**ABSTRACT**

Anaplastic large cell lymphoma (ALCL) is a T-cell lymphoma, accounting for <5% of non-Hodgkin’s lymphoma. Cutaneous involvement can be primary or secondary arising in systemic ALCL. The diagnostic feature in both is the presence of pleomorphic, CD30 positive hallmark cells. We present a case of ALCL in a 19-year-old male presenting as an ulcerated scalp swelling. Clinical impression was actinomycosis or scrofuloderma. Cytology smears showed large dispersed pleomorphic cells with hyperlobated nuclei and multinucleated giant cells. The differentials considered were ALCL, rhabdomyosarcoma, and poorly differentiated carcinoma. Immunocytochemistry (ICC) showed positivity for leukocyte common antigen (LCA) and CD30 while negativity for desmin, favoring ALCL. Computed tomography (CT) showed a lytic paravertebral lesion. Subsequently, both paraspinal and scalp lesions were biopsied and immunohistochemistry confirmed the diagnosis of ALCL. Thus, cutaneous involvement in ALCL can resemble inflammatory and other neoplastic lesions clinically and cytologically. Hence, a high index of suspicion and ICC can aid in the correct diagnosis on fine needle aspiration cytology (FNAC).

**Key words:** Anaplastic large cell lymphoma (ALCL); cutaneous; fine needle aspiration cytology (FNAC)

**Introduction**

Anaplastic large cell lymphoma (ALCL) is a T-cell lymphoma, accounting for <5% of all cases of non-Hodgkin’s lymphoma (NHL).

**Case Report**

A 19-year-old male presented with painful ulcerated scalp and neck swellings since 1 year [Figure 1a]. They were gradually increasing in size and showed intermittent purulent discharge. Incision and drainage was done twice but the lesion did not regress completely. Additionally, a skin biopsy had been done elsewhere which was suggestive of granulomatous inflammation. Thus, the clinical impression was actinomycosis or scrofuloderma. However, as the patient was not responding to treatment he was advised FNAC. Cytology smears were highly cellular and showed cohesive fragments and large dispersed cells with abundant dense cytoplasm, pleomorphic hyperlobated nuclei, small multiple nucleoli, and brisk mitosis [Figure 1c]. Amidst these were rare hallmark cells with horseshoe-shaped or reniform nuclei and basophilic cytoplasm [Figure 1d]. Few cells were elongated and clustered around blood vessels [Figure 1b]. Many multinucleated giant cells were seen as well. The background showed few mature lymphocytes and no lymphoglandular structures.
bodies were identified. The impression was a high-grade pleomorphic malignant tumor with differentials being ALCL, rhabdomyosarcoma, poorly-differentiated carcinoma, and melanoma. Immunocytochemistry (ICC) showed positivity for leukocyte common antigen (LCA) and CD30 and negativity for desmin, favoring ALCL [Figure 1e and f]. Computed Tomography (CT) additionally showed a lytic lesion in the L-3 paravertebral region. Subsequently, both paraspinal and scalp lesions were biopsied and they displayed the same immunohistochemistry (IHC) pattern as described above. In addition, tumor cells were positive for cluster of differentiation 3 (CD3) and negative for AE1/AE3, CD5, CD4, CD20, Paired Box 5 (PAX-5), B-cell lymphoma 2 (Bcl-2), OCT-2, Epstein–Barr virus latent membrane protein 1 (EBV-LMP1), and anaplastic lymphoma kinase-1 (ALK-1). The final diagnosis was ALK negative ALCL. The patient was started on chemotherapy and lesions regressed, however, the patient succumbed 8 months after diagnosis.

Discussion

ALCL is a T-cell lymphoma, characterized by cohesive proliferation of large pleomorphic cells expressing CD30.\(^1\) It occurs as two distinct clinical entities, a cutaneous and a systemic variant.\(^3\) Cutaneous involvement can be de novo or as an extranodal spread in a systemic ALCL.\(^2\) Both show the presence of pleomorphic, CD30-positive hallmark cells.\(^5\) It is important to differentiate primary cutaneous ALCL (PCALCL) from systemic ALCL with cutaneous involvement, as the former has an indolent course, a different treatment protocol and better long-term prognosis.\(^2\) Hence, patients should have complete staging with CT scans, bone marrow biopsy, and a complete blood count to rule out systemic involvement.\(^2\) It commonly presented as tumor nodules or papules.\(^2\) Multicentric cutaneous involvement and ulceration can occur and may mimic an inflammatory lesion clinically, as in our case.

