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Case Report

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A rare diagnostic case of angioimmunoblastic T-cell lymphoma

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ABSTRACT

Angioimmunoblastic T-cell lymphoma is a malignancy of mature T-cells. A 45 years old Sudanese female with generalized lymphadenomegalyreferred from Tayba hospital to Al-tayseer reference medical centre in histopathology and cytology laboratory department (Sudan) for her lymph node histopathology analysis. A surgical lymph node biopsy for histopathology analysis stained by H&E was performed and sections showed effacement of normal architecture of lymph node with disappearance of follicles and germinal center composed of polymorphic infiltrate of small tumour cells and large tumour cells. The small tumour cells showed irregular nuclei and clear cytoplasm. In this case report, we state that the delay of diagnosis was mainly a consequence of an insufficient clinical history, which led to an incomplete histological analysis, delay of reporting and need for second opinions for interpretation.

Keywords: Angioimmunoblastic T-cell lymphoma, lymph node, biopsy, immunohistochemistry stains

INTRODUCTION

Angioimmunoblastic T-cell lymphoma (AITL) is a malignancy of mature T-cells. It is characterized as a polymorphic lymphonodal lymphoid infiltrates accompanied by a prominent proliferation of endo-thelial venules and follicular dendritic cells. AITL was first described in 1974 by Frizzera et al. as angio immunoblastic lymphadenopathy with dysproteine-mia. [1] A short time later, the name was changed to immunoblastic lymphadenopathy, and then to lym-phogranulomatosis X in 1979. [2] AITL comprises 15–20% of all peripheral T-cell lymphomas and 1–2% of all non-Hodgkin lympho-mas (NHL). Most frequently, it occurs in aged patients, with equal prevalence between males and females. Typically, AITL displays aggressive behavi-our, which makes the diagnosis difficult and it must be differentiated from other malignant lympho proli-ferative diseases, drug reactions and viral infections. Patients with

AITL frequently exhibit B-symptoms (e.g., fever and weight loss) and a generalized enlargement of the lymph nodes. Other common symptoms include heaptomegaly, splenomegaly, polymorphic skin rash and pleural effusion. AITL is also associated with autoimmune phenomena. Polyclonal hypergamma-globulinemia occurs in approximately 50% of AITL cases. [3] Histological analyses of AITL specimens show effacement of the lymph node architecture, particularly in advanced stages. Malignant cells tend to distribute into interfollicular regions, and are typically positive for T-helper cell markers and T-cell receptors (TCRs) alpha and beta. [2, 4] Immunoblasts, often positive for Epstein–Barr virus (EBV), are frequently dispersed in paracortical regions. This characteristic can be confused with Reed-Sternberg cells, which can lead to a mistaken diagnosis of Hodgkin's lymphoma (HL). TCR gene rearrangeme-nts are found in 70% of cases. On the other hand, immunoglobulin gene rearra-ngements are found in only 10% of patients with AITL. [5]

There is no standard treatment for AITL. Consequently, patients may be treated with different drugs, including steroids, immunomodulators or by cytotoxic chemotherapy. However, the most commonly used treatment modality is the cyclophosphamide, vincristine, doxorubicin and prednisone (CHOP) regimen, associated or not with etoposide. This trea-tment is typically followed by autologous hemato-poietic stem cell transplantation. Further more, the natural history of AITL is characterized by several relapses, with a five-year overall survival of 30%. [6, 7]

In this case report, we analyzed the main clinical characteristics that make AITL diagnosis difficult. As AITL is a rare disease with a poor prognosis, an early and correct diagnosis is essential to improve survival and quality of life.

CASE REPORT

A 45 years old Sudanese female with generalized lymphadenomegaly (neck, abdomen, inguinal, supra-clavicular and axillar regions) referred from Tayba hospital to Al-tayseer reference medical centre in histopathology and cytology laboratory department (Sudan) for her lymph node histopathology analysis. The disease was first noticed three months previously.

