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Case Report
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Angioimmunoblastic T Cell Lymphoma: Typical Presentation of an Atypical Disease

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Abstract

Angioimmunoblastic T-cell lymphoma (AITL) is an uncommon T-cell type of non-Hodgkin lymphoma. Its clinical manifestations are typical of lymphoma, and may include maculopapular rashes resembling viral origin. Patients may present with seropositive polyarthritis, fever, pruritus, lymphadenopathy, night sweats, weight-loss and edema. Incongruous clinical symptoms raise the possibility of AITL, e.g. sick-sinus syndrome, collagen-vascular diseases such as rheumatoid arthritis and dermatomyositis. We report herein a case of AITL which is an uncommon example of how atypical diseases can be compounded by antitubercular-drug allergy, however, ultimately a small sub-centric cervical lymph-node biopsy and immunohistochemistry proved to be confirmative for AITL.

Keywords: Angioimmunoblastic lymphoma; Pulmonary tuberculosis; Lymphadenopathy

Introduction

Angioimmunoblastic T-cell lymphoma (AITL) is recognized as an uncommon T-cell type of non-Hodgkin lymphoma (NHL) [1,2]. AITL used to be called angioimmunoblastic lymphadenopathy with dysproteinemia (AILD) [3]. The clinical manifestations of AITL and AILD are typical of lymphoma, and may include maculopapular rashes (resembling viral rash) and seropositive polyarthritis, fever, pruritus, lymphadenopathy, night sweats, weight loss and edema. Patients can present with acute abdomen, disseminated infections with herpes virus type-6 and other viral infections. Incongruous clinical symptoms raise the possibility of AILD, *e.g.* sick sinus syndrome and collagen-vascular diseases, such as rheumatoid arthritis and dermatomyositis.

Case Presentation

A 54-year old female diagnosed elsewhere as sputum smear-negative pulmonary tuberculosis, was admitted with chief complaints of fever on and off, generalized weakness, cough with expectoration, rashes and itching of the whole body. She was a housewife a non-smoker, non-alcoholic but a regular tobacco-leaf chewer. She had no history of pulmonary tuberculosis or other chronic illness. Before hospitalization, she had received two-weeks of anti-tubercular treatment and diagnosed as sputum smear-negative pulmonary tuberculosis based on chest–X-ray finding and CT-scan abdomen showing abdominal lymphadenopathy. Following anti-tubercular treatment, the patient's symptoms persisted with generalized weakness, decreased appetite, weight-loss and generalized itching with rashes and therefore, she had been referred to our hospital for further management.

On clinical examination she had pallor+++, no icterus, cyanosis, clubbing or pedal edema. A single lymph node of size 1x1cm was palpable in right cervical region (firm, non-tender, freely mobile, not attached to underlying tissue, skin over the gland was normal). Pulse was 118/min, regular, normal in character. Blood pressure was 90/60mmHg. SpO_2 was 94% at room air and respiratory rate-22/min (thoraco-abdominal). Upper respiratory tract was normal. Lower respiratory tract was normal except coarse crepitations on auscultation all over the lung fields. Other systemic examination was normal. She was provisionally diagnosed to have Disseminated TB with Anti-tubercular drug induced allergy. Laboratory tests showed Hb-7.9g%, Platelet-73000/cumm, TLC-4, 500/cumm, DLC (N-48%, E-3%, L-43%, M-6%) with erythrocyte sedimentation rate (ESR) of 150mm/1st hr. Liver function Test/Renal function Test (LFT/RFT) and fasting blood sugar(FBS)

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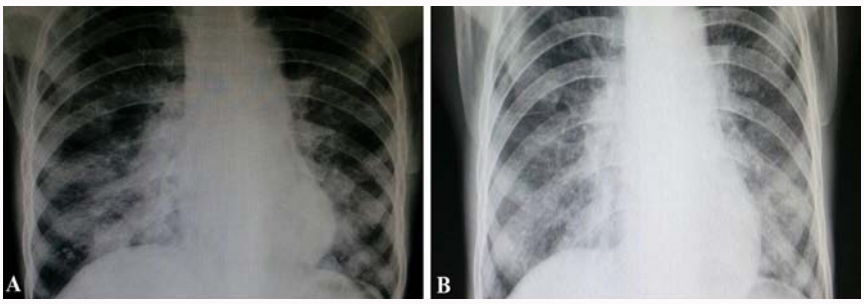

Figure 1: (A) CXR-showing bilateral reticulonodular shadows in mid and lower zones, (B) CXR-showing worsening of the earlier lesions.

were normal, with serum protein-6.8 g/dL, serum albumin-2.7g/dL and LDH-384U/L. Peripheral blood smear examination showed normocytic, normochromic anaemia with clumped RBC, leukopenia, thrombocytopenia and immune-hemolysis. Direct Coombs' test was positive.

