

Maxillo-facial Extraskelatal Myxoid Chondrosarcoma: A Case Report and Discussion

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In this report, we share our experience of a case of maxillo-facial extraskelatal myxoid chondrosarcoma, a very rare location for this neoplasm. In addition, a literature review is provided. The patient, a 61-year-old male, had a maxillary mass encroaching on the nasal cavity. After debulking, the tumor recurred, attaining its pre-surgical proportion in two months. The patient improved clinically with radiation and remained stable for about one year. However, he ultimately developed metastases in his lung which were treated with palliative chemotherapy with a good outcome lasting three months. We could find only eight reported cases of this tumor in the head region of which two are in the maxilla; hence, ruling out other primary sites is mandatory for a patient presenting with a primary head and neck mass. Surgical removal may be complicated because of the location. A combination of surgery and radiation is the management of choice, with palliative chemotherapy in metastasis.

Key Words: Extraskelatal myxoid chondrosarcoma; Maxillary sinus; Head; Radiation; Chemotherapy

Chondroma of soft parts and non-synovial chondrosarcoma are the two entities that are grouped under extraskelatal cartilaginous tumors. Under the latter category, the two soft tissue chondrosarcomas, namely myxoid and mesenchymal chondrosarcomas, are grouped. Extraskelatal myxoid chondrosarcoma (EMC), initially recognized by Stout and Verner in 1953, is a soft tissue malignancy with characteristic histomorphology.¹ It was defined as a distinct clinicopathologic entity by Enzinger and Shiraki in 1972.^{2,3} Two balanced translocations found to be present in EMCs are t(9;22)(q22;q12.2) or t(9;17)(q22;q11.2).^{4,5} The first translocation causes a fusion of the genes Ewing sarcoma breakpoint region 1 (*EWSR1*) and *NR4A3*, whereas the second results in *RBP56-NR4A3* fusion. The soft tissue of extremities especially that in the lower limbs, is the more common site of these rare tumors, in addition to the suprascapular region.^{1,6,7}

The present example of EMC arose in the maxillo-facial sinuses, a very unusual primary location for this tumor.

CASE REPORT

A north east Indian man, aged 61 years, presented with facial

swelling with dull aching pain in and around the left maxillary sinus, chronic nasal blockage and post nasal drip. He was in general good health. There was a history of rapid increase in the faciomaxillary swelling and symptoms for the past three and half weeks. There was a polypoid mass visible through the left nostril, though the site of origin was not clear on clinical examination. Imaging studies revealed a 6.3 cm expansile mass destroying the lateral part of the hard palate, the wall of the maxillary antrum, nasal cavity, nasopharynx, bilateral ethmoid, maxillary and left sphenoid sinuses (Fig. 1). The computed tomography (CT) scan of the other regions of the body ruled out other primary foci.

A complete curative resection would have been the ideal treatment; however, a tumor board deemed this to be impossible because of the location of the tumor and the extensive tissue involvement. Extensive mass debulking was carried out through maxillary and sphenoid sinusotomies. The gross appearance was fleshy and hemorrhagic with small areas of necrosis and extensive bony involvement. Light microscope revealed the tumor to be unencapsulated and lobulated with the tumor cells arranged in whorls, reticular pattern and trabeculae (Fig. 2) punctuated with areas of coagulative tumor necrosis, all arranged in a strongly alcianophilic, fibrillary, myxoid stroma (Fig. 3) having a prom-



Fig. 1. Computed tomography scan showing large paranasal and nasal mass.

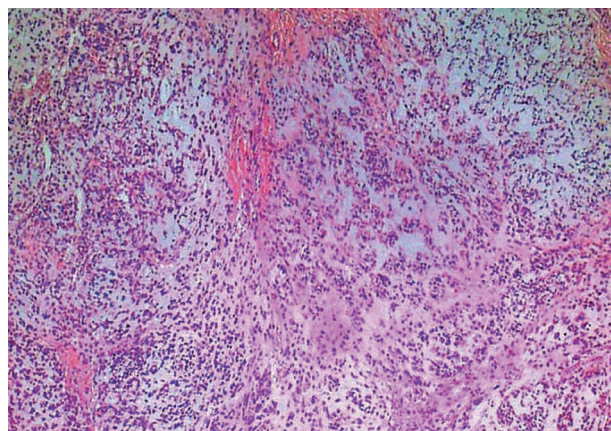


Fig. 2. Extraskeletal myxoid chondrosarcoma showing cords of cells in myxoid background.

inent capillary network. The tumor cells had a moderately pleomorphic, hyperchromatic nuclei with prominent nucleoli (Fig. 4). The amount of cytoplasm was moderate and eosinophilic. Some of the tumor cells had a rhabdoid appearance with eccentrically placed nuclei (Fig. 4). There was brisk mitosis, with about 5–7 mitotic figures/10 high power fields.