The diagnosis of ALCL by FNAC is not only difficult but challenging if it occurs at an unusual site such as the scalp, although the hallmark cell is a clue for the diagnosis.\(^4\) These are characteristically described as CD30-positive anaplastic pleomorphic cells with abundant amphophilic cytoplasm, reniform nuclei and paranuclear eosinophilic hof.\(^5\) These hallmark cells are known to show varied cytomorphology and cohesion with clustering around blood vessels, thus creating diagnostic dilemmas.\(^6\) In addition, associated multinucleated giant cells, Reed-Sternberg (RS)-like cells, lymphocytes admixed with eosinophils, presence of spindle cells, and absence of lymphoglandular bodies in ALCL smears makes it more difficult to diagnose ALCL.\(^5\)\(^6\) The entities that enter in differential diagnosis on morphology includes tumors that can show marked anaplasia such as Hodgkin lymphoma, diffuse large B-cell lymphoma (DLBCL), embryonal carcinoma, melanoma, and sarcoma.\(^3\) Medical literature describes the combination of hallmark and wreath-like multinucleated
giant cells to be predictive of ALCL on cytology.\textsuperscript{[5]} However, these cells may in some cases, be rare or even absent. Similar age group, RS-like cells and expression of CD30 creates an overlap with Hodgkin’s lymphoma but in the latter the number and the spectrum of pleomorphic and abnormal cells are less.\textsuperscript{[5,7]} Moreover, the nucleoli in RS-like cells of ALCL are basophilic and irregular and not eosinophilic as seen in Hodgkin’s lymphoma.\textsuperscript{[5,6]} Immunocytochemistry with PAX5 and CD15 will help resolve the dilemma as these are positive in Hodgkin’s lymphoma.\textsuperscript{[5,7]} DLBCL, embryonal carcinoma and rare high grade sarcoma can additionally show CD30 positivity.\textsuperscript{[8]} DLBCL expresses B-cell markers such as CD20 and does not express T-cell markers.\textsuperscript{[8]} Another characteristic feature of ALCL is the expression of ALK, seen in 72–85% of ALCL but is not observed in the other abovementioned tumors.\textsuperscript{[6]} ALK status of ALCL has not only diagnostic significance but also imparts prognostic implications for patients as ALK-negative cases have unfavorable clinical outcome.\textsuperscript{[5]} The average number of anaplastic cells in ALK-negative ALCL cases is more than ALK-positive cases.\textsuperscript{[9]} Thus, the accuracy of FNA in such anaplastic neoplasms can be increased by obtaining adequate aspiration material for immunochemistry which can be performed on smears or cellblock.\textsuperscript{[9]} The recommended immunostains would include CD45, CD20, CD15, PAX5,CD30, ALK, epithelial membrane antigen (EMA), CD3, cytokeratin, vimentin, placental alkaline phosphatase (PLAP), and human melanoma black-45.\textsuperscript{[5]} However, in view of restricted cytology material, the immunostains should at least include CD45, CD30, EMA, vimentin. The discussed case was positive for LCA and CD30 and negative for desmin on ICC, favoring ALCL. The IHC on scalp biopsy was positive for CD3 and negative for AE1/AE3, CD5, CD4, CD20, PAX-5, Bcl-2, OCT-2, EBV-LMP1, and ALK-1, thus rendering the final diagnosis as ALK negative ALCL. The correct diagnosis of ALCL has important clinical implications as it is a treatable form of lymphoma and has a much better prognosis than other types of T-cell lymphoma.\textsuperscript{[6]} Thus, the cytologist must be diligent in obtaining adequate additional material for ancillary studies to classify this anaplastic neoplasm.\textsuperscript{[5]}

Conclusion

Cutaneous ALCL can resemble an inflammatory lesion clinically and the morphology can mimic cells of other lymphoma, sarcoma or poorly-differentiated carcinoma on cytology. A high index of suspicion and procuring adequate material for ICC can aid in correct diagnosis on FNAC.

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Conflicts of interest

There are no conflicts of interest.

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