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CASE REPORT

Mesenchymal Chondrosarcoma arising in the Central Nervous System: A Diagnostic Pitfall

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ABSTRACT

Mesenchymal chondrosarcoma is a rare aggressive neoplasm affecting the bones of young adults. It also arises extraskeletal in CNS, soft tissue and other organs. Intracranial and those that originate from the dura mater are very rare. These tumors constitute an entirely different entity from classical chondrosarcoma. These are characterized by a bimorphic histological pattern composed of highly undifferentiated small round to oval cells and islands of well-differentiated hyaline cartilage with calcification and ossification. We hereby report a case of mesenchymal chondrosarcoma arising from the right tentorium cerebelli in a 40-year-old man with symptoms of mass effect. Histological examination demonstrated sheets of round to oval cells with islands of hyaline cartilage. The diagnosis of mesenchymal chondrosarcoma was made after a thorough microscopic assessment. Tumor in addition to cellular component also revealed a prominent cartilaginous component. We hereby discuss the morphological features of mesenchymal chondrosarcoma arising in the CNS, the differential diagnoses of small round-cell tumors within the CNS, and the differentiating features of mesenchymal chondrosarcoma from the other differential diagnoses.

Keywords: Mesenchymal chondrosarcoma, Small round to oval cell tumor, Meninges.

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INTRODUCTION

Mesenchymal chondrosarcoma is an aggressive tumor which mostly, but not exclusively, involves our skeletal system. Intracranial mesenchymal chondrosarcoma is an unusual but weIl-defined tumor. Involvement of the CNS by this tumor is extremely rare however, it is the most commonly reported extraosseus site of this tumor.[1-4]

Histologic subtypes are, conventional, dedifferentiated, clear cell and mesenchymal.[5] The conventional variety is the commonest and the mesenchymal variant is the rarest. The dedifferentiated and clear cell variants have not been reported in the CNS. Originally described by Lichtenstein and Bernstein in 1959, mesenchymal chondrosarcomas have been conventionally regarded to be a neoplasm of the bone.[6]

Both skeletal and extraskeletal tumors exhibit similar morphologic features. Though variations are common but a characteristic bimorphic pattern is described on microscopy, with islands of hyaline cartilage interspersed with diffuse sheets of undifferentiated small round to oval cells. The cartilaginous element is relatively well-differentiated and may resemble mature hyaline cartilage or low-grade chondrosarcoma. The transition between the cellular and cartilaginous components may be quite abrupt. Diagnostic pitfalls arise when only one of the two characteristic components is sampled for histological examination. Immunohistochemical staining is not very helpful, the small round cells stain positive for CD99, vimentin and leu.[7] No characteristic molecular marker reliably differentiates it from other round blue cell tumors of the CNS. Thus, the pathological identification relies mainly on the characteristic biphasic pattern.

CASE REPORT

A 40-year-old man, presented with history of headache, vomiting and blurring of vision for 1 month. He was treated with medication but symptoms persist and the headaches increased in severity. CT scan showed a dural based lobulated, enhancing lesion in temporopariatal region with moderate surrounding edema and midline shift (Fig. 1). A differential diagnosis of atypical meningioma was raised on radiological assessment. Patient underwent craniotomy. The mass was found to be adherent to the dura. Complete surgical resection was done.

Histological sections showed a hypercellular lesion composed of sheets of crowded hyperchromatic ovoid to spindle cells displaying some nuclear molding, finely to coarsely granular chromatin, inconspicuous nucleoli and scanty cytoplasm. Staghorn vasculature was evident. The lesion was seen to be attached to the dura. Sections also showed loosely arranged hypercellular lobules of chondroid cells (Fig. 2), with a rare showing binucleation and areas of calcification and ossification. No mitoses or rosette formation was identified. Immunohistochemical stains were performed using standard protocols. CD99 showed focal strong membranous immunoreactivity (Fig. 3). There was also positive staining with synaptophysin, and focal staining with CD56 and vimentin. Immunostaining for neurofilament protein, cytokeratin, neuron sensitivity enolase (NSE), epithelial membrane antigen (EMA) were negative. Ki-67 proliferation index was 25%. Differential diagnoses included medulloblastoma, monophasic synovial sarcoma, hemangio-

