

A rare case of Anaplastic Large Cell Lymphoma

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Abstract

Anaplastic large cell lymphoma is defined by a proliferation of large pleomorphic blasts and a constant expression of the CD30 molecule on all neoplastic cells, and has been clinically subdivided into a primary form and a secondary form. We are presenting a case of 54 year old male with multiple nodular lesions and a small non healing ulcer on it over left thigh along with inguinal lymphadenopathy since 3 months. Clinically the patient was diagnosed as Squamous Cell Carcinoma. FNAC from the lymphnode was done and cytodagnosis of poorly differentiated malignancy was given. However due to presence of few atypical cell, FNAC was done from skin nodule and diagnosis was given as poorly differentiated malignancy suspicious of anaplastic large cell lymphoma. Confirmation was done by skin biopsy and immunochemistry, tumor cells were positive for CD30,CD 3(focal) and Granzyme B.

Keywords: ALK, CD30, Embryo shaped nucleus, Granzyme B, Immunohistochemistry.

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Introduction

Anaplastic large cell lymphoma (ALCL) represents a generally recognized group of large cell lymphomas. ALCL was described for the first time in 1985. ALCL is defined by a proliferation of large pleomorphic blasts and a constant expression of the CD30 molecule on all neoplastic cells. Anaplastic large cell lymphoma (ALCL) is a biologic and clinically heterogenous subtype of T-cell lymphoma. Clinically, ALCL may present as localized (primary) cutaneous disease or systemic disease. These two forms of ALCL are distinct entities with different clinical and biologic features. Primary cutaneous ALCL (C-ALCL) is part of the spectrum of CD30+ lymphoproliferative diseases of the skin including lymphomatoid papulosis. Using conservative measures, 5-year disease-free survival rates are > 90%. The systemic ALCL type is an aggressive lymphoma that may secondarily involve the skin, in addition to other extranodal sites. Further, systemic ALCL may be divided based on the expression of anaplastic lymphoma kinase (ALK) protein, which is activated most frequently through the nonrandom t(2;5) chromosome translocation. Systemic ALK+ ALCLs have improved prognosis compared with ALK-negative ALCL.

Case Report

A 54 years male patient presented with high grade fever along with a non healing ulcer on left leg since 3 months. Clinical examination revealed multiple, soft, erythematous nodular plaque like indurated lesions of varying size on left leg. Nodules were rubbery and non tender. There was oedema of the left leg. Inguinal lymphadenopathy was present. There was no history of weight loss or any other constitutional symptoms. CT scan reported small paraaortic and mediastinal

lymphnodes and clinically, a diagnosis of squamous cell carcinoma was made.

Fine Needle Aspiration Cytology(FNAC) of the inguinal lymphnode was done using 18-G needle and a provisional diagnosis of poorly differentiated malignancy was made. However because of the presence of few atypical cells, an FNAC was performed from the skin nodule. Considering the presence of embryo like cells and clinical presentation, Anaplastic Large Cell Lymphoma was suspected.

Pathological Findings: FNAC smears from the inguinal lymphnode revealed scattered and few clusters of tumor cells. The cells were large, round to oval, with large hyperchromatic nuclei with irregular nuclear membrane and prominent nucleoli. The cytoplasm was scanty. Pleomorphism, mitoses and occasional bizarre cells were seen (**Fig 1**). Background contains lymphocytes and red cells. Hence a diagnosis of poorly differentiated malignancy was made. However considering the presence of few atypical cells, FNA from skin nodule was done.

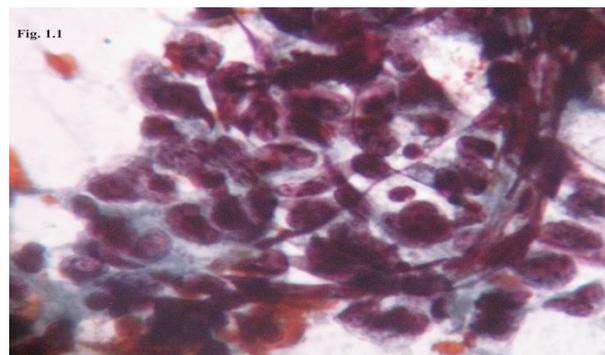


Fig. 1: Pleomorphic cells seen in loose cluster (FNAC from Lymph node PAP 40X)

FNAC smears from the skin nodule revealed few widely dispersed large “hallmark” cells that contain eccentric “kidney-shaped” or “embryo-like” nuclei, several prominent “rod-shaped” basophilic nucleoli, and abundant cytoplasm. There was pleomorphism. Mitotic figures were seen. The background comprised of abundant lymphocytes. Hence a diagnosis of poorly differentiated malignancy highly suspicious of anaplastic large cell lymphoma was made (Fig 2). Confirmation was done on skin biopsy and Immunohistochemistry.

