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Cutaneous Anaplastic Large Cell Lymphoma - A Case Report

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Abstract

Anaplastic large cell lymphomas are a group of lymphoproliferative disorders associated with a predominant CD30 positive infiltrate. A 43 year old male patient presented to the Dermatology department with multiple, painful lesions over his left arm of six months duration. Biopsy was suggestive of Non-Hodgkins Lymphoma - Anaplastic Large cell lymphoma (T cell type), ALK (Anaplastic Lymphoma Kinase) Negative. The histopathology showed characteristic hallmark cells with horshoereniform nuclei. Immunohistochemistry showed atypical cells which stained positively for LCA (Leukocyte common antigen), CD4, bcl2 and CD30. This case has been reported due to the rarity of the disease entity.

Keywords : Anaplastic large cell lymphoma, hallmark cells

Case Report

A 43 year old male patient presented with multiple, painful lesions over his left arm since six months. It initially started as multiple, small, raised erythematous nodules which increased in size and ulcerated. The lesion was associated with discharge which was initially watery and then foul smelling. Few of the lesions healed with scarring. The patient reported similar lesions on and off since the past 2 years.

On examination a 7x8 cm proliferative growth with everted edges was present over left arm on the medial aspect near the elbow, the base of which was covered with unhealthy granulation tissue. (Fig- 1) Two similar, smaller growths, 2x1 cm present over the left axilla with satellite nodules. (Fig-2) Axillary lymph nodes were enlarged, firm, mobile and non- tender.

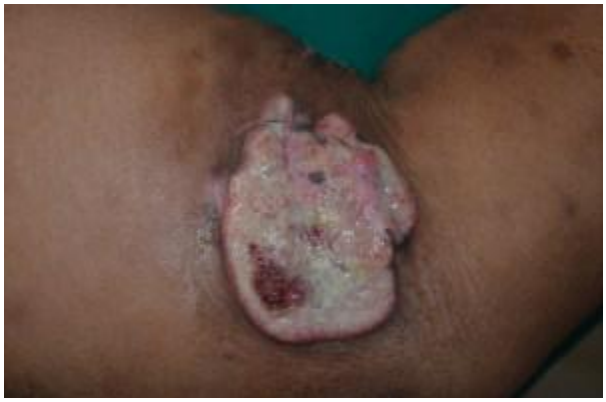

Figure 1 - Proliferative growth over medial aspect of left arm

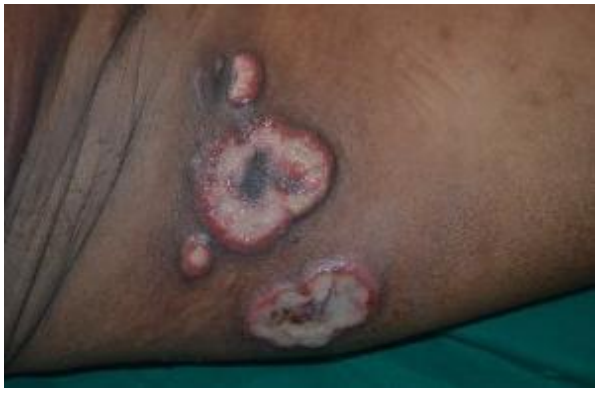

Figure 2 - Ulcerative growth with satellite lesions near left axilla

On investigation patient had elevated ESR and Mantoux was positive at 30 mm. Ultrasound abdomen and chest X-Ray were normal. HIV, HBsAg and HCV were negative. Automated AFB culture and fungal culture was negative. Gram's stain showed few pus cells.

Histopathological examination of a wedge biopsy specimen revealed an infilterating neoplasm composed of atypical cells arranged in sheets and islands. The cells were medium size to large with moderate amount of cytoplasm and large vesicular prominent nuclei. (Fig-3) The pleomorphic cells displayed a high nuclear-cytoplasmic ratio, irregular and indented nucleur membranes and prominent nucleoli. Scattered hallmark cells with horse-shoe/reniform nuclei were present. Many multinucleated pleomorphic giant cells were also seen .The adjacent dermis showed sclerosed collagen infilterated by patchy aggregates of lymphocytes and plasma cells.

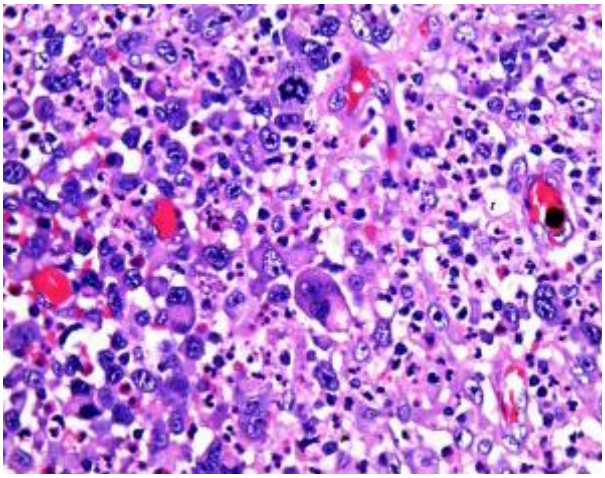

Figure 3 - Pleomorphic cells with prominent nuclei

Immunohistochemistry showed atypical cells which stained positively for CD30. (Fig-4) These cells were also positive for LCA, CD4, and Bcl-2. The atypical cells were negative for cytokeratin, CD20, CD3, EMA and ALK. (Fig-5)

