Intracranial extraskeletal mesenchymal chondrosarcoma

Ahmed Waliuddin, MBBS, MD (NS), *Abdulhakim B. Jamjoom,* MD, FRCS (SN), *Jaiyeola Thomas,* MD, FRCPath.

ABSTRACT

Intracranial extraskeletal mesenchymal chondrosarcoma is a rare malignant variant of chondrosarcomas. We present a 5-year-old Saudi male child who was brought to the Emergency Department with the complaints of headache, irritability, vomiting, and unsteadiness of gait with right hemiparesis. Radiological studies confirmed the presence of a space-occupying lesion in the left cerebral hemisphere of the brain. Through a left temporoparietal craniotomy a total macroscopic excision of the tumor was carried out, and the tumor was found attached to the dura at the base of the temporal fossa. The tumor was well circumscribed, extra axial in location, and was easily dissected from the other part of the brain. The histopathological examination revealed the tumor to be a mesenchymal chondrosarcoma. This rare tumor of the pediatric age group should be included in the differential diagnosis of all intracranial tumors with aggressive characteristics.

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Sarcomas of the brain and meninges are generally regarded as arising from pluripotential mesenchymal cells, or from their more differentiated descendants. These cells and their derived connective tissues form the dura, the leptomeninges and the pia-arachnoid extensions that surround the perforating cerebral blood vessels in the Virchow – Robin spaces. Fibroblasts, arachnoidal, and pial cells are therefore, the potential cellular sources of intracranial sarcomas.[1] The primary cartilaginous tumors of the central nervous system - chondroma, chondrosarcoma, mesenchymal chondrosarcoma, and myxoid chondrosarcoma constitute 0.16% of all the cranial and intracranial neoplasms.[2,3] Mesenchymal chondrosarcoma is a distinct, rare malignant neoplasm which is thought to have been derived from primitive cartilage mesenchyme and constitutes a very small subset of intracranial neoplasms. Although these tumors were initially thought to be tumors of the bone, almost half of them have an extra osseous origin, hence, the term extraskeletal mesenchymal chondrosarcoma. To date, 39 cases of intracranial extraskeletal mesenchymal chondrosarcoma have been reported in the published literature. In this study, we are reporting a case of intracranial extraskeletal mesenchymal chondrosarcoma in a child. We have included in our review those previously reported cases as well as ours, which were either dural in origin or were freely lying in the parenchyma and not associated with radiographic or surgical evidence of bony origin.

Case Report. A 4-year-old Saudi male child was brought to our hospital with a 2-month history of headache, dizziness, vomiting, irritability, and unsteadiness of gait. In addition, he had developed urinary incontinence and inability to hold objects with his right hand. He had no significant neonatal or

From the Section of Neurosurgery (Waliuddin, Jamjoom), Department of Surgery, and the Department of Pathology (Thomas), King Khalid National Guard Hospital, Jeddah, *Kingdom of Saudi Arabia*.

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Address correspondence and reprint request to: Dr. Ahmed Waliuddin, Assistant Consultant Neurosurgeon, Section of Neurosurgery, Department of Surgery, King Khalid National Guard Hospital, PO Box 9515, Jeddah 21423, *Kingdom of Saudi Arabia*. Tel. +966 (2) 6240000 Ext. 2071. E-mail: a_waliuddin@yahoo.com

family history. On examination, he was conscious and oriented with mild right hemiparesis. Funduscopy was normal, and there was no cranial nerve involvement. Routine laboratory investigations, namely, serum urea and electrolytes, complete blood count, and liver function tests were within normal limits. Plain x-ray of the skull showed a 'beaten copper' appearance and coronal suture diastases. A plain CT scan (**Figure 1a**) of the brain showed a large left temporoparietal mass measuring 9 x 8 x 6 cms. The lesion was hypodense causing compression of the left lateral ventricle and dilatation of the contralateral ventricle with periventricular lucency. The contrast CT scan was not carried out initially because the child was not sedated adequately. After appropriate sedation, MRI of the brain was carried out with and without gadolinium. The MRI (**Figures 2a & 2b**) confirmed the presence of a large concentric left temporal contrast-enhancing tumor causing midline shift towards the right side with evidence of subfalcine and impending uncal herniation. Soon after the MRI, the patient underwent a left temporoparietal craniotomy, and total macroscopic excision of an extrinsic, soft and moderately vascular tumor was performed. The base of the tumor was found adherent to the dura, which was easily detached from it, and the area of attachment was thoroughly cauterized. The patient tolerated the operation well, and there were no postoperative complications. The immediate postoperative CT scan (**Figure 1b**) showed no residual tumor. A metastatic work up was carried out post operatively, which did not show any evidence of metastases. An oncological referral was made, and radiotherapy was given. The target volume was defined by CT planning and a total dose of 5040 cGy, spread over 28 fractions using 180 cGy per fraction were given. Three months after surgery, the patient was admitted elsewhere following deterioration of his level of consciousness. A CT scan of the brain carried out at that time showed extensive tumor recurrence. As a result of the early extensive recurrence of tumor following surgery and radiotherapy and the relatively poor clinical status of the patient, further surgery and adjuvant therapy were not considered judicious. The patient ultimately died 4 months following the original presentation.

