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Case Report and Systematic Review

Angioimmunoblastic T-cell lymphoma associated with leukocytosis and lymphocytosis; a case report and systematic review

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Abstract

Background: Angioimmunoblastic T-cell lymphoma (AITL) is an uncommon lymphoma arising from follicular T-helper cells. Since this is a rare disease, diagnosis is unfortunately difficult. AITL responds to treatments, therefore by reviewing the characteristics of the available cases, we aimed to classify the available data for in-time diagnosis.

Objectives and data sources: A systematic search was performed on PubMed, Scopus, and Web of Science to January 5, 2023, to investigate the presence of peripheral blood lymphocytosis and leukocytosis in AITL cases.

Results: Among 129 papers, 41 articles with 46 cases were included. All 41 studies were checked in terms of quality by two independent reviewers using an eight-item Joanna Briggs Institute checklist for case report studies. We also reported a 57-year-old Iranian woman with AITL suspected rash. Complete blood count (CBC) analysis showed a significant lymphocytosis and leukocytosis of 26 and 37.5 × 10^9/L, respectively.

Conclusion: In the reviewed cases, male predominance was obvious. Lymphadenopathy was the most seen clinical presentation. Dermal abnormalities were presented in more than half of the patients. The prevalence of blood eosinophilia was also remarkable; CD3 and CD4 were expressed the most and CD7, CD8, CD30, and CD56 the least. Despite treatment, the mortality rate was high. In this systematic review, we tried to provide a complete classified review of all AITL cases with different types of leukocytosis to avoid future miss diagnosis of this rare lymphoma.

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1. Introduction

Hematological malignancies cause high mortality rates (1). Angioimmunoblastic T-cell lymphoma (AITL) is known as a rare malignant lymphoproliferative disorder (2, 3). Based on the 5th edition of the world health organization (WHO) haematolymphoid tumors classification in 2022, this neoplasm is a member of nodal T-follicular helper cell lymphomas which is renamed nodal T-follicular helper cell lymphoma, angioimmunoblastic type (nTFHL-AI) and comprised about 15-30% of peripheral T-cell lymphoma (PTCL) and 1-2% of non-Hodgkin lymphoma (NHL) cases (4, 5). Regardless of several progressions through these years, there are still difficulties in finding definite characteristics of AITL. Due to poor prognosis, this lymphoma is mostly detectable in advanced stages and it often leads to low survival rates (6). From a clinical point of view, patients often represent B symptoms (fever, weight loss, night sweats) and generalized lymphadenopathies. Less frequent manifestations are hepatosplenomegaly, pleural/pericardial effusion, joint pain and inflammation, and various skin complications such as papules, plaques, and nodular tumors (7-9). In AITL cases, immunological disorders like polyclonal hypergammaglobulinemia and autoimmune hemolytic anemia with warm autoantibodies might take place (10). In addition, other laboratory findings exhibit increased levels of lactate dehydrogenase (LDH) (60–71%), and β2-microglobulin (22–82%), besides anemia (with 33–65% occurrence) (11), thrombocytopenia (in 20-50% of patients) and lymphopenia (52-66%), though not many studies are available reporting lymphocytosis (5). It is worth noting that due to unspecific symptoms of AITL, diagnosis at early stages has remained a challenge. Moreover, leukocytosis and lymphocytosis are not common findings in the peripheral blood assessment of these patients. Thereupon, obtaining more information from a hematologic view is essential. To the best of our knowledge, few studies have focused on the hematologic aspect of AITL. In this paper, we described an AITL case with lymphocytosis and carried out a systematic literature review which provided a better insight into AITL, especially by emphasizing the relevant demographic and clinical characteristics, as well as the treatment and outcomes of this unique disease. This comprehensive review considers all challenging articles about AITL hematologic features.

2. Case presentation

A 57-year-old Iranian female was admitted in March 2022 with dermatological conditions which were presented a few weeks before admission. She was first referred to a dermatologist and given treatment for her diffused rashes and abscesses. After showing resistance to treatment, lymphoma was suspected. Complete blood count (CBC) revealed 37.5 × 10^9/L white blood cell (WBC) count with a high percentage of lymphocytes (69%), 27 × 10^3/µl platelets, 3.93 × 10^6/µl red blood cells (RBC), 11.6 gr/dl hemoglobin, and 36% hematocrit. Laboratory analysis of peripheral blood showed leukocytosis, anisocytosis, and lymphocytosis. The blood smear investigation demonstrated 70-75% of lymphoid cells with small and medium sizes. Also, few smudge cells were seen. The absence of blasts was identified (**Figure 1**). Biopsy of bone marrow was performed which showed severe infiltration of small lymphoid cells. Other nucleated elements were significantly decreased. Immunophenotyping results were positive for CD2, CD3, CD4, CD5, CD7 (with down expression), and CD10. CD8 and CD38 were negative in malignant cells (**Figure 2**). Chemotherapy with cyclophosphamide, vincristine, doxorubicin, and prednisone (CHOP) was given to the patient. She died after receiving the first cycle of CHOP.