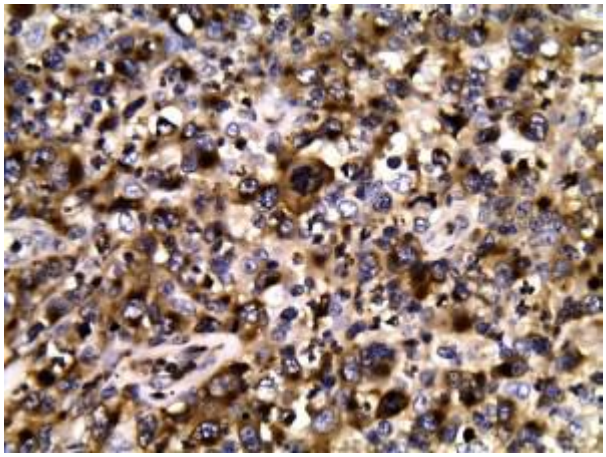

Figure 4 - CD30 positive staining on immunohistochemistry

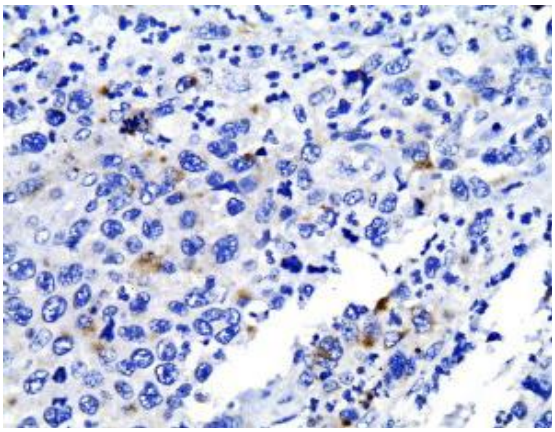

Figure 5 -Pleomorphic cells showing ALK negative staining

The patient was referred to an oncologist for surgical excision and chemotherapy.

Discussion

Primary cutaneous anaplastic large cell lymphomas are non- Hodgkin's lymphomas characterized by clonal proliferation of skin homing malignant T-lymphocytes. This disease represents about 30% of the primary cutaneous T-cell lymphomas.[1] Defining features include absence of systemic involvement at time of presentation, indolent course, spontaneous remission and low recurrence rate after therapy. Histopathologically it is denoted by presence of anaplastic (rarely pleomorphic or blastic) cells which are the major components of the inflammatory infilterate.

It was first described in 1985 as a separate clinical entity based on its characteristic pleomorphic cells expressing CD30.[2] The CD30 molecule belongs to the tumour necrosis factor receptor family and is found on the surface of activated T and B cells. Although the underlying mechanisms for development of ALCL is mostly unknown, chromosomal aberrations which lead to clonal expansion of CD30+ T-cells have been implicated.

This disease is usually seen in adults and presents as large solitary or multiple often ulcerative nodules, plaques or tumours commonly seen on the trunk or localized to a limb as in our case. It is commoner in males with a male: female ration of 1.5-2:1. Approximately 10% of cases progress to involve extracutaneous sites. [3]

The histologic clue to the diagnosis of ALCL, cutaneous or systemic, is the presence of large lymphoid cells, with an eccentric horsheoe or reniform nucleus, prominent eosinophilic nucleoli and abundant cytoplasm.[4] These cells exhibit a high nuclear:cytoplasmic ratio and are known as "hallmark cells".

Immunohistochemistry of ALCL is of mature activated T-lymphocytes. Apart from CD30, the cells generally express markers such as CD 4 and CD 25. Normal T-cell markers such as CD2, CD3 and CD5 can be lost.

The CD positive lymphoproliferative disorders maybe primary (localized to the skin) or secondary with systemic involvement. The systemic form is associated with the t (2; 5) translocation that results in the protein NPM-ALK.[1] This is a fusion gene between nucleophosmin (NMP) and a receptor tyrosine kinase gene, ALK, which encodes an activated tyrosine kinase that has oncogenic potential. As both forms present with overlapping features it is not possible to differentiate the two on purely histopathologic grounds.[5] The cell surface marker EMA or epithelial membrane antigen is usually not expressed in the primary cutaneous variant. It is important to distinguish between the two forms as secondary forms have a poorer prognosis and require aggressive therapy.

Primary ALCL is both chemosensitive as well as radiosensitive. Disease related 5-year survival rates have been reported to be around 95% with 20% of lesions showing spontaneous mode of resolution.[1]

Standard treatment of single or localized primary cutaneous ALCL comprises of local excision or radiation. (6)Chemotherapeutic measures are indicated for systemic involvement or disease that is refractory to local measures. This includes the CHOP regimen (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone) and systemic methotrexate. About 83 % of patients achieve complete resolution with the CHOP regimen. [7]

In chronically relapsing disease, autologous stem cell transplantation has been found to be effective. [2]

.References

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