Histopathological examination. The tumor was lobulated and biphasic with well differentiated cartilaginous areas alternating with cellular areas consisting of small oval to spindle shaped mesenchymal cells with hyperchromatic nuclei in an interlacing and hemangiopericytomatous pattern. Foci of cellularity showed abrupt cartilaginous differentiation (**Figures 3a & 3b**). The tumor showed areas of necrosis with peritheliomatous aggregates of residual tumor cells. The tumor appeared to arise from the dura, which has large congested peripheral vascular channels, some of which are thrombosed. Immunostaining showed strong positive reaction of the cellular areas with vimentin, S-100 reaction was particularly marked in the chondroid areas and GFAP showed positivity in the cellular and chondroid areas. The diagnosis of extraskeletal mesenchymal chondrosarcoma was established.

Discussion. The term mesenchymal chondrosarcoma was coined by Lichtenstein and Bernstein[4] in 1959, based on their findings of a group of unusual chondroid tumors of the bone, which microscopically showed poorly differentiated spindle connective tissue with focal areas of cartilage or chondroid matrix. Although they were first thought to be tumors of the bones, it is now apparent that almost 50% of these tumors occur in extraskeletal sites.[1] According to Guccion et al,[5] of the 75 cases of mesenchymal chondrosarcoma reported in the literature up to 1973, nearly half were extraskeletal in origin. For the sake of convenience, the extra skeletal sites can be separated into 2 types – those occurring in the muscles and soft tissues and those occurring in the central nervous system (CNS). The most common location of the mesenchymal chondrosarcoma in the CNS is the craniospinal meninges, and the first report of an intracranial mesenchymal chondrosarcoma was in 1962 by Dahlin and Henderson.[6]

The other chondrosarcomas encountered intracranially are the classic chondrosarcomas and the myxoid chondrosarcomas. The classic chondrosarcomas are tumors of the elderly occurring between 40-60 years of age with a male preponderance. It occurs more frequently at the base of the skull, is usually avascular, and does not show any 'tumor blush' on angiography. This tumor is locally invasive, and recurrences are known to occur. Histologically, they differ from mesenchymal chondrosarcomas in their greater pleomorphism, with maturity of cartilage cells and less prominent cellular stroma.[3]

Mesenchymal chondrosarcomas are tumors of the younger age group ranging from 10-30 years with an almost equal sex distribution.[1,7] These tumors are usually found in the supratentorial compartment and are mostly attached to the meninges. The gross appearance of these tumors, as observed at operation, is described as circumscribed masses with a smooth knobby surface, firm on palpation and variable in color from grey to red. The cut surface is usually gritty due to focal calcification and often described as chondroid. In our case, the above description was observed.[1,2,7] The usual presentation of the intracranial

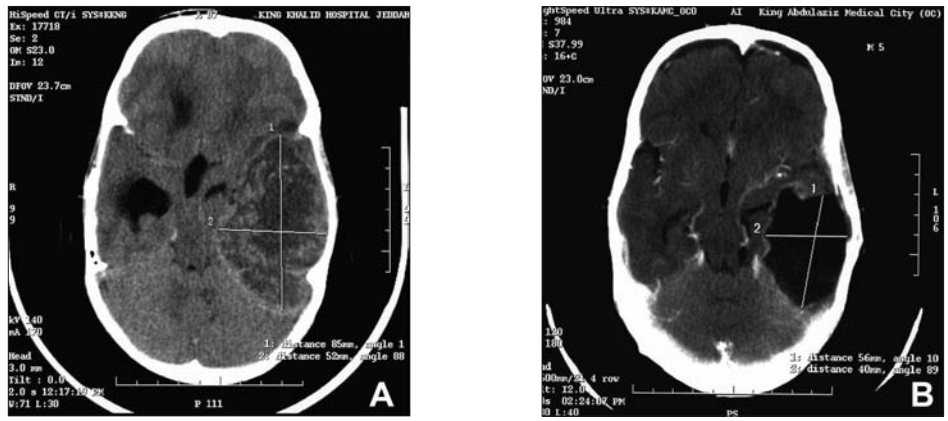

Figure 1 - **(A)** Non-contrast CT scan showing a large left temporoparietal extra-axial mass. **(B)** A post-operative contrast enhanced CT scan showing gross total excision of the mass.

