

A LOW GRADE TUMOR, EXTRA SKELETAL MYXOID CHONDROSARCOMA, WITH METASTATIC POTENTIAL: A CASE REPORT

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Abstract

Extraskeletal Myxoid Chondrosarcoma (EMC) is a rare soft tissue sarcoma of uncertain differentiation characterized by abundant myxoid matrix located in the soft tissues. It affects mainly the soft tissues of the proximal end of long bones. EMC has a male preference, and this occurs in soft tissue area in patients who are more than 40 years old. The present case was 63 year old female diagnosed as EMC on histopathological examination with immuno-histochemical confirmation and after eight months presented with pulmonary and inguinal metastasis. EMC is a rare tumor should be considered in the differential diagnosis of myxoid soft tissue neoplasm. Therefore, a multi-modal approach, having distinct clinical, cytological, histo-pathological, immunohistochemical features and cytogenetics analysis, must be necessary in establishing a more definitive diagnosis, which may finally lead to a more targeted and specific treatment for patients.

Keywords: Extraskeletal myxoid chondrosarcoma, Inguinal metastasis, low grade tumor, IHC

Introduction

Extraskeletal Myxoid Chondrosarcoma (EMC) is an extremely rare soft tissue sarcoma. It was first described in literature by Stout and Verner in year 1953[1], and later in year 1972 Enzinger and Shiraki [2] coined EMC as a different clinico-pathological entity in their study on 34 cases. EMC is extremely rare low grade malignant mesenchymal neoplasm of vague differentiation with main characteristic of presence of abundant myxoid matrix located in the soft tissues. The soft tissues of the proximal end of long bones are the commonest site of involvement by EMC [3]. EMC has strong tendency for local recurrence with percentage of 37 to 48% while literature suggests its metastatic potential around 50% with most common site of involvement is pulmonary metastasis [4]. EMC has more male preponderance as compared to females with age of presentation is around 40 years [5,6]. As per the concern of present case with similar diagnostic findings on histopathological examination of above

knee amputation specimen with their confirmation on immuno-histochemical (IHC) examination and after eight months presented with pulmonary and inguinal metastasis.

Case History:

A 63 year old female patient presented with small swelling in posterior part of left knee joint. On local examination 8x4cm lump was identified having increased local temperature, erythema with dilated veins over swelling and skin involvement was also notified. The patient's past history suggests that her mass was slowly progressive in nature over several months and it was mildly tender to the touch. On radiological investigation, MRI showed the well defined lesion 8.5x8.0x7.0 cm at the left popliteal fossa. The lesion was causing breach in the cortex posteriorly and was extending into lower femur. Posteriorly lesion was displacing the muscles and extending upto subcutaneous tissue and skin. On post contrast images it showed heterogenous

enhancement and extension into joint involving the cruciate ligament and upper tibia. Finding suggestive of large lobulated mass lesion in the popliteal fossa showing both intra-osseous and intra-articular extension. USG whole abdomen showed normal study. X ray chest showed cardiomegaly with bronchitis.

FNAC of left knee joint was done outside and it showed mildly cellular smears with scattered atypical cells in hemorrhagic background. These cells were plasmacytoid with high N:C ratio. Some cells showed intracytoplasmic vacuolation. Final impression on FNAC smears was given as features suggestive of positive for malignant cells.

The trucut biopsy from left popliteal fossa region revealed a malignant tumor appears to had lobulated appearance. Tumor cells were loosely cohesive with moderate to abundant amount of thick eosinophilic cytoplasm and markedly pleomorphic, hyperchromatic nuclei. Many of these tumor cells had rhabdoid appearance and final diagnosis of trucut biopsy was given as features suggestive of rhabdomyosarcoma. Immunohistochemical (IHC) staining of trucut biopsy showed expression for vimentin only. The CD99, Desmin, SMA, S-100, EMA, CK –PAN, Bcl-2 were negative. Ki67 score was 10-12%. On IHC report impression was malignant mesenchymal tumor with features suggestive of Pleomorphic cell sarcoma.

