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Case Report

Oncology Section

A Case of Angioimmunoblastic T-Cell Lymphoma

KANCHAN DASHARTHRAO DEVDE[1], AMOL GAJANAN ANDHALE[2], AMOL SHANKAR DONGRE[3], HIMANSHI KAUSHIK[4], PRERNA TEKULWARE[5]

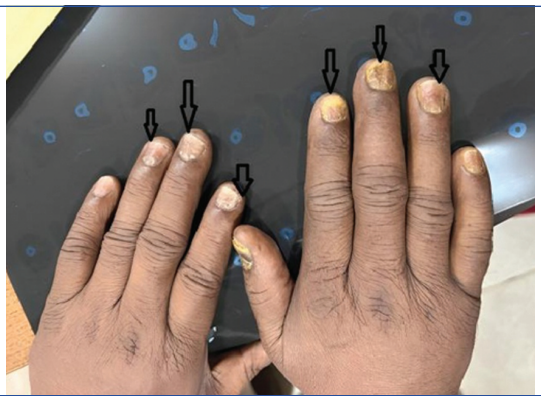
ABSTRACT

Angioimmunoblastic T-cell Lymphoma (AITL) is a rare type of peripheral T-cell lymphoma characterised by an aggressive clinical course and a poor response to current therapies. There is currently no standard of care for treatment. A case of a 59-year-old male with a history of diabetes mellitus and hypertension presented to the emergency department with chief complaints of intermittent fever, difficulty walking, and generalised weakness. The patient was evaluated for these complaints, and a general examination revealed multiple cervical, axillary, and inguinal lymphadenopathy. Further evaluation with a Positron Emission Tomography-Computed Tomography (PET-CT) scan showed Fluorodeoxyglucose (FDG) uptake in the bilateral cervical and supraclavicular lymph nodes. A biopsy of a cervical node revealed sheets of intermediate-sized lymphoid cells, with a few scattered large cells and macrophages, favoring a diagnosis of lymphoma. Further Immunohistochemistry (IHC) was required to determine the final diagnosis. IHC results were positive for CD3, CD2, CD10, PD1, ICOS, CD7, and CD4, which further supported the diagnosis of AITL. The patient was then planned for chemotherapy with the Cyclophosphamide, Adriamycin, Oncovin, and Prednisolone (CHOP) regimen on a 21-day cycle. After four cycles of the CHOP regimen, the patient presented with abdominal distention and bilateral lower limb swelling, requiring multiple blood transfusions due to low haemoglobin levels. Bone marrow biopsy findings suggested hypocellular marrow with atypical lymphoid cells, indicating progression of the disease. The patient was subsequently planned for second-line chemotherapy, considering the patient's poor performance status, with the single agent Azacitidine. The patient was also advised to undergo Epstein Barr Virus (EBV) testing but was lost to follow-up due to poor performance status.

Keywords: IHC, Nail dystrophhy, CHOP, Bone marrow

CASE REPORT

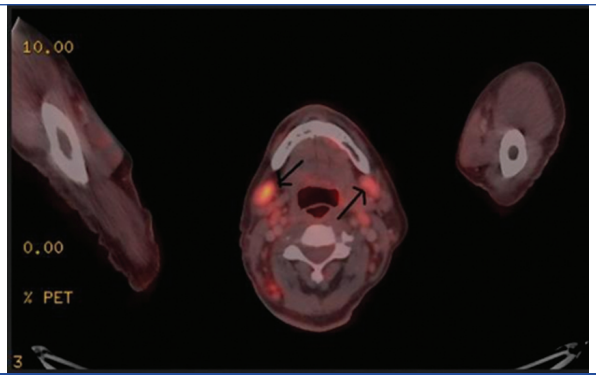
A 59-year-old male, known to have hypertension and type 2 diabetes mellitus, has been on medication for three years. He presented to the emergency department with chief complaints of generalised weakness, intermittent fever, decreased appetite, and weight loss over the past eight months. His clinical examination revealed pallor, as well as axillary, cervical, and inguinal lymphadenopathy, along with nail dystrophy of both hands, as shown in [Table/Fig-1]. The patient was further evaluated with a PET-CT scan and laboratory parameters mentioned in [Table/Fig-2]. The PET-CT scan findings suggested FDG uptake in the bilateral cervical and supraclavicular lymph nodes [Table/Fig-3].



