# Systemic Variety of Anaplastic Large - Cell Lymphoma

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## Abstract

We present a case report of a patient with very aggressive course of anaplastic large-cell lymphoma. The patient had nonspecific complaints of easy fatigability and progressive breathlessness and had generalized lymphadenopathy. Initial investigations revealed pancytopenia. Bone marrow examination revealed presence of atypical cells. Liver biopsy showed portal tracts infiltrated by atypical lymphoid cells. Fine-needle aspiration of the lymph node finally confirmed anaplastic large-cell lymphoma. Patient succumbed to the illness.

***Keywords:*** Lymphoma, Pancytopenia.

## Introduction

Anaplastic large-T-cell lymphoma (ALCL) comes under the category of non-Hodgkin lymphoma and is its morphologically and immunologically distinct subset. It is characterized by the proliferation of pleomorphic large neoplastic lymphoid cells, which express the CD30 antigen (Ki-1 antigen), usually growing in a cohesive pattern and preferentially spreading in the lymph node sinuses.[1 2]

Two distinct clinical forms of primary ALCL are recognized: limited to the skin and systemic. Systemic ALCL has an aggressive clinical course and patients frequently present with systemic symptoms, advanced-stage disease and extranodal localisations.[2] Response to treatment and overall survival of systemic ALCL in children are good. In adults it is not clear.

## Case Report

A 55-year-old male presented with complaints of abdominal discomfort, easy fatigability for past 1 month. He also had complaints of fever for last 5 days, which was high grade and not associated with chills, rigors, rash or joint pain. There was also history of acute onset of exertional breathlessness for 5 days which was not associated with cough or change in posture. There was no history of orthopnea, paroxysmal nocturnal dyspnea, hemoptysis, weight loss, abdominal distention, or vomiting, nor did he have any history of jaundice, hematemesis, malena, diarrhea, constipation, or bleeding per-rectum. There was no history of headache, convulsion, and loss of consciousness. No past history of diabetes mellitus, hypertension, tuberculosis. Patient was non-smoker and non-alcoholic. On examination, patient was conscious, oriented, and febrile (oral temp: 100.2 °F). The pulse rate was 100 beats/minute, regular. Blood pressure was 100/60 mm Hg, respiratory rate 22 breaths/minute, abdomino-thoracic and regular. Pallor was present, no icterus, cyanosis or clubbing was present. Left supraclavicular lymphnode was palpable which was 2×3cm in size, non-tender and rubbery in consistency.

Bilateral inguinal lymph nodes were palpable, maximum size of 2 cm. Examination of chest revealed bronchial breath sounds in right infraclavicular region. No crackles were present. In abdominal examination there was hepatomegaly of 3 cm, and splenomegaly both firm in consistency, no free fluid was present. Cardiovascular and neurological

examinations were normal. Preliminary investigations showed hemoglobin level to be only 2.4 g/dL. Total leucocyte count was 2100/cu mm (polymorphs 50%, lymphocyte 42%, eosinophil 4%, monocyte 4%). The platelet count was 90,000/cumm. Blood urea was 49 mg/dL, serum creatinine 0.9 mg/dL, sodium 140 meq/dL, and potassium 3.5 meq/dL. Chest X-ray showed a nodular opacity in right upper zone and a patchy opacity in right lower zone. Ultrasound abdomen revealed an enlarged liver of 16.7 cm with mild increase in echogenicity and coarsened echotexture. Portal vein of 17 mm, and spleen of 8.2 cm was seen. Multiple enlarged lymph nodes in periportal, peripancreatic and paraaortic region were seen, largest being 3.2×2.1 cm.

Management in emergency was done with oxygen therapy, packed red cells transfusion, intravenous ceftriaxone, and pantoprazole. Myeloproliferative disorder was suspected and bone marrow aspiration was performed. Peripheral smear revealed polymorphs 32%, lymphocytes 45%, monocytes 2%, eosinophils 2%, myelocytes 2%, metamyelocytes 2% and atypical cells 15%. Red blood cells were normocytic normochromic; few macrocytes, and macroovalocytes were also seen. Platelets were reduced.