Chest X-Ray-showed bilateral reticulonodular shadows (mid and lower zones, Figure 1A-B). CT-thorax showed paratracheal lymph node, nodular opacity and patchy air space consolidation in bilateral lung parenchyma associated with mediastinal lymphadenopathy (Figure 3B, C). CT-abdomen showed peripancreatic and para-aortic lymphnode. Bronchoscopy revealed no endo-luminal pathology (Figure 3A). Broncho-alveolar lavage fluid analysis showed benign respiratory lining epithelial, alveolar macrophages and few inflammatory cells. Biopsy of very small single right cervical lymph-node with Haemotoxylin and Eosin (H&E) staining and immuno-histochemical analysis established the diagnosis of angio-immunoblastic T-cell lymphoma (Figure 4A-H). Ziehl Neelsen (ZN) stain for acid fast bacilli (AFB) of lymphnode was negative. Patient was managed with Tab. prednisone 40mg/day and planned for cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP) regimen, however, she was discharged on request and later lost to follow up.

Discussion

AITL contributes 1-2% of NHL and 10-20% of peripheral T-cell lymphoma (PTCL) in US. It mostly affects elderly population (median age-59-65 years) with slighter greater preponderance in males [2]. The most common presentation is generalized lymphadenopathy, hepatomegaly and splenomegaly (74%) with B-symptoms (70%) (fever, weight-loss, night-sweats). Skin involvement occurs in around 50% of patients. AITL can mimic tuberculosis and patients may be treated with anti-tubercular drugs but later on AITL could be diagnosed based on lymph-node biopsy [4]. AILD associated with proliferative glomerulonephritis has also been reported earlier, though it is an extremely rare event [5]. Pulmonary findings are varied and include hypoxemia, but some patients have interstitial pneumonia or broncho-pneumonia. Patients with broncho-pneumonia can have opportunistic infection such as *Pneumocystis jiroveci* pneumonia. Cases with shortness of breath and peripheral edema have also been reported earlier [6].

The pathogenesis of AITL remains unclear. In some cases the disease is preceded by an allergic reaction, infection or drug exposure. Laboratory findings could be pancytopenia, circulating immune complexes, anti-smooth muscle antibodies, autoimmune-hemolysis, cold agglutinins, para-proteinemia and presence of anti-cardiolipin antibodies. Rheumatoid factor and cryoglobulins are rare. But ESR is raised in most cases, LDH levels are commonly increased, polyclonal

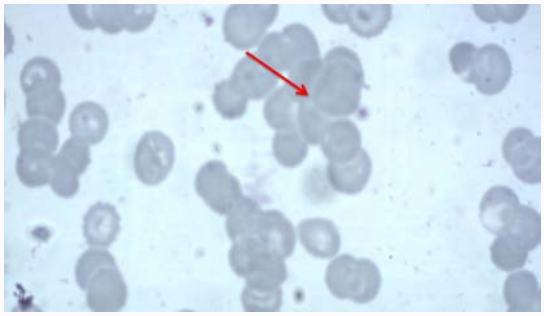

Figure 2: Peripheral Smear showing RBC clumps indicative of immune mediated hemolysis.