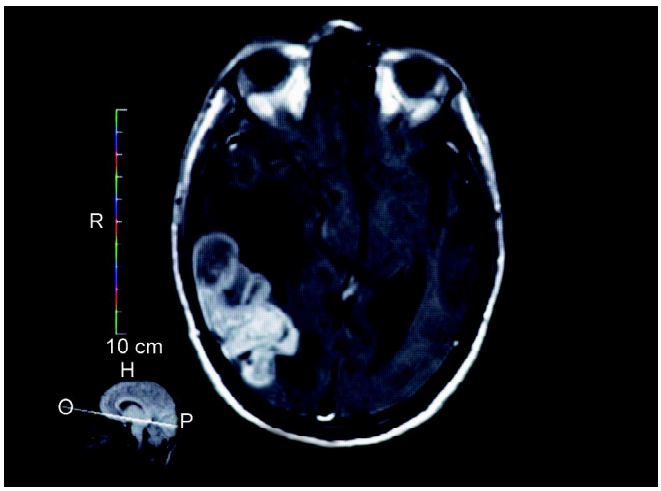

Fig. 1: CT scan showing a dural based lobulated, enhancing lesion in temporoparietal region

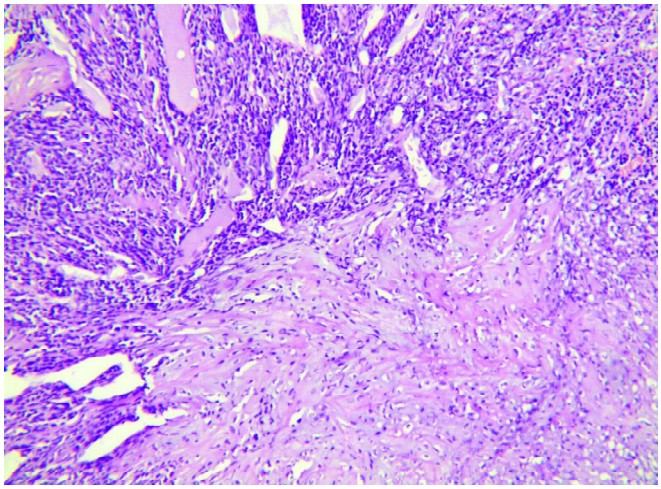

Fig. 2: A tumor composed of small round to oval cells with a cartilaginous component (hematoxylin and eosin stain)

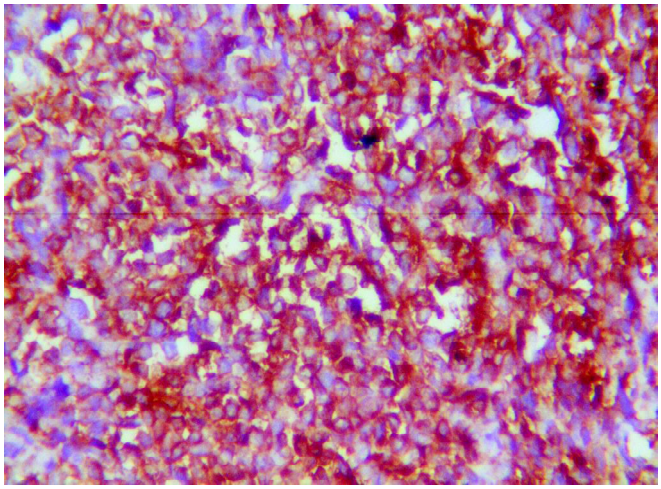

Fig. 3: Positive staining for CD99 immunohistochemical stain

pericytoma, meningioma and atypical teratoid/rhabdoid tumor. However, these were deemed unlikely given the PAS positivity of the tumor cells and results of the immunoperoxidase panel. The chondroid cells showed positive nuclear staining with S100.

The combination of hypercellular zones of anaplastic small blue to oval cells and islands of hyaline cartilaginous tissue showing mild atypia seen in this case were highly suggestive of mesenchymal chondrosarcoma.

DISCUSSION

Mesenchymal chondrosarcoma is a rare malignant tumor which usually affects young adults in their second to third decades.[5,6] It has traditionally been regarded as a neoplasm of bone. However, extraosseous examples involving areas such as somatic soft tissues, mediastinum, reported in the literature in recent years,[7,8] CNS is now considered the most common site of extraosseous mesenchymal chondrosacroma.[9] The CNS can be involved by direct extension from a nearby primary osseous (cranial or spinal), a lesion of dural origin, or by arising directly within the brain parenchyma.[10]

Macroscopically mesenchymal chondrosarcomas show a firm, lobulated variegated red-brown gray surface.[1] They appear well-circumscribed, but they may infiltrate brain or invade adjacent bones.

Morphological assessment of both extraosseous and osseous lesions showed the same characteristic biphasic appearance.[11] The two elements are composed of islands of hyaline cartilage and sheets of undifferentiated round to oval small cells.[5,6,9] The cartilaginous component is well-differentiated and may appear as benign hyaline cartilage, low-grade chondrosarcoma.[5] Staghorn vascular spaces are characteristic of these lesions. The two characteristic components can show an abrupt transition; however, occasional cases show a gradual merging of the two components. More importantly, presence of each component is highly variable and diagnostic problems arise when a limited biopsy only shows one component.

