

## Case Report

### Rare Presentation of Anaplastic Large Cell Lymphoma and HTLV1 Positivity: A Case Report and Review

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## Abstract

Anaplastic large cell lymphoma (ALCL) is a biologic and clinically heterogeneous subtype of T-cell lymphoma, which may present as localized (primary) cutaneous disease or widespread systemic disease. Primary cutaneous ALCL (C-ALCL) is part of a spectrum of CD30+ lymphoproliferative diseases of the skin with excellent prognosis. HTLV-1-associated lymphomas include adult T-cell lymphoma and leukemia (ATL), which is characterized by a clonal expansion of CD4+ T lymphocytes frequently associated with skin rash, lymph node and visceral involvement, and hypercalcemia. ATL rarely resembles ALCL and CD30 positive. We report a patient with single ulcerative skin mass lesion which showed an ALCL in biopsy, and immunohistochemistry analysis revealed that cells expressed CD30 positive. He did not respond to systemic therapy, and in this setting I found that he is anti-HTLV1 positive. I added zidovudin and interferon to his chemotherapy but he did not response again. Skin mass was completely resolved with local radiation, but he had systemic relapse after 3-4 month and finally died because of disease severity and treatment complication. Due to the various presentations of cutaneous T-cell lymphoma which we cannot exactly classify, there is a strong need for more data and a revision of the original classification.

**Keywords:** Cutaneous T Cell Lymphoma; HTLV1; ALCL

## Introduction

Anaplastic large cell lymphoma is a peripheral T-cell lymphoma with a different behavior, both biological and clinically [1]. Anaplastic large cell lymphoma may be clinically presented as a widespread systemic disease or a primary localized cutaneous disease. These two forms of ALCL are distinct entities with different biological and clinical features. Primary cutaneous ALCL is a rare CD30+ lymphoproliferative disease of the skin characterized by solitary or locoregional occurrences of reddish nodules or tumors, with a tendency to ulcerate. Progression toward extracutaneous and systemic disease is rare (5-10%) and most commonly occurs with regional nodal involvement. Primary cutaneous has a favorable prognosis, and includes 5-year disease-free

survival rates of >90% [2]. A rare subset of Cutaneous-ALCL patients with extensive limb disease has been reported, who have a worse treatment and survival outcome [3].

Adult T-cell lymphoma leukemia (ATL) is a peripheral T-cell lymphoma that is characterized by a clonal expansion of CD4+ T lymphocytes frequently associated with blood and bone marrow involvement, lymphadenopathy, hepatosplenomegaly, hypercalcemia, lytic bone lesions, and skin rash [4, 5]. ATL is most prevalent in Southwestern Japan, the Caribbean basin, inter-tropical Africa, the Middle East (especially northeast of Iran), and in African American populations in the Southeastern United States [6-8]. ATL occurs at least 20 to 30 years after the onset of HTLV-1 infection and is more common in adult males [7]. We report here a rare

skin presentation of ATL. The case reported here is notable for its poor prognostic subtype of primary cutaneous ALCL and HTLV1 positivity in primary cutaneous ATL.