[Table/Fig-1]: Dorsal aspect of both hand showing 20 nails. dystrophy (black) arrow.

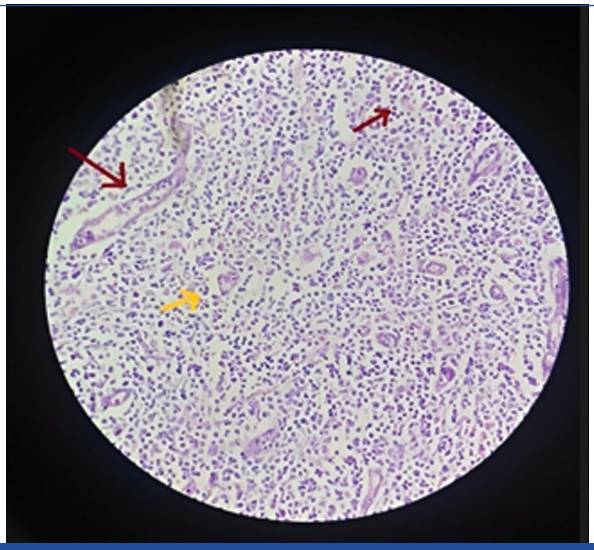
Parameters	Patient value	Reference range
Hb (g/dL)	10	13-15
Whole blood cell count (mm^3)	2500	4000-11000
Platelet (mm^3)	100000	1.5-4×105
Haematocrit (%)	36	40-60
Lymphocyte (%)	30	20-50
Neutrophil (%)	60	30-60
Lactate Dehydrogenase (LDH) (U/L)	340	140-280
Sodium (mmol/L)	129	136-144
Potassium (mmol/L)	4	3.7-5.2
Calcium (mg/dL)	7	8-10
Creatinine (mg/dL)	1.1	0.7-1.5
Albumin (g/dL)	2	3.5-5.5
Protein (g/dL)	5	6.6-8.3
Bilirubin (mg/dL)	1	0.3-1
Serum Glutamic Oxaloacetic Transaminase (SGOT) (U/L)	38	7-55
Serum Glutamate Pyruvate Transaminase (SGPT) (U/L)	25	8-48
Alkaline Phosphatase (ALP) (U/L)	121	40-129

[Table/Fig-2]: Blood investigations findings of the patient.



[Table/Fig-3]: PET-CT scan FDG avid-up take in bilateral cervical lymphnode (Black arrow).

A cervical lymph node biopsy was performed, and microscopic examination revealed sheets of intermediate-sized lymphoid cells, with a few scattered large cells and macrophages, as shown in [Table/Fig-4], favouring the diagnosis of lymphoma. Further IHC was conducted to determine the type of lymphoma. The IHC results were positive for CD3, CD2, CD10, PD1, ICOS, CD7, and CD4, which further supported the diagnosis of AITL.



[Table/Fig-4]: Cervical lymph node histopathology under 40x microscope showing small to intermediate sized lymphocyte with (red arrow) macrophage (yellow arrow).

The patient was then planned for chemotherapy with the Cyclophosphamide, Adriamycin, Oncovin, and Prednisolone (CHOP) regimen on a 21-day cycle. After the fourth cycle of the CHOP regimen, the patient presented with intermittent high-grade fever, anemia, thrombocytopenia, and ascites, for which he required multiple blood transfusions. Further bone marrow evaluation revealed the presence of atypical lymphoid cells, suggesting involvement of the bone marrow by the disease, indicating clinical and haematological progression despite CHOP therapy.

Considering the patient's general condition, chemotherapy was switched to the single agent injection Azacitidine (75 mg/m^2) and oral Cyclosporine (100 mg twice daily). The patient tolerated the first cycle of Azacitidine well. He was also advised to undergo Epstein Barr Virus (EBV) testing but was lost to follow-up due to his poor general condition.