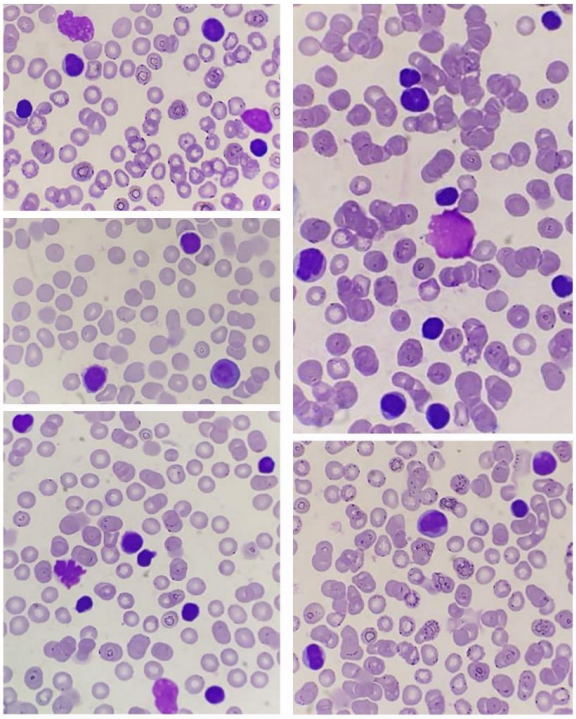

Figure 1. Peripheral blood smear showed small and some medium-sized lymphocytes. Some lymphocytes have cleaved nuclei. Few smudge cells are present.

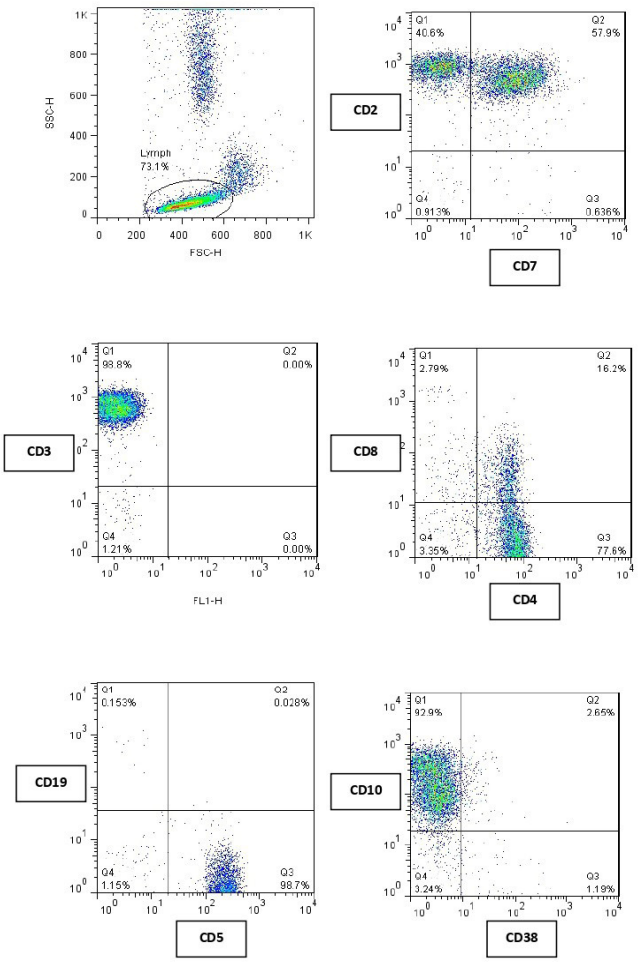

Figure 2. Immunophenotyping demonstrates the positivity of CD2/CD3/CD4/CD5 with a down expression of CD7 and negativity of CD8. CD4/CD8 dual marker was negative and aberrant expression of CD10 was observed.

3 Methods

3.1. Protocol and registration

The Preferred Reporting Items for Systematic Reviews (PRISMA) (**Figure 3**) were followed, for carrying out this article (12).

3.2. Eligibility criteria

All case report studies that stated hyperleukocytosis in AITL patients were included. All the duplicate papers besides unavailable full-text studies in English were excluded. Studies that reported incomplete data or irrelevant subjects were also excluded.