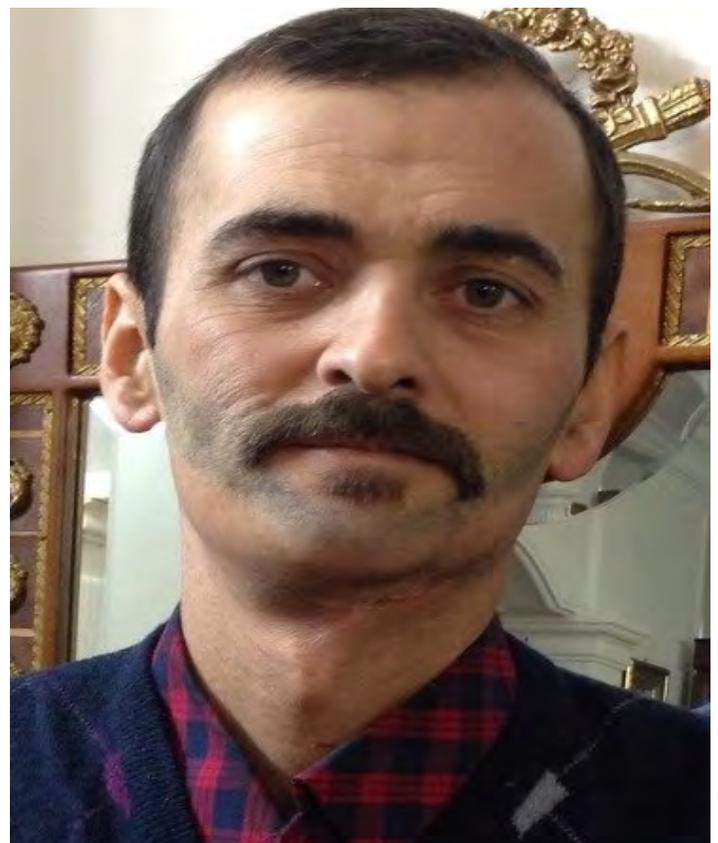
### Case Report

A 37 year-old man is presented with a single ulcerative mass in the submandibular area (figure 1). This mass began from 3-4 month prior to the presentation. In history and physical examinations, he did not have any other signs or symptoms. Biopsy was performed from a skin mass, and the result showed the diffuse infiltration of large lymphoid cells with chromatin-poor nuclei and prominent nucleoli, cells have abundant cytoplasm with eccentric and sometime kidney shaped nucleus. Immunohistochemistry analysis revealed that cells expressed CD30 positive, CK negative, LCA positive, CD3 positive, and CD20 negative, which are features that were consistent with anaplastic large T-cell lymphoma. A complete hemogram including CBC and peripheral smear, as well as a biochemical and serologic test showed no abnormalities, only LDH elevated slightly (LDH=576). Peripheral blood smear and bone marrow biopsy was normal. CT scans of the neck showed the superficial soft tissue mass to be 21\*27cm in the left submandibular area with several lymph nodes around it. CT scans of the chest, abdomen, and pelvis showed no systemic involvement.



**Figure 1.** Skin mass in T cell lymphoma before treatment.

Chemotherapy was started with cyclophosphamide, doxorubicin hydrochloride, vincristine sulfate, and prednisone (CHOP). After 4 cycles there was not a good response and there was only about a 30% decrease in the size of mass. Considering that we are in an endemic area for the HTLV1 infection, I checked it for him and the results was positive, therefore I added zidovudine and interferon to his chemotherapy [9]. Again, we did not have a good response. Due to the locoregional disease, I referred him for local radiation and the ulcerative mass was resolved completely (figure 2). However, he came back with bone pain in the pelvis and weight loss of about 8-10 kg three months later. Whole body scan and Pelvic MRI showed a mass lesion in pelvis, and he had a relapse. At this setting, CBC and LDH was normal, but ESR was elevated (ESR=75). After that he did not come back and I was informed that he had died after 2-3 month due to the severity of the disease and treatment complications.



**Figure 2.** T cell lymphoma after treatment with radiation therapy.

### Discussion

The patient was presented with primary cutaneous ALCL (PCALCL), which led me to initially believe that his condition should be completely treated and he should have a good prog-

nosis. However, his relapse within the short interval changed my opinion. Being in an endemic area for HTLV1 (Mashhad, Northeast of Iran), I searched in the literature for this discrepancy and requested anti-HTLV1 for him. I found a recent report that described a subset of Cutaneous-ALCL patients with extensive limb disease who have worse treatment and survival compared with patients who do not have extensive limb disease [3]. In some special cases, co-expression of CD30/CD56 causes further progression of the disease [10]. Also, some cases were reported of adult HTLV1 related lymphomas having pathologic characteristics resembling ALCL, but considered to be CD30+ ATLL subtypes. The expression of CD30 in some patients may result in confusion with ALCL. The cytologic features and immunophenotype findings are pathognomonic of ATLL, but definite diagnosis require confirmation by serologic evidence of HTLV1, or to show viral antigen or DNA by molecular technique [11].

A case report from Korea (non-endemic area for HTLV1) also described patients with unusual presentation of ATLL, skin plaques and nodules, testicular mass without involvement of blood and bone marrow, and CD30 expression which histologically showed anaplastic large cell lymphoma [12]. Another study showed that patients with diffuse CD30 positive adult T-cell leukaemia/lymphoma have unusual clinical and immunohistological findings and are frequently presented with extranodal tumors and lymph node enlargement, and rarely with leukaemic changes, bone marrow involvement, or hypercalcaemia [13].

In another study in 52 patients with cutaneous ATL, histologic patterns resembling mycosis fungoides were found in 19 cases and ALCL was found only in two cases, which in contrast of our patient, were chronic and smoldering ATL. In this study, the author emphasized that it is important to differentiate between primary and secondary cutaneous ATL and classify the cases histologically in order to better evaluate the prognosis. They identified two forms of primary cutaneous ATL, primary cutaneous smoldering and primary cutaneous tumor. The smoldering type presented longer survival and histological aspects suggestive of better prognosis, in contrast to the primary cutaneous tumor type that had shorter survival and histological characteristics suggestive of worse outcome [14].

A study from Japan describe that, two types of cutaneous ATL thought to originate from skin include cutaneous tumor and erythematopapule types, and patients with cutaneous ATL show neither leukemic involvement nor invasion of tumor cells into the lymph nodes for at least six months[15]. All cases of cutaneous ATL resembling ALCL reported until now were multiple skin lesions and there are no presentations about single tumoral skin lesion, which we saw in our patient.

## Conclusion

As we can see across different the studies, there are different presentations of cutaneous ATL and ALCL, especially in regard to the primary type, and ATL was not included as occurring primarily in the skin in the last WHO and in the WHO/EORTC classifications of cutaneous lymphomas[16]. Therefore, there is a need for more studies and data collection around this entity.

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