Vimentin and synaptophysin were the only immunohistochemical markers that were positive. S100 was focally positive. MIB-1 index was 20%. The alcianophilia of the matrix and lack of lipoblasts ruled out liposarcoma. Cytokeratin and epithelial membrane antigen were negative and that ruled out consideration of carcinoma. On electron microscopy, the tumor cells

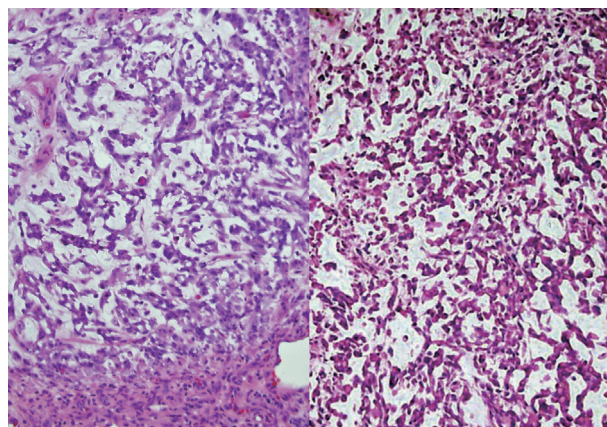


Fig. 3. Networking cords and whorls of cells in myxoid stroma.

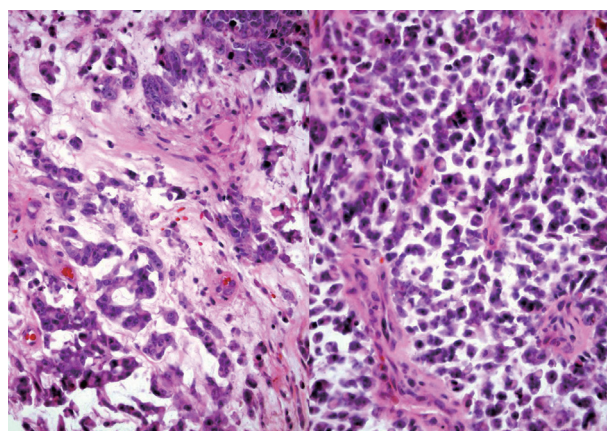


Fig. 4. Cells with eccentric nuclei and pleomorphism (rhabdoid morphology).

contained multiple well formed golgi complexes, rough endoplasmic reticulum, and microvilli with scalloped cytoplasmic membrane with some of these showing glycogen deposits, features common to chondrocytes.

The paraffin embedded tissue was subjected to fluorescence *in situ* hybridization using *EWSR1* probe to detect t(9;22) gene translocation and was positive (Fig. 5). However, t(11;22), normally typical for Ewings sarcoma and present in EMC in more than 50% of the cases, was negative.

Post operatively, a wait and watch approach was adopted without using chemotherapy, since EMCs typically fare poorly with chemotherapy. However, the tumor started to expand in size again and reached post-resection dimensions in two to three months and caused visual impairment on the left side.

This recurrent tumor was subjected to radiotherapy starting at the sinonasal cavity and the left orbit and that was followed by additional tomotherapy. The course through the radiation therapy was uneventful. The patient's vision was almost restored

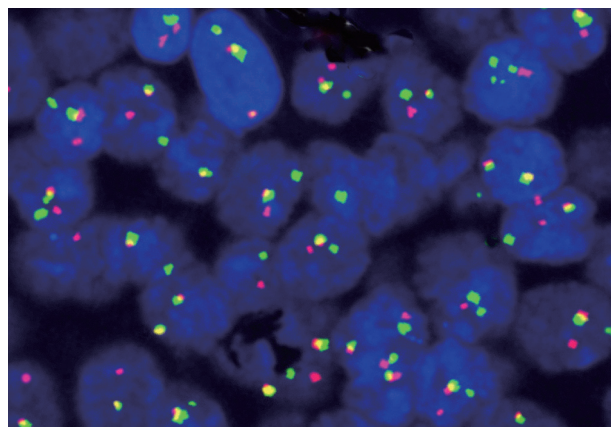


Fig. 5. Fluorescence *in situ* hybridization with Ewing sarcoma break-point region 1 (*EWSR1*) probe (Vysis) showing the characteristic translocation.

to normalcy and the symptoms of nasal congestion and blockage were relieved.

The patient was in good health for about eleven months after the original resection in the sinus, but he again presented with dry cough and pleuritic chest pain. Previously non-existent pulmonary masses were revealed on a chest X-ray. High resolution CT revealed some large lung parenchymal, subpleural and peribronchial masses. In five weeks, the patient suffered more recurrences with brain metastases and worsening ipsilateral visual impairment. He was managed palliatively with eight cycles of doxorubicin based chemotherapy, which lasted six months. There was some symptomatic improvement and cessation of progression of the visual impairment. A metastatectomy for the brain mass was performed before the last cycle of the chemotherapy regimen. After this last cycle of the chemotherapy regimen the patient had improved significantly, but in three months he was admitted with uncontrolled bouts of dry cough, dyspnea, extreme loss of weight and seizures. There were recurrent brain metastases along with liver metastases. Symptomatic therapy was unsuccessful and he was beyond salvage. He expired after 2 weeks of suffering from an intracranial bleed.