DISCUSSION

Angioimmunoblastic T-cell Lymphoma (AITL) is a rare type of peripheral T-cell lymphoma that accounts for approximately 10-15% of cases of non-Hodgkin lymphoma and 1-2% of all peripheral T-cell lymphoma cases. It is associated with a poor outcome [1]. The median age of presentation is 65 years, with equal prevalence in males and females. AITL is primarily a CD4 T-cell disorder, featuring dysregulated B cells and endothelial cells [2]. Patients typically present with fever, weight loss, urticaria, papules, red nodules, skin lesions, generalised lymphadenopathy, and organomegaly [3]. Skin manifestations range from urticarial lesions to nodular tumours. Prodromal symptoms have been reported in 20-50% of AITL patients [4]. EBV has been found to play a role in the pathogenesis of AITL by activating helper T cells and leading to tumour development [5]. The diagnosis of AITL is based on histopathological examination, but it lacks specific pathological features.

In 1974, Frizzera G et al., described a reactive lymphoproliferative disease affecting T cells as AITL [6]. The WHO classified AITL as a peripheral T-cell lymphoma in 2001. The pathophysiology of AITL remains largely unknown. An allergic reaction, infection, or medication exposure can also precede the condition [7,8]. A TET2 mutation may be responsible for the disease's multi-lineage character, as it affects early haematopoietic progenitor cells, potentially creating a malignant potential for both B and T cell lineages, and possibly leading to adverse outcomes in other cell lines [9]. A study analysing the genetic abnormalities in patients with AITL showed that various mechanisms are likely present, with several pre-existing mutations being the most frequent [10]. AITL has been treated using various regimens, with anthracycline-based chemotherapy considered the first line [11]. It has been found that 61% of AITL patients achieve a complete response with anthracycline-based chemotherapy, with a 32% five-year overall survival rate and an 18% recurrence-free survival rate [12]. The chance of complete remission is higher with high-dose chemotherapy followed by autologous stem cell transplant [13].

The diagnosis of AITL remains challenging due to the absence of specific diagnostic criteria. Various prognostic factors have been identified, including age over 60 years, an LDH level more than twice the upper limit of normal, involvement of more than two extranodal sites, B symptoms, and bone marrow involvement. Some studies have also found that raised β2M and C-Reactive Protein (CRP) levels at the time of diagnosis are associated with worse progression-free survival [14,15]. B symptoms such as fever, weight loss, nail changes, and lymph node involvement were the initial presentations of this patient. The patient showed clinical improvement following the first four cycles of the CHOP regimen. However, after the fourth cycle of chemotherapy, the patient progressed clinically, presenting with ascites and pancytopenia due to bone marrow involvement. Optimal treatment for AITL remains an unmet need. Deeper knowledge of the disease biology and novel therapeutic approaches are required to improve outcomes.

CONCLUSION(S)

AITL is a rare disease with complex symptoms. Since the disease biology remains unknown and AITL has limited targeted therapeutic options, this patient presented with cutaneous involvement and showed disease progression during therapy, indicating the need for aggressive treatment. Autologous stem cell transplant is also an option for this condition, but this patient was not a candidate for transplant due to his general condition.

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PARTICULARS OF CONTRIBUTORS:
1. Senior Resident, Department of Medical Oncology, Jawaharlal Nehru Medical College, Wardha, Maharashtra, India.
2. Senior Resident, Department of Neurology, Jawaharlal Nehru Medical College, Wardha, Maharashtra, India.
3. Professor and Head, Department of Medical Oncology, Jawaharlal Nehru Medical College, Wardha, Maharashtra, India.
4. Senior Resident, Department of Medical Oncology, Jawaharlal Nehru Medical College, Wardha, Maharashtra, India.
5. Junior Resident, Department of Pathology, Jawaharlal Nehru Medical College, Wardha, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Kanchan Dasharthrao Devde,
Flat No. 402, Subhadra Mansion, Sawangi, Meghe, Wardha-442001,
Maharashtra, India.
E-mail: drkanchandevde@gmail.com

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