Histopathology showed a variable admixture of lymphocytes, neutrophils, histiocytes and large highly atypical cells showing marked pleomorphism. The nuclei of these cells were embryo shaped with prominent nucleoli (Fig 3). Cytoplasm was abundant. Mitotic activity was also seen. Immunohistochemistry confirmed the diagnosis as the tumor cells were positive for CD30, Granzyme B and CD3(focal) and negative for CD20 and CD8.

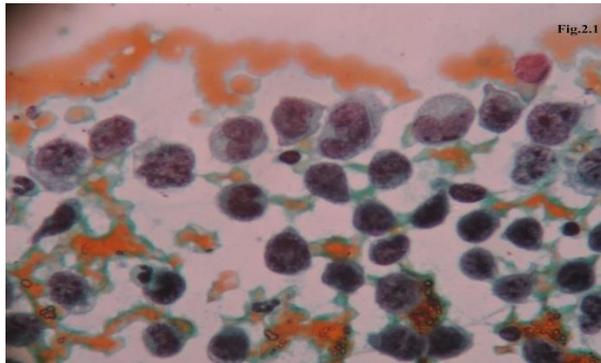


Fig. 2: Embryo nucleus with moderate cytoplasm (FNAC from skin nodule PAP 40 X)

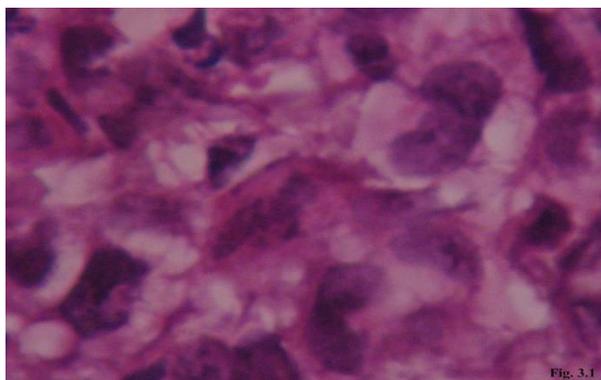


Fig. 3: Embryo nucleus seen. (H&E 40 X)

Discussion

The diagnosis of ALCL relies on recognition of distinctive morphologic clues and immunopositivity for CD30 and occasionally ALK protein. ALCL occurs as two distinct entities—a systemic disease or a localized (primary) cutaneous disease.^(1,2) The updated World Health Organization (WHO) classification now recognize this systemic ALCL into ALK-positive and

ALK-negative disease.⁽¹⁾ According to one study, skin involvement was 21%, bone 17%, lung 11% and liver 8%, with a rare involvement of central nervous system and gut.^(2,3)

Primary C-ALCL accounts for approximately 9% of all cutaneous T-cell lymphomas and affects older patients. It has rarely been described in the pediatric population.^(4,5) Most patients with primary C-ALCL present with localized skin tumors. Generalized lesions are seen in about 20% of the patients.⁽⁶⁾ Extracutaneous involvement is most commonly in regional nodes. Notably, C-ALCL lesions are known to regress spontaneously. C-ALCL patients have an excellent prognosis, with a 5-year disease-specific survival exceeding 90%, as confirmed by several studies.^(5,7)

Based on ALK status, there is a similar distribution of nodal (ALK+, 54% vs ALK-, 49%) and extranodal disease (ALK+, 19% vs ALK-, 21%),⁽⁶⁾ The most frequent extranodal sites in ALK- ALCL include bone, subcutaneous tissue, bone marrow, and spleen, whereas in ALK+ patients, the most common sites are skin, lung, liver, bone, and bone marrow.⁽⁸⁾ There are rare reports of ALCL presenting as a leukemic disease, typically occurring in children and associated with a poor prognosis.⁽⁹⁾

In our case, based on clinical presentation, diagnosis of Squamous cell carcinoma was made. However due to presence of few abnormal cells, diagnosis of squamous cell carcinoma was ruled out. Also the overlap is possible between ALCL and Hodgkin lymphoma (HL). Cutaneous involvement in HL is usually nonspecific. Primary cutaneous Hodgkin lymphoma is even more rare.⁽³⁾ Immunophenotyping reveals reactivity of Hodgkin and Reed-Sternberg cells for CD30. CD15 is frequently expressed but can be negative. CD45R0 is not expressed³. Other differential diagnosis included were sarcoma and melanoma which were ruled out on IHC.

A definitive diagnosis of ALCL is possible on careful interpretation of cytologic features and the proper application of immunocytochemical study to cytology samples. Majority of the ALCL cases have lymphadenopathy likely to be superficial. However extranodal disease is an important component of ALCL. It is important for cytopathologist to consider ALCL in the differential diagnosis of lesions characterised predominantly by discohesive, pleomorphic cells especially when anaplasia and/or horse shoe shaped nuclei are present, and it is therefore essential to obtain adequate material for ancillary testing at the time of procedure. ALCL is a good 5 year survival rate.

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