Histochemical and immunoperoxidase profile of mesenchymal chondrosarcoma is not very helpful in distinguishing it from other differential lesions.

Mesenchymal chondrosarcoma is a very difficult tumor to be diagnosed as the histological appearance is quite similar to hemangiopericytoma and angioblastic meningioma. These neoplasms are usually misdiagnosed.[1,12,14]

A tumor composed of round to spindle cells arising in the brain raises several differential diagnoses. These include Ewing sarcoma/PNET, medulloblastoma, hemangiopericytoma, monophasic synovial sarcoma, menengioma and atypical teratoid/rhabdoid tumor. Our case was further complicated as it showed several mutual clinical, radiological and pathological features of meningioma. Furthermore, CD99, a characteristic IHC stain positive in Ewing sarcoma/PNET, may also be seen in other tumors such as mesenchymal chondrosarcoma, hemangiopericytoma and synovial sarcoma.[9,15]

Hemangiopericytoma is also a meningeal-based tumor. It show characteristic staghorn vessels with spindle to oval cells which may be seen in mesenchymal chondrosarcoma.[15] Morphological criteria that will help to differentiate a chondrosarcoma from a hemangiopericytoma are very subtle; however, the presence of well-defined nodules of well differentiated, benign appearing hyaline cartilage, with frequent central clacification and ossification and the presence of positive PAS staining in our case made this diagnosis unlikely.[16]

Medulloblastoma is also another important differential diagnosis, as it shows sheets of similar round blue cells, and Homer-Wright rosettes are only present in less than 40% of cases. However, medulloblastoma was thought to be unlikely in our patient due to the dural-based location, presence of glycogen-rich cytoplasm and CD99 positivity.[13,15]

Monophasic synovial sarcoma may also display a prominent hemangiopericytomatous vascular pattern, cytokeratin and EMA positivity, all of which were lacking in our case.[6]

Our case also lacked rhabdoid cells and EMA positivity, which ruled out the possibility of atypical teratoid/rhabdoid tumor.[9]

Rushing et al in clinicopathological study of 13 cases of CNS mesenchymal chondrosarcoma focal S100 in the cartilaginous component in all cases and CK and GFAP positivity in 25% cases.[17]

Use of immunohistochemistry and electronmicroscopy is often not helpful. So there is an increasing reliance on the utilization of molecular testing, and these include RT-PCR, looking for EWS-FLI1 and EWS-ERG (or other EWS variants) fusion transcript, and FISH, looking for characteristic chromosomal translocation t(11;22)(q24;q12) or other variant translocations, such as t(21;22)(q22;q12).[6,16] Sensitivities and specificities of 91 and 100%, respectively, have been reported with FISH, and this is considered a confirmatory test if positive.[15] However, it is noted that 5% of these tumors have no detectable chromosomal translocation and in these cases, making the correct diagnosis is quite challenging.[18]

Nearly 50 cases of intracranial mesenchymal chondrosarcoma have been reported in the literature. However, clinicopathologicoradiological details of some earlier cases are vague and unclear. It is hoped that there will be more reports in the future that will help in raising the awareness of this entity within the CNS.

Prognosis of mesenchymal chondrosarcoma is poor. These tumors show aggressive behavior as compared to other chondrosarcomas.[19,20]

Scheithauer and Rubinstein were the first to notice in 23 patients which were followed for 3 years that long-term disease free survival is of limited significance.[13] Out of 23 patients 15 had local recurrences. Spinal or distant metastasis occurred in 65%.

Kabayashi et al in his case report described one patient who had local recurrence twice, 13 and 16 years after initial resection. Patient died after 18 years.[18]

Radical removal is the management of choice. Preoperative embolization may be useful when the tumor is highly vascular.[1,21] Postoperative radiotherapy has also shown better outcome in some cases. Considering that these tumors have an aggressive behavior and as these are radiosensitive in some cases[3] radiotherapy has been indicated especially after subtotal resection.

CONCLUSION

Extraskeletal mesenchymal chondrosarcoma is a malignant neoplasm which is rarely encountered in the CNS. It pursues an aggressive clinical course and metastasizes in high percentage.[3] Among 5 and 10 years survival rates of 54.6 and 27.3% respectively have been reported.[3] Experience with cranial or spinal mesenchymal chondrosarcoma is limited. Mesenchymal chondrosarcoma should be considered in the differential diagnosis of any small dural or parenchymal based, spindle to round cell lesion. Correlation with the clinical and radiological information is mandatory, especially to ascertain that the lesion has been removed completely. Adequate material to assess morphology, displaying both cellular and cartilaginous components, appropriate immunohistochemistry and molecular testing are mandatory to exclude other differential diagnosis. A high index of suspicion is the mainstay to the diagnosis of this rare entity.

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