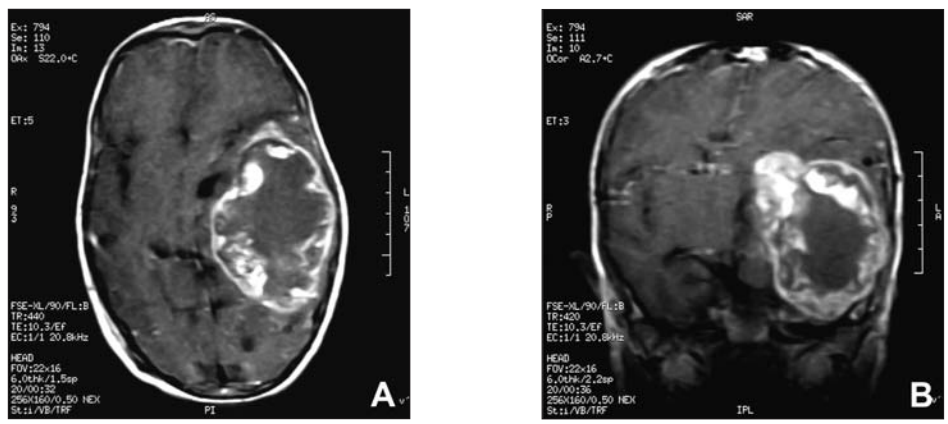

Figure 2 - **(A)** Pre-operative T1 weighted Gadolinium-enhanced MRI scan revealing left temporoparietal, extra axial mass in an axial plane. **(B)** Pre-operative T1 weighted Gadolinium-enhanced MRI scan revealing left temporoparietal extra-axial mass in a coronal plane.

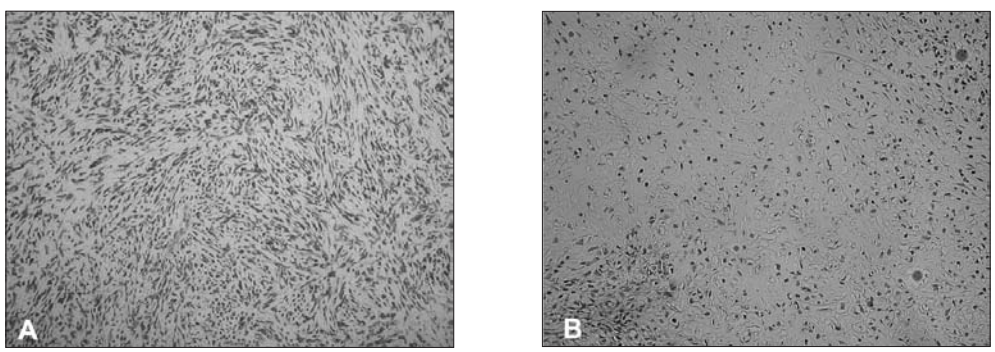

Figure 3 - **(A)** Undifferentiated oval to spindle shaped cells arranged in sheets (Hematoxylin & Eosin, X 100). **(B)** Abrupt transition between the undifferentiated cells and islands of cartilage (Hematoxylin & Eosin, X 100).

extraskeletal mesenchymal chondrosarcomas are those due to raised intracranial pressure. However, other symptoms and signs can occur, which are due to their direct compressive effect on other anatomical structures, depending upon their location. Scheithauer and Rubinstein,[1] reported a case presenting with third and sixth cranial nerve palsy. Of interest, there are only 3 cases that have presented with initial subarachnoid hemorrhage followed shortly by intracerebral hemorrhage.[1,8] However, this occurrence in very rare. There is enough evidence to suggest that this tumor can present like any other intracranial space-occupying lesion and exhibit signs depending on its location, size, and vascularity. Histologically, the tumor has a biphasic pattern composed of highly cellular, undifferentiated round to oval somewhat spindle shaped mesenchymal cells with scanty cytoplasm randomly arranged in sheets containing scattered islands of well-differentiated cartilage. The typical transition between these 2 stages is very abrupt. Immuno-histochemistry using S100 protein antibodies show positive staining in the cartilaginous areas and small cell components are positive for vimentin. At times, this tumor may closely resemble a hemangiopericytoma or a cartilage containing meningioma, but the identification of cartilaginous areas in association with undifferentiated cell component is sufficient to exclude those tumors.[9]

