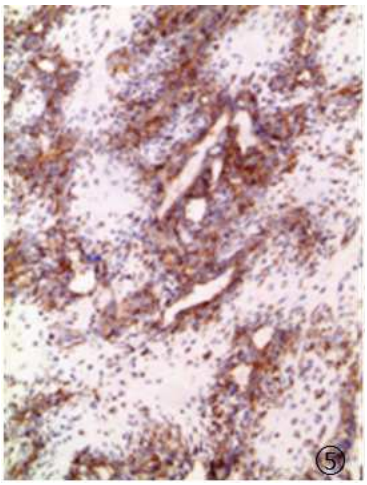

Figure 5. *Undifferentiated small round cells positive for CD99, EnVision two-step.*

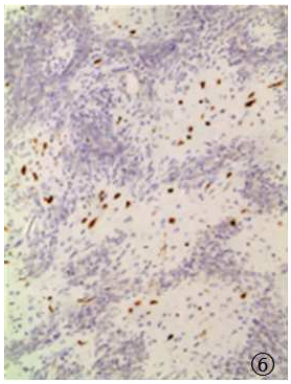

Figure 6. *S-100 positive chondrocytes in cartilage islets, EnVision two-step method.*

4. Discussion

MC is a rare malignant mesenchymal tumor that accounts 2% ~ 10% for the majority of primary chondrosarcoma, the incidence rate is 0.2 ~ 0.7/100,000. It is more common in the ribs, spine, mandible, pelvis, and femur, and rarely occurs in extra-osseous soft tissue, and intracranial primary is even rarer. It has been reported in the literature that chondrosarcoma at the base of the skull may originate from the cartilage of the base of the skull, which can be either chondrosarcoma at the origin, or malignant transformation of chondroma; there are also very few reports of fibochondrosarcoma or chondrosarcoma induced by postoperative radiotherapy in patients with meningioma [1]. The 2th patients in this group developed MC 28 years after meningioma. In the past 40 years, about 60 cases of intracranial chondrosarcoma with clear treatment data and follow-up records have been reported in the literature [2, 3], the youngest was 2 months [2], and the oldest was 71 years old [4]. Between 10 and 30 years old, the average age is 24.1 years old, and the lesions are mostly in the telencephalon.

Imaging examination: CT scan showed an oval or lobulated soft tissue mass with slightly low density, plaque calcification or ossification, and the tissue between calcifications showed low, isodensity, with clear boundary, and some cases of mass It is connected with the skull base by a wide base, and can invade inside and outside the skull. After enhancement, the area without calcification shows mild uneven enhancement. The more calcified components, the more mature the tumor differentiation, and vice versa. On MRI T1-weighted images, the tumor showed mixed shadows of equal and low signal, while T2-weighted images showed mixed shadows of high and low signals, and the calcified areas in the tumor were no signal areas. Slightly heterogeneous enhancement after enhanced scan, no enhancement in the calcified area. Cerebral angiography showed that the tumor was rich in blood supply and variable vascular distribution. It is difficult to distinguish it from meningiomas on imaging [5]. CT and MRI of the 2 cases in this group both showed intracranial and extracerebral mass, the tumor edge was smooth, and the base of the mass was connected to the meninges during the operation, so

meningiomas were considered in both imaging and clinical diagnosis.