Bone marrow was hypercellular with paucity of hemopoetic precursors. Marrow was infiltrated by atypical cells which comprised 75-80% of marrow-nucleated cells that showed nuclear indentation, eccentric nuclei, and moderate amount of cytoplasm and were negative for myeloperoxidase (MPO) and periodic-acid-Schiff (PAS) stain. An impression of non-Hodgkin lymphoma (NHL) (acute nonmyelogenous leukemia) with spill over was made. Liver biopsy showed portal tracts infiltrated by atypical lymphoid cells of same morphology of that in bone marrow. Similar cells were also seen in sinusoids. Hepatocytes were normal. The findings were suggestive of lymphoma/ leukemic deposit. Fine-needle aspiration of the lymph node finally confirmed anaplastic large cell lymphoma T-cell NHL of high grade. Anaplastic lymphoma kinase (ALK) was positive and CD 30 positive T cells were also seen (Fig. 1). Chemotherapy was planned but unfortunately the patient succumbed to his illness on the next day of investigations.

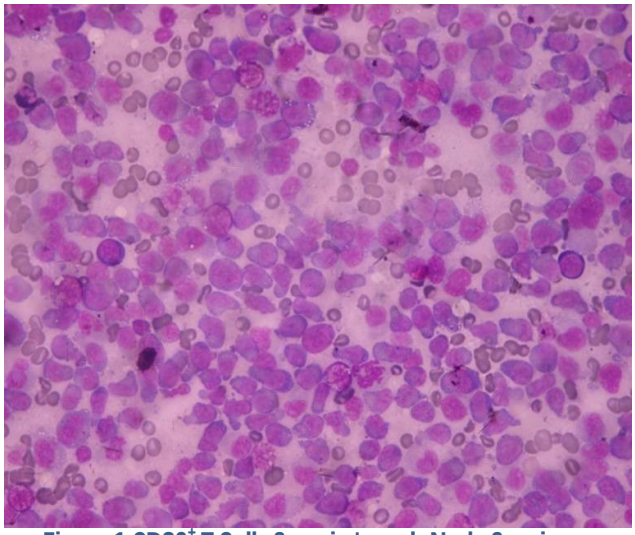

**Figure 1.CD30$^+$ T Cells Seen in Lymph Node Specimen**

## Discussion

Anaplastic large-cell lymphoma (ALCL) is a type of non-Hodgkin lymphoma involving aberrant T-cells. They are distinguished from other lymphomas by their anaplastic cytology and constant membrane expression of the CD30 antigen (an activation marker for B or T cells). It is seen as two distinct clinicopathologic subtypes. Systemic anaplastic large cell lymphoma (ALCL), which includes anaplastic lymphoma kinase (ALK)-positive and ALK-negative ALCL can present as secondary involvement of the skin as part of extranodal disease. The other one is primary cutaneous ALCL (PC-ALCL), according to the 2008 WHO classification, is part of the primary cutaneous CD30$^+$ T-cell lymphoproliferative disorder, which is a spectrum of diseases having lymphomatoid papulosis (LyP) at the benign end of the spectrum and PC-ALCL at the malignant end.[3] Major clinical features include frequent cutaneous and extranodal involvement, presentation at a younger age, and male predominance.[1,2] Patients with the ALK-positive systemic ALCL (median age, 24 years) are generally younger than the patients with primary cutaneous-ALCL and ALK-negative systemic ALCL (median age, 61 years). PC-ALCL has a better prognosis than the systemic type. Around 25% of patients with PC-

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ALCL show spontaneous regression. The evaluation of patients with any lymphoproliferative malignancy should include a detailed history and physical examination, with close attention paid to the presence of systemic B symptoms, lymph node involvement, organomegaly, and evidence of cutaneous involvement.

Meticulous examination of the lymph node specimen is required for diagnosis. Immunophenotypic and immunohistochemical studies are critical in the definitive diagnosis of ALCL. Major immunophenotypic features of ALCL include $CD30^+$, $CD15^-$, $PAX\text{-}5^-$, and $CD45^+$. Sixty percent of cases express one or more T-cell antigens ($CD3^+$, CD43, or CD45RO). Anaplastic lymphoma kinase (ALK) protein may be detected in most cases (60-70%) of systemic ALCL by immunohistochemistry. Treatment involves mainly chemotherapy, response to which is usually good. Doxorubicin-based combination chemotherapy stands out as a reference regimen from the trials of peripheral T-cell lymphomas.[2,5] The CHOP regimen is the most common therapy for systemic ALCL. Brentuximab vedotin, a CD30-specific antibody-drug conjugate composed of a chimeric monoclonal antibody linked by a dipeptide linker to a cytotoxic antitubulin agent, monomethyl auristatin E (MMAE) is used in cases of refractory and relapsed cases.[2,6,7]

This case was important because the patient had a systemic type of anaplastic lymphoma, ALK-positive at 55 years of age where usually cutaneous variety is seen. Also he had subtle signs and symptoms and had a very aggressive course of the disease that he succumbed to his illness in just a month.

**Conflict of Interest:** None

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