On radiological assessment, plain skull x-ray may reveal signs of increased intracranial pressure like 'beaten copper' appearance and sutural diastases as was seen in our patient.[10] A CT scan shows these tumors to be either hypodense, isodense or slightly hyperdense to the brain before contrast administration. After contrast administration, they enhance homogeneously but may show ring like enhancement. Magnetic resonance imaging is probably the imaging method of choice for evaluation. These tumors are either hypointense or isointense to brain on precontrast T1 weighted images and enhance strongly after gadolinium administration. Intracranial mesenchymal chondrosarcomas can resemble a meningioma, hemangiopericytoma or an arterio venous (AV) malformation. On angiography, the tumor can give a "blush" or appear like an AV malformation.[3,11] This high vascularity of the tumor could be responsible for a number of reported cases, which have suffered intra-operative hemorrhage. As they are extremely vascular, preoperative evaluation with angiography is advised and embolization of the feeding vessels before excision should facilitate their removal.[7]

Extraskeletal mesenchymal chondrosarcomas have a tendency to be locally aggressive and recurrences are quite common as it is a more malignant type of chondrosarcoma.[2] Extracranial metastases have been reported to have occurred in the lumbar vertebra, ribs, heart, and several intra abdominal structures.[3,10] They have been documented to have occurred in approximately 15-20% of the patients, usually after a long quiescent period.[2] In a series of 12 patients, Scheithauer and Rubinstein[1] observed recurrence in 6 patients occurring over a period of a few months to 9 years. Since recurrence may be a late event, they suggested that the ultimate prognostic significance of 3-5 year survival is of limited value. The longest surviving patient survived 2 recurrences in 18 years. Rushing et al,[9] in their clinico-pathologic and flow cytometric study found that survival may be shorter for those patients with high S-phase fraction and a high Ki-67 staining frequency.

On reviewing the literature on cases of intracranial extraskeletal mesenchymal chondrosarcoma, we found 39 documented cases.[1,3,6-11] Out of the 39 cases, 31 cases were extra-axial with documented dural connection and 8 were parenchymal without dural attachment. Out of these 8, 5 were in the cerebrum and 3 were in the cerebellum. In the reported 39 cases, 32 were supratentorial and 7 were in the infratentorial compartment. In the supratentorial compartment, the preferential location has been observed in the frontal and parietal regions. Of the 39 cases reported in the literature, 17 were males and 22 were females, and there does not appear to be any preponderance of either sex.[3,11] On grouping the cases by age, there were 5 cases in the first decade of life, 18 in the second decade, 7 in the third, 2 in the fourth, and 3 in the fifth, one in the sixth, and 3 in the seventh decade. It was observed that the highest prevalence occurred in the second decade, followed by the third and then the first decade. The prevalence of the cases fell sharply from the fourth decade to the seventh decade. The youngest patient was 6 months old and the oldest was 68 years old. Our case reported here was 4 years old, falling within the first decade. It thus confirms the fact that extraskeletal mesenchymal chondrosarcoma is a tumor of the younger age group.

There is no generalized consensus regarding the optimal therapy of extraskeletal mesenchymal chondrosarcoma. However, there is unanimity of opinion about gross total macroscopic excision, which should be the final aim, although it is not sufficient to stop the recurrence and spread of the tumor.[1,7,9-11] There is conflicting evidence regarding the efficacy of radiation therapy and its justification has been based on the high incidence of local recurrence and the aggressive nature of the tumor.[3,10-12] The beneficial effects of radiation therapy have been documented by the fact that there was tumor size reduction on

comparing CT scan pre- and post- radiation.[2] In view of the reported incidences of tumor metastases to the other systems, chemotherapy to avoid such metastases in conjunction with radiotherapy has been advocated.[10-12] However, it must be emphasized that first attempt gross total macroscopic excision followed by adjuvant radiotherapy and chemotherapy should be the recommended line of management. Although adjuvant treatment (radiation and chemotherapy) appears to offer some benefit in prolonging life, the prognosis for mesenchymal chondrosarcomas is one of frequent recurrence, occasional metastases and ultimately death.

Despite the availability of sophisticated neuro-imaging techniques, the direct tissue examination and histological evaluation are crucial to the diagnosis, hence, the importance of expert pathological assessment cannot be overemphasized. It has been stressed that a solitary dural based lesion with such aggressive behavior on neuro imaging in a pediatric age group should raise suspicion of this tumor, and it is reasonable to include it in the differential diagnosis. Furthermore, it is important to follow up these patients with appropriate imaging studies on a regular basis, in order to identify recurrences early.

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