The patient later underwent above knee amputation. The tumor was identified in the left popliteal fossa which measured 6.0x3.5x3.5 cm in dimension. Cut surface of tumor was nodular and comprising of gelatinous material along with few cystic spaces. The underlying bone seem to be involved by tumor grossly. Histologic examination revealed a malignant tumor forming lobules. Stroma is chondromyxoid in most of the areas. Tumor cells are loosely cohesive, present singly or in small groups and mostly present at the periphery of the lobule. Tumor cells have moderate to abundant eosinophilic cytoplasm. Nuclei are markedly pleomorphic and hyperchromatic. Few mitotic figures are seen. Tumor is infiltrating sub-cutaneous adipose tissue and underlying bone. Large areas of necrosis are seen. Overlying skin is remarkable. IHC staining demonstrated a positive immunohistochemical (IHC) reaction for vimentin, NSE, S-100 and EMA. The Desmin, Myogenin, Smooth Muscle Actin (SMA), Cytokeratin-PAN and Synaptophysin immunostains were all negative.

Based upon histological examination and IHC, the final diagnosis of EMC was given. The patient refused to take any treatment at that time and returned back after seven months for further management. Her CECT thorax and abdomen findings are suggestive of soft tissue density nodule in bilateral lung field, probably metastasis with inguinal lymphadenopathy. FNAC left inguinal fungating swelling shows round to oval pleiomorphic cells having adundant pale cytoplasm, which at places is showing vacuolations. Nuclei show anisonucleosis, coarse chromatin and prominent nucleoli. Mitotic figures are seen. These tumor cells are entangled in chondroid material with chondromyxoid stroma background. She was started on tyrosine kinase inhibitor (Tab. Gefitinib 250 mg once daily) and was planned for external beam radiotherapy (EBRT) with a total dose of 30Gy in 10 fractions over 2 weeks.

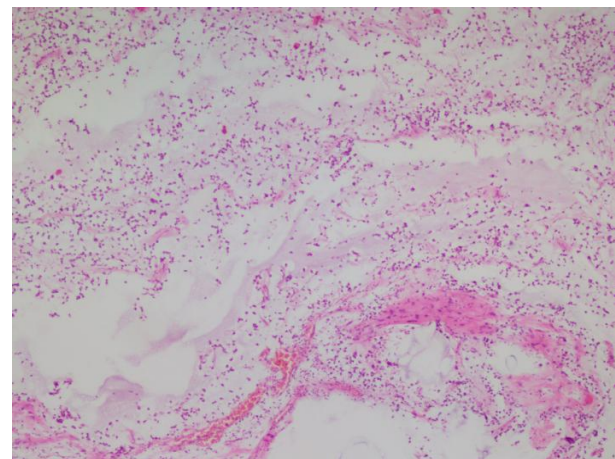


Figure 1: H&E stain of EMC shows tumor forming lobules (10x)

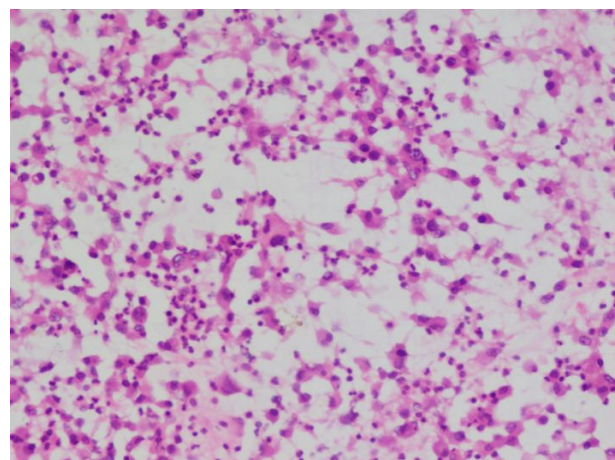


Figure 2: H&E stain of EMC showing markedly pleiomorphic nuclei (20x)

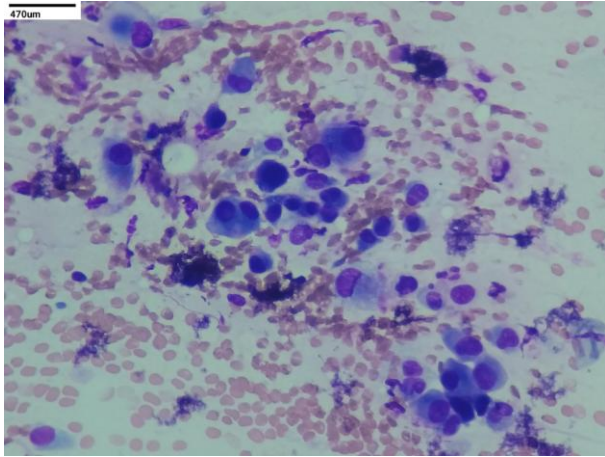


Figure 3: Cytological smear of FNA inguinal swelling shows markedly pleiomprhic tumor cells (MGG stain, 40x)

