Research Paper

Volume : 4 | Issue : 12 | December 2015 • ISSN No 2277 - 8179

Medical Science

KEYWORDS : extraosseous, Chondrosarcoma, multiple.

Multifocal Extraskeletal Myxoid Chondrosarcoma: A Case Report

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ABSTRACT

Extraosseous myxoid chondrosarcoma constitute about 2 % of all chondrosarcomas and are relatively rare. Most common sites involved are extremities, thorax and retroperitoneum. These are biologically similar to high grade sarcomas. Osteoblastic, chondroblastic and fibroblastic variants have been described. Here we report a case of extra osseous myxoid chondrosarcoma in a 65 yrs old female who presented with painless mass in her right forearm for last 2 years which was gradually increased in size. We are sharing our approach to diagnosis and management of the patient. Best treatment options include surgical resection for localized disease. But here we are dealing with the multiple extra osseous chondrosarcoma which was treated with Anthracycline based systemic therapy.

Introduction

Extra osseous myxoid chondrosarcoma is a malignant mesenchymal neoplasm located in the soft tissue without any attachment to the skeletal system and produces chondroid material. Extra osseous myxoid chondrosarcomas typically occur in the extremities, with thigh being the most common site. They occur at all ages but typically around the age of 50 yrs [1].

Case report

A 65 years old female patient presented to us with painless swelling in dorsomedial aspect of right forearm **(figure 1)** and posteromedial aspect of left thigh for last 2 years. These swellings were initially small pea sized and increased to its present size in the course these years. On examination, there was an oval shaped swelling about 4 X 6 cm in dorsomedial aspect of right forearm and another swelling of about 5 X 7 cm in the posteromedial aspect of left thigh. Both the swelling were non tender, firm to hard in consistency and fixed to the underlying muscle. A swelling of 3 X 3 cm was also noted in posterior triangle of neck. Three Right sided axillary lymph nodes were palpable, the largest of which was 2 X 2 cm in size. An enlarged left sided inguinal lymph node about 3 X 2 cm was also noted. X-ray of right Forearm showed no obvious bony lesion or injury, but there was a soft tissue shadow (mass) devoid of any calcifications **(figure 2)**. Contrast Enhanced Computed Tomography (CECT) Scan of Thorax revealed multiple enlarged lymph nodes in Right axilla **(figure 3)** and CECT scan of Abdomen showed enlarged left iliac group of Lymph nodes **(figure 4)**. Fine Needle Aspiration Cytology (FNAC) from the Left cervical swelling revealed malignant neoplasm and FNAC from the Right forearm swelling revealed myxoid chondrosarcomatous deposits. Excision biopsy from the cervical mass was done and histopathological examination (HPE) exhibited multinodular architecture composed of cords or strands of small cells immersed in a myxoid matrix **(figure 5)**; the cells were ovoid or spindle shaped with a deeply eosinophilic cytoplasm and exhibited hyperchromatic nuclei; a picture suggestive of moderately differentiated chondrosarcoma. Immunohistochemistry (IHC) was positive for S100, Ki67 & EMA and negative for SMA. Hence the case was diagnosed to be highly aggressive extraskeletal myxoid chondrosarcoma.

The patient was started on palliative Chemotherapy with Inj. Ifosfamide (4g/m2) i.v. D1 to D3 and Inj.Epirubicin (40mg/m2) i.v. D1 to D3; the cycle was repeated every 21 days. Mesna was given along with Ifosfamide as per directives. Three cycles of chemotherapy was administered. A progressive decrease in the size of the right forearm tumor and the left thigh mass was seen in subsequent fallow ups. The 3rd cycle was delayed due to anemia and neutropenia. But after three cycles of chemotherapy the patient was lost to fallow up.

Discussion

Extra osseous myxoid chondrosarcoma (EMC) is an aggressive soft tissue lesion with high rates of local and distant recurrence and delayed disease related death. It is a misnomer insofar as the tumor is really of uncertain differentiation with no convincing evidence of cartilaginous origin. In reality it is an infrequent tumor of soft tissues, forming around bones.