gamma-globulins are common and direct Coombs' test can be positive [7,8]. Radiographic findings may show bilateral mediastinal and hilar lymphadenopathy, pleural effusion, interstitial/alveolar shadow and atelectasis. Diagnosis is usually very challenging, however, biopsies of bone-marrow, lymph-node, and skin are key tools. The gold standard for diagnosis in such cases is biopsy of affected lymph-node. A variety of T-cell associated antigens can be used to confirm tumor cells in AITL, such as CD3+, CD4+, CD8−,CXCL13+, CD10+, BCL6+, CD19, CD20, CD1a, Tdt, CD21, and CD23+ [2,9]. In this case, it was confirmed using in CD3+, CD15-, CD30+ and CD 20- antigens, as illustrated in figure 4, (D-H). The clonality of cells can be detected with T-cell clonality, eventually detected in 75% of cases. First line of treatment is anthracyclin based therapy-which can achieve complete remission in 61% with 5-year survival rate of 32% and recurrence-free survival rate of 18%. Clinical course of AITL can be aggressive, with a median survival of less than 3-year regardless of type of treatment. It can evolve into high grade symptoms of B-cell or T-cell type, Epstein Barr Virus (EBV) positive B-cell lymphoma and chronic lymphatic leukemia. Unfortunately, most patients die of infections, due to immunological compromise [10].

The key findings in favour of AITL as shown in this case, were symptoms of itching, rashes, fever, weight-loss, cervical lymphadenopathy, pancytopenia, autoimmune-hemolysis, DCT-positive, raised ESR, raised serum protein, decreased albumin, raised LDH, CRP positive, ANA Positive and CXR showing bilateral reticulo-nodular shadows. CT-Thorax had nodular opacities and patchy air-space consolidation in bilateral lung parenchyma associated with mediastinal lymphadenopathy. CT-abdomen showed lymphadenopathy with histopathological confirmation of cervical lymph-node.

Conclusion

Increased awareness and high degree of clinical suspicion,

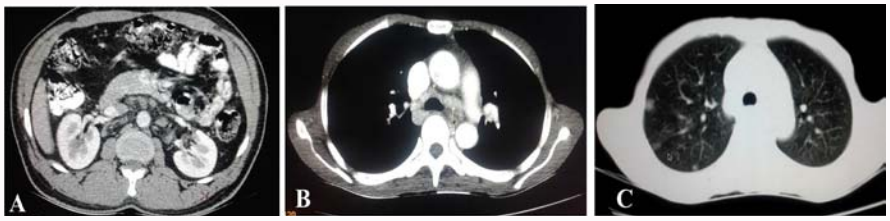

Figure 3: (A) CT-abdomen (Axial) showing peri-pancreatic lymph node (B)CT thorax (Axial) Mediastinal window showing paratracheal lymphnode, (C) CT thorax (Axial) showing nodular opacity, patchy airspace consolidation.

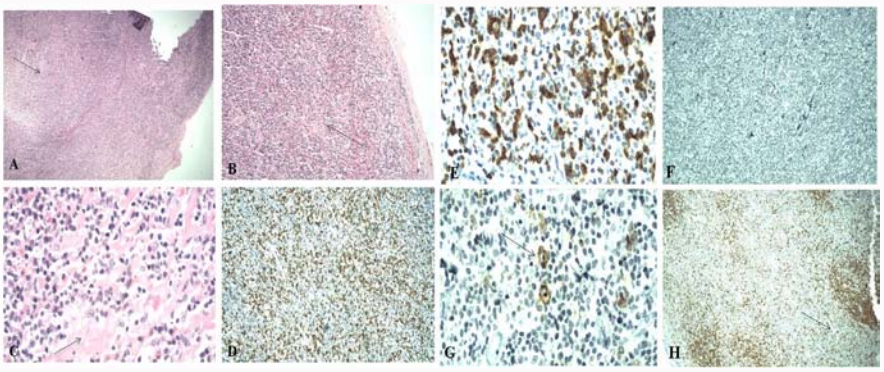

Figure 4: (A) H & E section of lymphnode showing Pseudonodule formation (B) Low Power view of H & E section of lymphnode showing Hyaline Changes and Medium and Large sized population of Lymphocytes (C) High Power view of H & E section of Lymph Node showing Hyaline Changes, Immunoblasts and Medium Sized Lymphocytes. (D) IHC (CD3+) Scanner view ; (E) IHC (CD3+) High Power, (F) IHC CD 15- Scanner View; (G) IHC (CD30+) Immunoblasts High Power View; and (H) Scanner View CD 20- Lymphoma Cells.

coupled with advanced imaging and histopathological technique can enable the diagnosis of such cases, which can be often misdiagnosed as tuberculosis. Even biopsy, histological and immune-histochemical analysis of very small superficial lymph-nodes can establish the diagnosis of AITL. Therefore prompt diagnosis may improve the survival and quality of life.

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