3.3. Information sources and search

We did an electronic search of PubMed, Scopus, and Web of Sciences to Jan 5, 2023, without language restrictions. The whole search results with these search

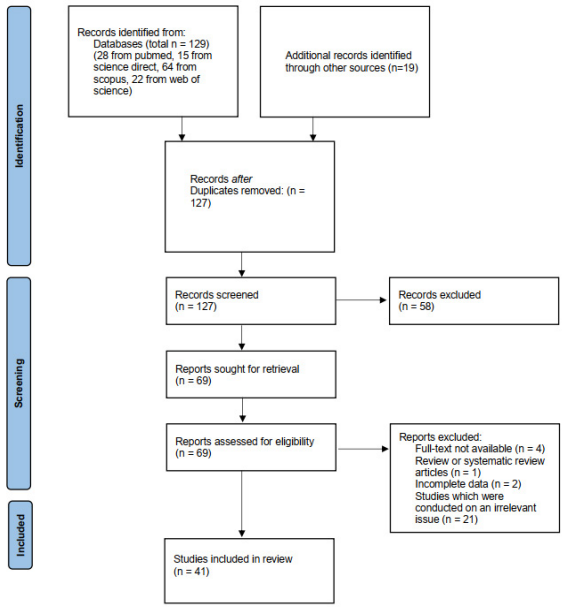

Figure 3. PRISMA flowchart

("angioimmunoblastic lymphoma" OR "Immunoblastic Lymphadenopathy" "angioimmunoblastic T-cell lymphoma" OR "angioimmunoblastic lymphadenopathy with dysproteinemia and lymphogranulomatosis" OR AITL) AND ("hyperleukocytosis" OR "leukocytosis" OR "neutrophilia" OR "lymphocytosis" OR "eosinophilia" OR "monocytosis") were first searched and then merged into Endnote V.8. All reference lists from the included studies and relevant systematic reviews were hand searched for additional studies.

3.4. Selection criteria

After the search was completed, all search results were imported to EndNote V.8, and then duplicates were omitted. The titles and abstracts were skimmed in the screening stage first, and then the full text of selected records was scanned by two independent reviewers, keeping only those matching with inclusion and exclusion criteria. A third reviewer revised the records in case of discrepancy, and if present, it was resolved by consultation and consensus.

3.5. Data collection process and data items

Two reviewers examined the full texts, independently and tabulated the relevant data using a researcher-made checklist. The following items were sought from the articles: author name and year of publication, demographic data, clinical presentation, underlying conditions, treatment, and outcomes (**Table 1**).

Table 1. Characteristics of cases with AITL and leukocytosis

Author name, year	Demographic data/ Underlying conditionsrs	Clinical presentation	Nationality	Country	Lymphadenopathy (diffused / focal)	Leukocyte count (10^6/L)	Presence of CD markers	location of involvement	Misdiagnosis	EBV	Treatment	Outcome
Argov et al, 2009	M/ 46/ -	AP/ weight loss	Arabic	Israel	Diffused (Detected by CT scan)	No leukocyte count was mentioned (Eo= 30%)	Inguinal LN= CD3+/ CD4+	LN	-	Neg	CHOP	Treated
Arora et al, 2016	F/ 64/ Dermatomyositis	Fever/ night sweats/ weight loss/ weakness/ pruritus/ petechiae/ Tachycardia/ edema/ Pale skin/ mucosal dryness/ LAD/ HSM	-	USA	Focal	17500 (Atypical lymph=9275/ 53%, Neut=7526/ 43%)	Inguinal LN= CD4+/ CD5+/ CD10+/ CD3+(weakly)/ CD21+/ CD79a-/ CD20-/ CD34-/ CD30-/ CD8- BM= CD4+/ CD5+/ CD10+/ CD3-/ CD8- PB= CD45+/ CD2+/ CD4+/ CD5+(bright)/ CD7+/ CD10+/ CD3-/ CD8-	LN PB BM	-	Neg	CVAD/ methotrexate/ cytarabine	Passed away
Baseggio et al, 2006	Case 1: M/ 51/ -	LAD/ splenomegaly/ skin lesions/ fever	-	France	Diffused	Leukocytosis at the first diagnosis: 15300 5 months later: 11400 (Lymph= *6100/ 53.5%)	LN and PB= CD4+/ CD2+/ CD5+/ CD7+/ CD10+(numerous in LN)/ CD3-	LN PB	-	-	-	-
	Case 2: M/ 55/ -	LAD	-	France	Diffused	These data are collected 1 year after diagnosis: 19500 (Lymph=11320/ 58%)	LN and PB= CD4+/ CD3+/ CD2+(dim)/ CD5+(dim)/ CD7+(dim)/ CD10+	LN PB	-	-	-	-
Burns et al, 2020	M/ 84/ congestive heart failure, ET	weight loss/ weakness/ LAD/ rash/ splenomegaly	Caucasian	USA	Diffused	No leukocyte count was mentioned (Eo= 17.7%, Mono=19.4%)	BM= CD4+/ CD8+ Axillary LN= CD2+/ CD3+/ CD4+/ CD5+/ CD7+/ CD10+(subsets)/ CD30+(subsets)/ CD23+	LN	-	Neg	CEOP	Passed away