In contrast to the more common skeletal chondrosarcoma of bone, EMC seldom contains mature cartilage, and there is no convincing evidence of cartilaginous differentiation. Ultrastructurally, EMC is characterized by densely packed intra-cistern microtubules and prominent mitochondria, whereas these are not apparent in skeletal chondrosarcoma. In addition, a non-random reciprocal translocation t(9;22), resulting in fusion of the *EWSR1* and *NR4A3* genes, is present in about 50% of EMCs[2-4] and is not seen in skeletal chondrosarcoma, which supports the idea that the two diseases have different molecular lineages. Most osseous myxoid chondrosarcomas show reciprocal translocations that fuse *NR4A3* in 9q22-q31.1 with one of four partners: *EWSR1* in 22q12 (the most common), *TAF15* in 17q11, *TCF12* in 15q21, or *TFG* in 3q12[5]. By gene profiling, extraskeletal myxoid chondrosarcomas constitute a distinct genomic entity, showing up-regulation of several genes, including *NMB*, *DKK1*, *DNER*, *CLCN3*[6]. *In situ* hybridization confirmed that *NMB* is highly expressed in extraskeletal myxoid chondrosarcoma but not in other sarcoma types, suggesting its potential value as a diagnostic marker. Somewhat surprisingly, the up-regulated genes seen in two different profiling studies had only limited overlap [6].

Middle ageds to elderly individuals are most prone to this tumor formation. Most of these tumors occur deep within the body tissue, though a few have been found beneath the skin surface. The most common location for this tumor is the thigh, followed by knee, buttocks, and trunks. Extra osseous myxoid chondrosarcomas can grow to large sizes and compress other tissues and organs, causing restriction of movement and pain at local site. Diagnosis of EMC is confirmed by biopsy and IHC. They can present with complications such as damage to vital nerves or vessels, damage to the underlying bone, lung or lymph node

metastasis. For localized disease without any metastasis, wide local excision with negative margin is the treatment of choice. If the tumor is not fully removed, there is a high chance of recurrence. Vascular embolization of the tumor, by blocking the blood vessels feeding the tumor, is used to provide temporary relief from the symptoms and reduce blood loss, during a surgical procedure. EMCs are rare, but malignant tumors that are not yet completely understood. Long-term prognosis depends on a combination of factors, such as, age of the individual, tumor size and stage at detection, type and location of the tumor, Ki-67 value and its response to treatment and medical therapy. EMCs usually grow slowly and long survival is typical, even in the face of metastatic disease, which usually occurs in the lung[7].

In our patient we could not carry out definitive surgical resection as the disease was multifocal. Hence we started systemic chemotherapy with palliative intent. It has been postulated that anthracyclin based therapy, either as single agent or with Ifosfamide may be active in such a setting[8]. We administered Epirubicin and Ifosfamide based chemotherapy with Mesna support. Grade 3 hematological toxicity was encountered after the 2nd cycle which resulted in delay of the 3rd. Assessment after the 3rd cycle exhibited partial response as per RECIST guidelines.

We conclude that multifocal extraosseous myxoid chondrosarcoma is a rare disease which is sensitive to anthracyclin based chemotherapy. Role of such regimen in neoadjuvant or adjuvant systemic therapy in this disease may be explored in the future.

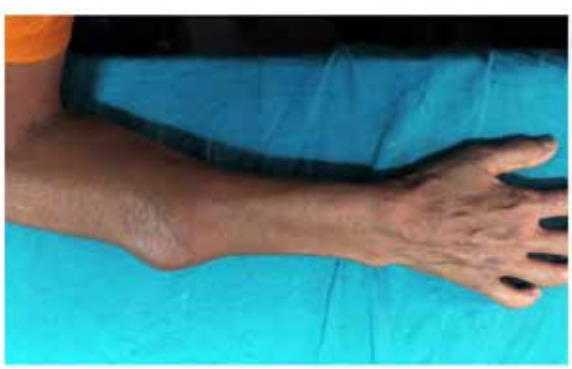

Figure 1 - the progressively increasing painless oval swelling of (4 X 6) cm in dorso-medial aspect of right forearm which was non tender, non pulsatile, firm to hard in consistency, fixed to the underlying muscle and without any edema or scar over the swelling.