At admission toTayba hospital, the complete blood count showed 10.7 g/L hemoglobin, 16.4×10^9/L white blood cell count with 23% lymphocytes and 10×10^3/µl platelets. The peripheral blood film report showed normocytic normochromic, neutrophil leukocytosis with few reactive lymphocytes and severe thrombocytopenia. Furthermore, a bone marrow biopsy demonstrated hypercellular bone marrow, megakaryopoiesis is overactive, erythron-poiesis is active with mild micronormoblastic maturation and dyserythropoietic, active granulopoiesis with ordered maturation and increased eosinophilis, mild lymphocytosis, no L.D bodies, focal areas show-ed excess infiltration by lymphoid cells and mono-nuclear cells, areas of ill-defined granuloma noted in trephine biopsy, no abnormal cells seen, no fibrosis and the conclusion of bone marrow report was sug-gested workup of T.B and immunohistochemistry to rule out lymphoproliferative disorder.The patient was submitted to an Echocardio-graphy scan that showed presserved L.V systolic func-tion, E.F 55%, dilated L.A and M.V.B with severe M.R=R.H.D. A surgical lymph node biopsy for histopathology analysis stained by H&E (Figure 1A and B) was performed and sections showed effacement of normal architec-ture of lymph node with disappearance of follicles and germinal center composed of polymorphic infilt-rate of small tumour cells and large tumour cells. The small tumour cells showed irregular nuclei and clear cytoplasm. The large tumour cells showed vesicularnuclei and prominent nucleoli with rare Reed Stern-berge like cells and multinucleated giant cells. High endothelial venules, eosinophiles and plasma cells are noted.

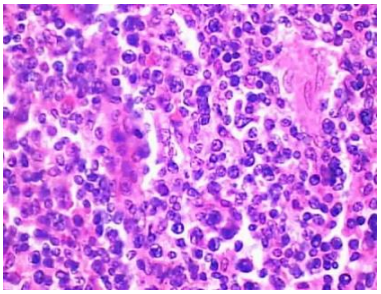

Figure 1. A: Angioimmunoblastic T. cell Lymphoma Composed of small tumour cells with irregular nuclei and clear cytoplasm. (H&E X10)

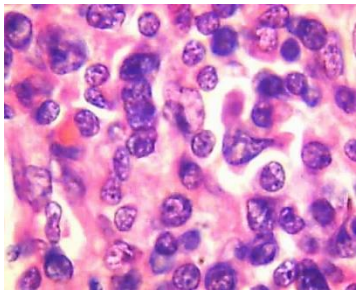

Figure 1. B: Angioimmunoblastic T. cell Lymphoma Composed of large tumour cells with vesicular nuclei and prominent nucleoli. (H&E X100)

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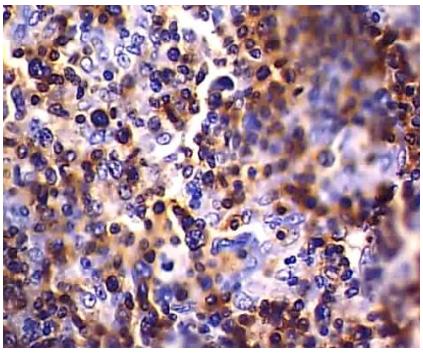
The immunohistochemistry stains (Figure 2A-C) showed polyclonal features with positive CD3 of most small cellstumour, some population are positive for CD20, CD15 and CD23. Tumour cells are negative for CD30, CD5 and CD1a. The patient complained with symptoms including: high fever, night sweats and skin rash.



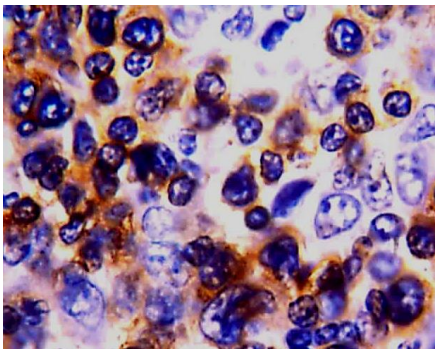


Figure 2. A: Immunoglobulin (CD3) incorporated; Figure 2. B: Immunoglobulin (CD3) incorporated in the cytoplasm of malignant cellsin the cytoplasm of malignant cells
(Immunoperoxidase method with DAB chromogen X10).(Immunoperoxidase method with DAB chromogen X100).

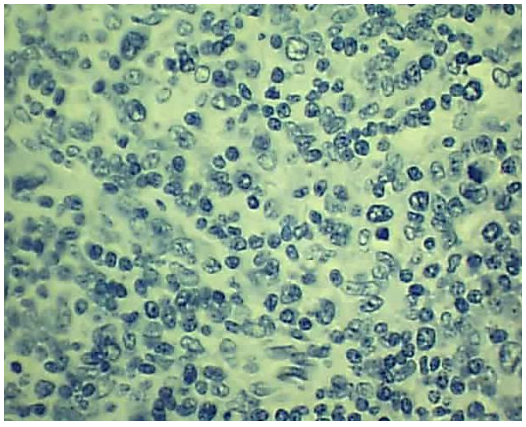


Figure 2.C: Immunoglobulin (CD30) is negative for malignant cells
(Immunoperoxidase method with DAB chromogen X10).

