



Received on 05 May, 2015; Received in revised form 18 October, 2015; Accepted on 14 December, 2015

PRIMARY ANAPLASTIC LARGE CELL LYMPHOMA OF BONE: MANAGING THE MISCELLANEOUS!

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Keywords:

ALCL, Bone, Chemotherapy, CHOP, Non-hodgkin lymphoma, Rare.

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Abstract: Anaplastic large cell lymphoma (ALCL) represents 2 to 3% of non-Hodgkin lymphoma (NHL). Anaplastic lymphoma kinase negative (ALK-) subtype accounts for 15-50% of all ALCL. Primary bone involvement in lymphoma is uncommon and constitutes less than 1% of all lymphomas and 4-5% of all extranodal NHL. Hence extra-nodal primary bone involvement in ALCL is even rarer. We report the 14th case of primary ALCL in a 38 year old Indian female. Other than the uncommon site, there is no reason not to keep NHL as differential diagnosis, as the condition responds too well to standard treatment.

INTRODUCTION

Primary bone involvement in lymphoma is uncommon and constitutes about 7% of all malignant bone tumors and less than 1% of all lymphomas. Primary bone involvement may be the presentation in 4-5% of all extranodal NHL.¹ Anaplastic large cell lymphoma (ALCL) represents 2 to 3% of non-Hodgkin lymphoma (NHL). Anaplastic lymphoma kinase negative (ALK-) subtype accounts for 15-50% of all ALCL.^{2,3} Hence extra-nodal primary bone involvement in ALCL is even rarer.

To the best of our knowledge only 13 cases of ALCL with primary bone involvement have been described in literature, so far.⁴⁻¹⁰ This case is 14th overall and 2nd ALK- case of ALCL with primary involvement of bone/s.

CASE REPORT

A 38-year-old woman consulted orthopedic department in our tertiary care center with seven months history of pain and swelling of right shoulder; insidious in onset, gradually progressive and associated with restricted overhead abduction movement. Managed symptomatically for couple of months, she had

no relief. Six months later, she also noticed a pea-sized painless lump on left lateral aspect of scalp which rapidly increased in size to 5x4 cm at presentation (Figure 1 and 2). No associated systemic symptom like night sweats, fever, weight loss, lump elsewhere over the body or gynecological complaint was there.

Figure 1



Figure 2



Magnetic resonance imaging (MRI) scans of right shoulder region revealed destructive and expansile lesion along distal end of clavicle with surrounding extension of 4.8x4.5 cm.

Bone scan showed an increased uptake in right clavicle's lateral end and left parietal bone of skull. Routine blood counts, biochemical and serologic parameters (including the lactate dehydrogenase level) and bone marrow examination were within normal range.

Histological examination of tissue biopsy from lateral end of clavicle showed poorly differentiated malignant round cell neoplasm (Figure 3). Immunohistochemical examination revealed that the atypical cells were positive for Vimentin and LCA (Figure 4, 5). On further analysis they were found to be hematolymphoid malignancy with closest resemblance to CD30 positive and ALK negative anaplastic large cell lymphoma.

Figure 3 H&E stain 20X

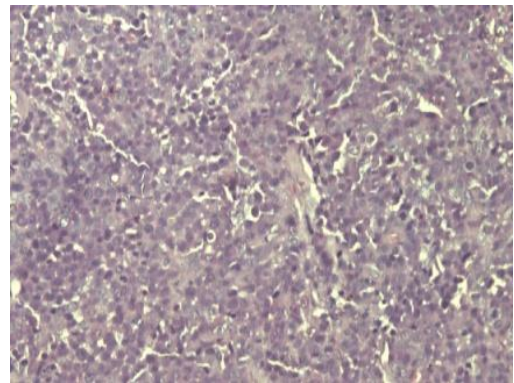


Figure 4 LCA stain 20X

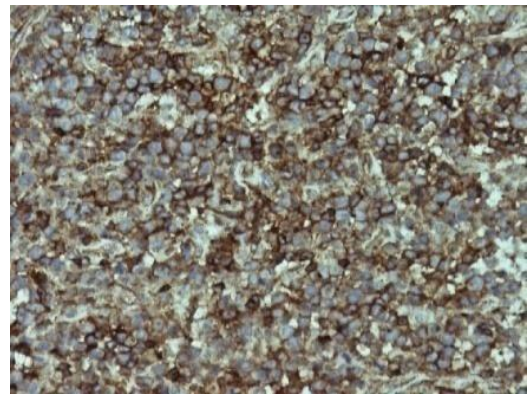
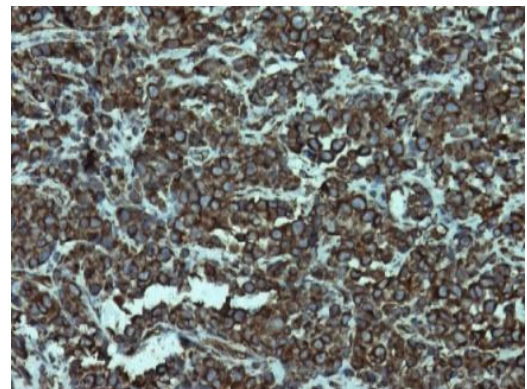


Figure 5 Vimentin 20X



Clinical examination and imaging studies revealed no evidence of significant lymphadenopathy or hepato-splenomegaly.