Microscopically, MCs are characterized by bidirectional differentiation and consist of small undifferentiated cells and hyaline cartilage islands with different degrees of differentiation. Undifferentiated mesenchymal cells are round or short spindle-shaped, with rare cytoplasm, round or oval nuclei, hyperchromatic, inconspicuous nucleoli, and rare mitotic figures. Small round cells can be seen scattered scattered hyaline cartilage islets, cartilage islets of varying sizes, uneven distribution. Some cartilage islets were differentiated and mature, showing cartilage lacuna, and some cartilage islets were poorly differentiated, and the cells were similar to undifferentiated small round cells. The boundary between undifferentiated cells and cartilage islets is not clear, and tumor cells can be seen in the transition zone to form cartilage. In some areas, tumor cells can be seen around blood vessels in a hemangiopericytoma-like structure. Immunohistochemistry may help make a definitive diagnosis. Sox9 is useful as a specific immunohistochemical marker because MCS can show strong nuclear reactivity for SOX9, indicative of a chondroid lineage [6]. Madiha et al [7] reported NKX3.1 is a useful immunohistochemical marker in differentiating mesenchymal chondrosarcoma from its histological mimics.Also, it showed chondrocytes S-100 (+), small round cells CD99 and vimentin (+), Collagen II in the small cell area and cartilage area (+). Microscopically, it needs to be differentiated from a variety of tumors. (1) Meningiomas: associated with cartilage and bone Metaplastic meningiomas are indistinguishable from MC on imaging, but immunohistochemical markers suggestive of EMA, SSTR2 and PR (+), S-100 (-) and lack of MC characteristic bidirectional differentiation can help identify. (2) Extraosseous Ewing's sarcoma: microscopically uniform small blue cells with the similar immunophenotype as MC, but common primitive neuroectodermal rosette-like structures and lack of cartilage islands, NKX3.1 expression was not seen in any case of Ewing's sarcoma [7] for identification. And extraskeletal Ewing sarcoma fluorescence in situ hybridization detection can show EWSR1 gene translocation. (3) Solitary fibrous tumor/ hemangiopericytoma: tumor cells are round, oval or spindle-shaped, irregularly arranged around blood vessels, lacking scattered cartilage islands and positive for CD34 and STAT6, which can be differentiated from MC. (4) Malignant lymphoma of soft tissue: The tumor cells are diffusely distributed, and there is no connection between the cells and a thin fibrous stroma is formed. Positive CD45 and B or T lymphocyte-associated antigens are helpful for diagnosis. (5) Small cell metastatic carcinoma: It often occurs in males aged 50 to 60 years. The tumor cells are distributed in solid, nested or cord-like shape, and a rosette-like structure can be seen locally. Differential diagnosis Mainly based on immunophenotype: metastatic cancer cells CK or CgA, Syn, NSE, CD56 and TTF-1 (+), CD99 (-). (6) Synovial sarcoma: it can also be morphologically Hemangiopericytoma-like arrangement and sheets of short spindle cells, accompanied by regional calcification or cartilage metaplasia, are easily confused with MC, but the immunophenotypes of CK and EMA are both (+), detected by fluorescence in situ hybridization A SYT-SSX fusion gene was shown to aid in the identification.

The genetic abnormality of MC is mainly manifested as chromosomal variation, among which Robert-sonian13;21 chromosomal translocation is common, but the form of variation varies greatly. Gatter et al [8] reported that chromosome 8 may be the only cytogenetic mutation in the disease. However, other chromosomal translocations have been reported, such as t(4;19) (q35;q13), t(6;10) (p21;q22) and t(1;5) (q42;q32) [9-11]. Nyquistet al [10] reported a case of MC showing t(1;5) (q42;q32) as the only karyotype aberration, and found a new fusion between IRF2BP2 and IRF2BP2 by fluorescence in situ hybridization detection and whole transcriptome sequencing analysis. A translocation between the transcription factor CDX1 gene was subsequently confirmed by Panagopoulos et al [12]. In addition, Wang et al [13] found HEY1-NCOA2 fusion gene in recurrent cases, especially in an atypical clinical and histological context. The chimeric fusion is generated from an intra-chromosomal delection between exon 4 of HEY1 (8q21) and exon 13 of NCOA2 (8q13). This fusion is specific for MCS, and has not been found in other types of CS, such as dedifferentiated or conventional CS. The IRF2BP2-CDX1 fusion has aiso been identified in MCS, and was reported in a HEY1-NCOA2-negative case pf MCS. This fusion is generated by a translocation between exon 1 of the IRF2BP2 gene on chromosome [14].Atsuhito et al [15] reported a case of Intracranial mesenchymal chondrosarcoma diagnosed by HEY1-NCOA2 gene fusion, IRF2BP2-CDX1 fusion and IDH1/2 mutations were negative.

MC has a poor prognosis and is prone to local recurrence and distant metastasis. Treatment includes surgery, adjuvant chemotherapy, and radiation therapy. If surgery cannot be completely removed, postoperative radiation therapy can reduce the risk. Salvati et al [4] counted 55 cases of intracranial MC and found that 23 patients who received postoperative radiotherapy had a longer survival time. Some studies have suggested that radical excision followed by adjuvant radiotherapy increase 5-year survival rates [16]. Herrera et al [17] believed that adjuvant chemotherapy could be used for cases with rapid recurrence and metastasis. Studies have shown that chemotherapy combined with radiotherapy is effective for poorly differentiated MC, and neoadjuvant chemotherapy combined with surgery is also effective for well-differentiated tumors [18]. At present, the number of cases of γ-knife in the treatment of intracranial and extraskeletal MC is gradually increasing. Although only a few cases have been reported so far, γ-knife has shown a better therapeutic effect through postoperative follow-up [19]. Xiao et al [20] also believed that the efficacy of the combination of γ-knife surgery and radiotherapy was worthy of recognition, and the patients had no obvious postoperative neurological deficit and evidence of rapid recurrence after treatment.Recent studies have considered IDH mutations as a

target for the treatment of chondrosarcomas [21].

5. Conclusion

Intracranial mesenchymal chondrosarcoma are rare entities and highly aggressive.As with the tumor, surgery and radiotherapy with or without chemotherapy may lead to a favorable outcome.

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