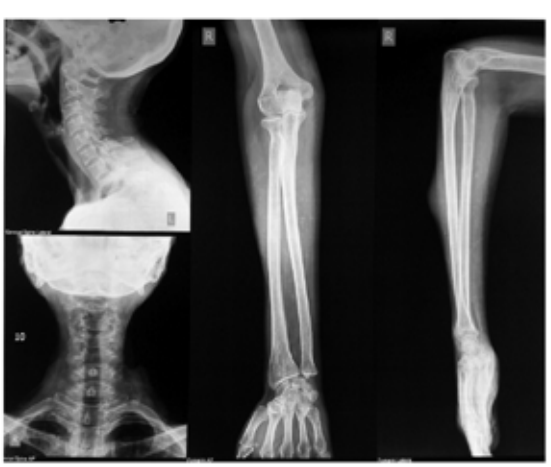

Figure 2 – X-ray neck and right forearm AP & Lateral view shows a left cervical swelling and a soft tissue swelling in the dorsal aspect.

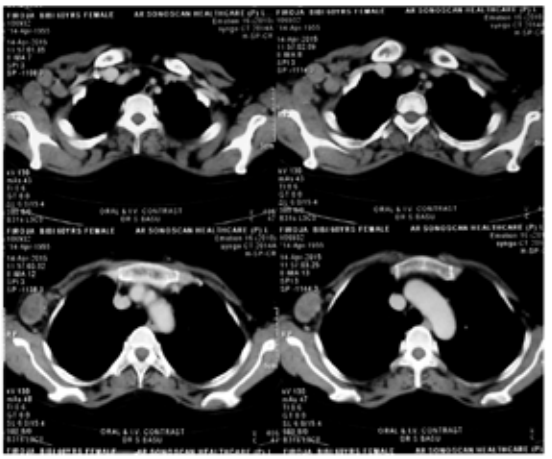

Figure 3 – axial slice of contrast enhanced CT scan thorax showing multiple lymph nodes in right axilla.

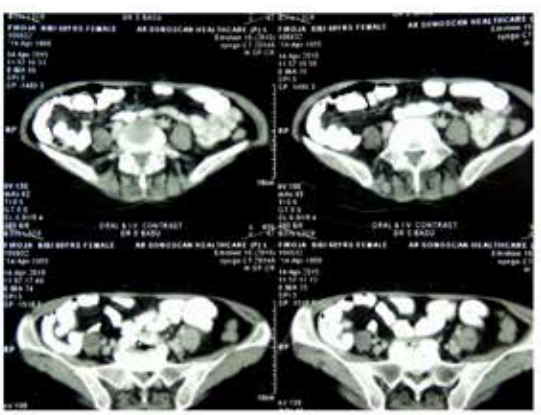

Figure 4 – axial slice of contrast enhanced CT scan of abdomen showing multiple left iliac groups of lymph nodes.

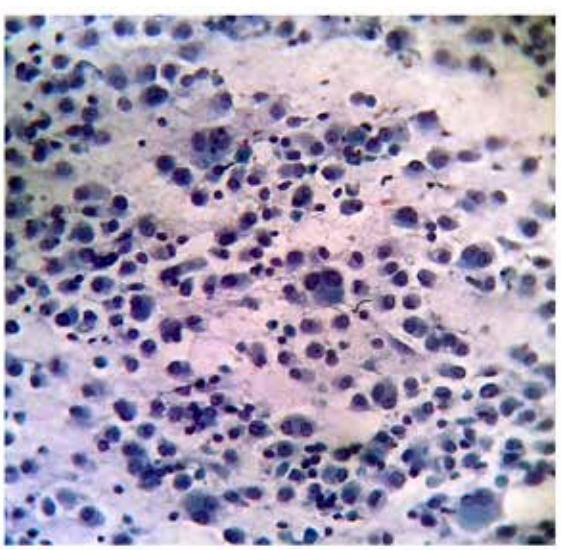

Figure 5 – histopathological examination of the biopsy specimen of left cervical lymph nodes revealed multinodular architecture and were composed of cords or strands of small cells immersed in a myxoid matrix. The cells were ovoid or spindle shaped with a deeply eosinophilic cytoplasm and exhibited hyperchromatic nuclei. Areas composed of large atypical cells with prominent nucleoli were also observed.

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