TREATMENT & OUTCOME

After explaining all pros and cons of treatment options, patient opted for local radiotherapy for painful shoulder followed by chemotherapy. Six courses of CHOP (Cyclophosphamide $750\text{mg}/\text{m}^2$ day 1, Doxorubicin $50\text{mg}/\text{m}^2$ day 1, Vincristine $1.5\text{mg}/\text{m}^2$ day 1 and P.O. Prednisolone 100mg day 1-5) were planned. To our expectations, disease responded very well. After 2 weeks of radiotherapy to shoulder, pain was 90% relieved and mass decreased. Three weeks after first course of chemotherapy, there was no clinical evidence of gross disease at either site (Figure 6, 7).

Figure 6



Figure 7



Three more courses of chemotherapy were given to consolidate. Three months after completion of chemotherapy, PET-CT (Figure 8a, 8b) revealed no evidence of metabolically active disease. Monthly follow up is planned for one year. The patient remains healthy and free of symptoms as of now (four months after completion of treatment).

Figure 8a

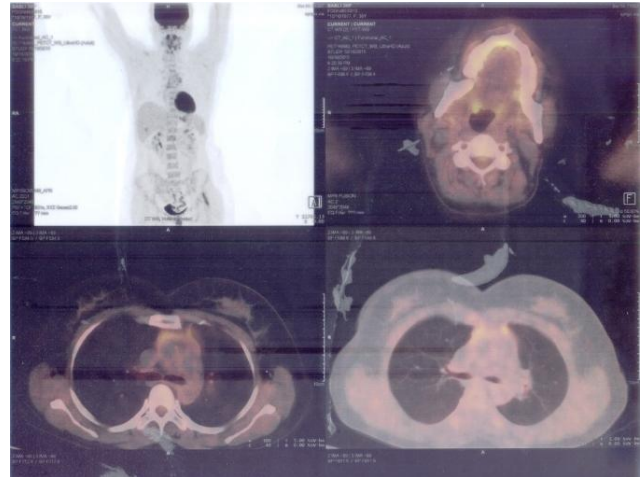
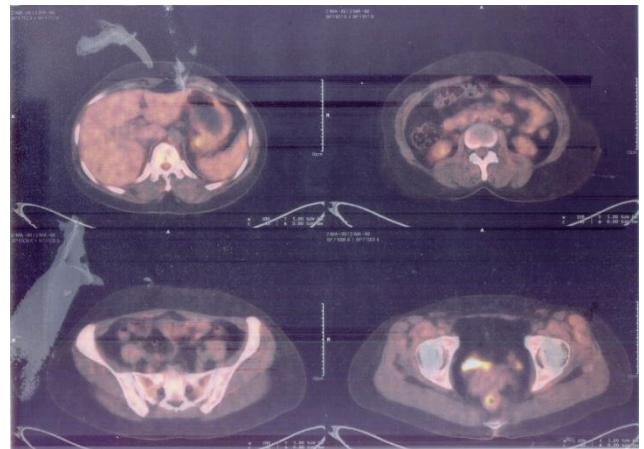


Figure 8b



DISCUSSION

ALCL was first described by Stein et al in 1985 as pleomorphic large cell lymphoma with a strong expression of the Ki-1.¹¹ ALCL is further sub-typed as ALK positive (ALK+) and ALK negative (ALK-) based on the expression of anaplastic lymphoma kinase (ALK) and is important because of the positive linkage

between the presence of ALK and the prognosis of the patient.¹²

ALK+ ALCL occurs earlier in life and accounts for 10 to 30% of all childhood NHL. It frequently involves both lymph nodes and extranodal sites including the skin, lung, bone, soft tissue and gastrointestinal tract. Disease has a more favorable prognosis with five-year survival as high as 80 to 90%. In contrast, ALK- are characterized by a higher age and advanced stage at diagnosis. Extranodal involvement is less common and prognosis is poor with an overall five-year survival of approximately 40%. ALK+ ALCL exhibits predominance for the involvement of bone, bone marrow and subcutaneous tissue whereas ALK- ALCL is more likely to invade the liver and the gastrointestinal tract.^{13, 14}

Primary involvement of the bone in lymphoma is rare and was first described by Oberling in 1928.¹⁵ After extensive search through medical literature, only 13 cases (excluding this one) of ALCL are known with extranodal involvement of the bone/s. The ratio of ALK+ and ALK- turns out to be 12:1. This is the 2nd case of ALK-negative ALCL.

When seen first by orthopedician; ewing's tumor, rhabdomyosarcoma, metastasis from elsewhere were kept as differential diagnosis. When subjected to imaging multiple myeloma was also among the differentials. Histopathological examination revealed it to be round cell tumor and now differentials included neuroectodermal tumor, lymphoma and metastatic deposits from lung. Marker study by IHC, made the diagnosis of ALK- ALCL. Primary involvement was ascertained by ruling out involvement of any other nodal or extranodal site by means of thorough clinical, radiological and marrow examination.

On review of literature, it appears that a younger age, advanced-stage of disease,

multiple bone involvement, and non-large cell histology are associated with decreased survival as compared with an older age, localized disease, single bone involvement respectively.^{7,9}

CONCLUSION

High clinical suspicion and early immunopathological diagnosis followed by aggressive treatment approach seems to be the right protocol. These kind of cases are likely to be a transient presentation of aggressive systemic microscopic disease that is yet to be clinically apparent. Outcome is rewarding with radiotherapy and modern chemotherapy just like in usual cases of lymphoma.

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How to cite this article:

Mittal S, Verma Y, Chauhan AK, Kaur P, Khurana A, Bansal N: Primary anaplastic large cell lymphoma of bone: managing the miscellaneous! *OncoExpert* 2016; 2(1):25-29