PAS special stain showed positive for blood vessels invasion (Figure 3).

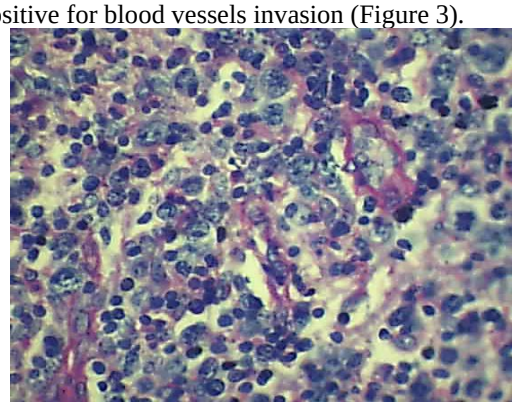


Figure 3. The blood vessels invasion-stained magenta red color by PAS stain X40.

DISCUSSION

AITL is an aggressive malignancy. It is the second most common peripheral T-cell lymphoma in Western countries. Although many patients achieve complete remission, disease relapse is frequent, and the recent years overall survival is less than 50%. The clinical symptoms of AITL are not specific and, consequently, the diagnosis can be complex and sometimes delayed. The clinical features of AITL are more related to immune dysfunction than to tumor growth. For example, AITL symptoms include skin rash, fever, generalized lymphadenopathy and polyclonal hyper-gammaglobulinemia, which are common featurees of infections and autoimmune disorders. [3]

The gold standard for AITL diagnosis is excisional lymph node biopsy. However, to save time and to avoid exposure to invasive procedures, many centers perform a core biopsy to obtain samples for pathological analyses. Unfortunately, the samples obtained by core biopsy can be insufficient to perform a complete immunohistochemical panel and ensure the correct diagnosis.

Previous studies have shown that the accuracy of a lymphoma diagnosis based on core biopsies varies from 68% to 94%. [8] Inadequate core biopsies are associated with misdiagnoses or delayed diagnoses. Gupta et al. compared lymph node biopsies acquired with either fine-needle aspiration or surgical excision in 100 patients. They found that the rates of accurate diagnoses based on fine-needle aspirations were 77% in reactive hyperplasia, 75% in NHL, and 85% in metastatic carcinoma. A recent meta-analysis showed that core biopsies provided adequate material for histology in 95% of cases, particularly in salivary gland lesions, but inadequate material in 39 (2.6%) cases of lymphadenopathies of the head and neck. In differentiating between malignant lymphoma and reactive lymph nodes, core biopsies showed a high false-negative rate and a low negative predictive value (85%). [9]

A full histological and immunohistochemical analysis of the lymph node is essential for the differentiation between AITL and other diseases. For example, it can differentiate between large cells with two or more nuclei, which are frequently observed in AITL tumor microenvironments, and Reed-Sternberg cells. [3, 4]

Singh et al. demonstrated that 17/17 patients with AITL in the leukemic phase harbored a distinct population of $CD3^{-}/CD4^{+}$ T-cells in the peripheral blood. Furthermore, this phenotype was highly specific to AITL because it was found in only 1/40 patients with other T-cell lymphomas in the leukemic phase. They showed that this phenotype provided a positive predictive value of 94% for a diagnosis of AITL. Those authors concluded that immune-phenotyping peripheral blood with flow cytometry might be a useful method for achieving a differential diagnosis of AITL, even though the aberrant T-cell population occurs at a very low frequency in peripheral blood. [10] Therefore, this assay should be part of lymphoma investigations, especially in inconclusive cases, because it can save time and improve the accuracy of diagnosis.

In this case report, we state that the delay of diagnosis was mainly a consequence of an insufficient clinical history, which led to an incomplete histo-logical analysis, delay of reporting and need for second opinions for interpretation. We also strongly recommend that to obtain an accurate and precise diagnosis for AITL, PAS stain should be performed firstly to recognize the capillary invasion which facili-tate the early diagnosis. Ancillary studies, such as peri-pheral blood immunophenotyping and PCR detection of TCR rearrangements, are very important tools to establish differential diagnoses, and should be part of the investigation to improve the accuracy or to confirm the diagnosis of AITL.

Conflict of interest

The authors declare no conflict of interest.

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