DISCUSSION

Myxoid and mesenchymal chondrosarcomas are the two well known extraskelatal or soft tissue chondrosarcomas. A few incidences have been reported on mesenchymal chondrosarcomas in the head and neck region.⁷

EMCs are more common in the extremities, especially in the lower limbs where occurrences in the thigh and the popliteal

fossa are very common.⁸ However, some rare sites have been reported for EMC which include the supraclavicular region,⁹ the intra abdominal wall and female genitalia.⁶ Very few cases have been reported in the head and neck. There has been one reported case each in the chin,⁷ infratemporal fossa,¹⁰ cerebellopontine angle,¹¹ masticator space,¹² and orbit.¹³ Nasal cavity^{1,7} and maxillary sinus^{8,14} have reported two cases each.

EMC, a tumor of unknown etiology,¹ is more common in males and is usually seen in patients after the fourth decade. Several theories may be put forward to explain the histogenesis. Similar to other chondrosarcomas, previous surgical or accidental trauma may be important, as is inhalation of chemical carcinogens such as hydrocarbons.⁸ Primitive cartilage forming mesenchyme or synovial intimal cells could be one of the sources of this tumor. Chondroblastic differentiation has also been suggested.¹⁵ Probably this is why this tumor most commonly arises close to tendons and ligaments.^{9,15} However, the very inconsistent S100 positivity, lack of true cartilage and cartilage forming matrix proteins in the majority of cases raise doubts about the chondroid origin of this neoplasm.¹⁶ Neuroendocrine differentiation has been demonstrated by some authors through immunohistochemical and ultrastructural studies. The present concept is that it is a mesenchymal tumor of uncertain origin.¹⁶

The classical EMC is a low grade tumor with a well circumscribed, lobulated architecture composed of cells in cords and whorls having hyperchromatic round to oval nucleus and finely fibrillar eosinophilic cytoplasm. The matrix is loose, fibrillar and myxoid and the tumor is mitotically not very active.⁷ Most EMCs behave in a less aggressive manner than chondrosarcomas of bone. However, there are prognostic variations depending on cellularity, cellular maturity and differentiation and amount of myxoid matrix.⁷ Also, histological grade is a prognostic determinant.¹⁷ Dedifferentiated EMC is assumed to be more aggressive.¹² However, even low grade EMCs have a tendency to recur and metastasize despite an indolent course.⁵

The present case behaved aggressively, probably due to its high grade, hypercellular histology, brisk mitosis and its lack of differentiation, in addition to age (more than 50 years) and deep location. In addition, the atypical features that may be found in a high grade EMC are rhabdoid phenotype, geographic necrosis and anaplasia.^{17,18} The lungs, soft tissues, bones, regional lymph nodes, subcutaneous tissue, brain, bones and testes are the documented secondary sites.^{9,15,19,20} Local recurrence and metastases can both develop after long time intervals.¹

Histologically, the other chondroid tumors such as chondromyxoid fibroma, myxoid chondrosarcoma etc in addition to chor-

doma, parachordoma, mixed tumors of salivary gland, and myxoid liposarcoma would figure in the differential diagnoses.^{6,10}

In terms of immunohistochemistry, the tumor cells are positive to vimentin. The expression of S-100, the epithelial membrane antigen and neurofilament¹¹ have been found to be inconsistently positive while synaptophysin positivity has also been reported by some authors.¹⁷

This tumor has been genetically and phenotypically characterized by Meis-Kindblom *et al.*⁴ in their extensive study of 117 cases in 1999. The authors conclude the high rate of local recurrence and the futility of histological grading in this entity. They however refer to EMC as a low grade sarcoma which was however not supported by the behavior of the present tumor.

The initial treatment of choice is wide excision, followed by radiotherapy or chemotherapy. Radiation therapy is believed to be superior to chemotherapy. Among the chemotherapeutic agents, a wide variety has been used, some of which include mesna, doxorubicin, ifosfamide, dacarbazine and cisplatin.⁹ Interferon alpha 2b, gemcitabine, methotrexate, and imatinib have also been used.⁵

EMC itself is a rare sarcoma with predilection for the limbs. Even more rarely it may originate in the region of the head. Hence it is imperative to rule out metastases from other primary sites. Since the tumors in the head cannot be surgically resected completely, radiation therapy plays a very significant role in the treatment of this neoplasm. Chemotherapy is useful in palliation. Although a combination of adriamycin/ifosfamide proved to be useful in the palliative treatment of the patient presented in this report, newer agents are needed to successfully treat this sarcoma.

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