Discussion:

EMC was first described in literature by Stout and Verner in year 1953 [1]. The literature suggests that it is an exceptional entity representing less than 3% of all soft tissue sarcomas [7]. The lower extremities are the most common location followed by trunk and males are more commonly than than females with ratio of 2:1 and most common age of initial presentation is in the fifth and sixth decades of life [8]. In most of the cases, the clinical symptoms are usually non-specific, including slowly progressive palpable mass and presence of tenderness on touch [9]. Radiological examination are usually non specific with low density lesion on CT scan. On MRI, lesion usually exhibit both high signal intensity and low signal intensity on on T2 and T1 weighted MRI scans respectively [10]. The size of growth varies from 100 mm to 250 mm approximately. On gross examination, the tumor usually exhibit a multinodular configuration with well-defined margin and usually an incomplete fibrous capsule. Cut surface shows gray to brown discoloration with areas of gelatinous appearance, which is often accompanied by presence of intralesional hemorrhage [11]. The most common microscopic features of EMC include myxoid ground substance usually present in background with entrenched tumor cells along with arrangement of tumor cells in the form of anastomosing cords or clusters of uniform round to spindle shaped cells with bland nuclear chromatin and inconspicuous nucleoli, and few tumor cells have cleaved or grooved nuclei suggesting chondroblast like derivation; all of which were identified in our case. However, the tumor usually does not exhibit cartilaginous differentiation. The mitotic activity is also rare in most previous

reported cases. Other cell types have also been reported in previous literature including epithelioid cells with vesicular nuclear chromatin and prominent nucleoli, also rhabdoid cells with abundant clear cytoplasm and presence of hyaline cytoplasmic globules; as found in our case in trucut biopsy and surgical specimen, or anaplastic cells i.e, range of anaplasia is from small blue looking cells to spindle cell morphology to pleomorphic cells. However, other differential diagnosis of myxoid soft tissue tumor should also be considered include myxoid liposarcoma, myxofibrosarcoma, malignant fibrous histiocytoma (MFH), myxoid peripheral nerve sheath tumor (MPNST), myxoma and chordoma [12]. However, EMC has no specific immunohistochemical staining but vimentin is generally expressed in all the cases with focal positivity of S-100 protein and epithelial membrane antigen (EMA), as in our current case. Few previously reported cases of EMC showing variable immunohistochemical reaction for synaptophysin, chromogranin, and NSE, suggesting neuroendocrine differentiation of EMC [13].

In electron microscopy, the characteristic, but not specific, feature of EMC are the presence of parallel microtubules and abundant REG [14]. Few previous studies had shown that EMC may have positive immunohistochemical reaction for Leu-7 and EMA but all the previous studies shown that EMC are usually negative for keratin, SMA and desmin [15]. Cytogenetical analysis of EMC showed that it is associated with recurrent chromosomal translocation t (9; 22) (q22; q12) in about 80% of cases, usually examined by reverse transcriptase polymerase chain reaction technique on paraffin fixed tissue [4]. So, ancillary technique such as immunohistochemical staining, cytogenetical analysis and electron microscopy are also valuable tool for diagnosis of EMC [11]. The choice of treatment is total surgical resection of the initial tumor and / or metastasis lesion. It has been reported in few previous studies that EMC usually does not respond to chemotherapeutic drugs and results regarding response of radiotherapy treatment are variably discordant. So role of radiotherapy and chemotherapy as first line treatment is questionable. As per the concern of metastatic EMC, the most common site is the lung metastasis followed by soft tissue, lymph nodes, bone, and brain [14].

Conclusion:

EMC, a low grade tumor with uncertain metastatic potential, is extremely uncommon entity which should be always considered as differential diagnosis when there is abundant myxoid change in soft tissue tumors. Because, a multi disciplinary approaches are essential for establishing definitive diagnosis, such as clinical, cytological, histo-pathological, immuno-histochemical features and finally by molecular analysis, so that specific treatment is given in terms of more targeted therapy for disease improvement and final outcome.

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