Table 1. (Continued)

Author name, year	Demographic data/ Underlying conditionsrs	Clinical presentation	Nationality	Country	Lymphadenopathy (diffused / focal)	Leukocyte count (10^6/L)	Presence of CD markers	location of involvement	Misdiagnosis	EBV	Treatment	Outcome
Chang et al, 2007	M/ 82/ -	Dyspnea/ fever/cough/ poor appetite/	-	Taiwan	Not detected at the first admission	9910 (Neut=6520/ 65.8%, Lymph=1407/ 14.2%, Eo=1189/ 12%)	Inguinal LN= CD3+/CD10+ Pleural biopsy= CD10+	LN Pleura	Parasites associated with EPE	-	the patient refused chemotherapy	Passed away
Chen et al, 2016	M/ 47/ -	Rash/ fever/ LAD/sweat	-	USA	-	19100 (Eo=10696/ 56%)	Inguinal LN= CD45+/ CD3+/ CD5+/ CD8+/ CD4(loss)/ CD7(loss)/ CD10+(partly)	LN BM	DRESS syndrome	Pos	chemotherapy	Treated
Cunningham et al, 1985	M/ -/ Kimura's disease	Pruritic papular dermatitis/ LAD	-	USA	Diffused	No leukocyte count was mentioned	-	-	-	-	-	-
Genovesi-Ebert et al, 2005	M/ 42/ -	AP / LAD	Caucasian	Italy	Diffused (Detected by echo scan)	28000 (Neut=392/1.4%, Lymph=980/3.5%, Eo=22288/ 79.6%)	LN= CD3+	LN	HES	-	CHEP/ cytarabine, bleomycin, vincristine, methotrexate, leucovorin	Passed away
Goenka et al, 1996	F/ -/ -	fever/ abdominal mass/ ascites/ diarrhea/ LAD	-	USA	Diffused	No leukocyte count was mentioned (eosinophilia)	-	-	-	-	combination chemotherapy	Passed away
Gregory et al, 2019	M/ 54/ -	LAD / B-symptoms	-	Australia	Focal	No leukocyte count was mentioned (eosinophilia)	Inguinal LN= CD3+/CD10+/ CD21+	LN	-	Neg	CHOEP / IVAC/ Brentuximabvedotin/Ciclosporin / (PAD)/Romidepsin/ Gemcitabine/ Panobinostat/ Azacitidine	Treated

Table 1. (Continued)

Author name, year	Demographic data/ Underlying conditionsrs	Clinical presentation	Nationality	Country	Lymphadenopathy (diffused / focal)	Leukocyte count (10^6/L)	Presence of CD markers	location of involvement	Misdiagnosis	EBV	Treatment	Outcome
Grossman et al, 2022	MM/ 68/ osteoarthritis	Skin lesions/ weight loss/ arthritis	-	USA	Diffused (Detected by CT scan)	3900 (Mono=702/ 18%)	Skin= CD4+/ CD3-(variable)/ CD5-(variable)/ CD7-(variable)/ CD20+(<5%)	Skin	-	Neg	Azacitidine / CHOP	Treated
Hirose et al, 1990	Case 1: M/ 62/ -	LAD/ HSM/ pleural effusion	-	Japan	Diffused	7900 (Neut= 6320/ 80%)	PB and LN= CD3+/ CD4+/ CD8+/ CD20+ PB= CD5+, CD8- and CD4+ on vacuolated lymphocytes	LN PB	-	-	CHOP	Passed away
	Case 2: M/ 68/ -	fever/ LAD/ AP/ ascites/ Hepatomegaly	-	Japan	Diffused	15500	PB, Ascites and Inguinal LN= CD3+/ CD4+ PB= CD3+ and CD4+ on vacuolated lymphocytes	LN PB	-	-	-	Passed away
Imoto et al, 1991	F/ 62/ -	fever/ LAD	-	Japan	Focal	No leukocyte count was mentioned (lymphocytosis)	-	LN	-	-	Prednisolone/ combination chemotherapy/ alpha-IFN	Treated
Jang et al, 2015	M/ 73/ -	fever/ LAD/ HSM	-	Korea	Diffused (Detected by CT scan)	30500 (Plasma cells=7625/ 25%)	Cervical LN= CD10- BM= CD3+ on malignant T-cells/ CD138+/ CD20+ PB= CD19+, CD20-, CD38+, CD138+ on B-cells/ CD3+ and CD4+(co-expression), CD2+, CD5+, CD7- and CD10- on T-cells	LN BM	-	Pos	CHOP	Treated

Table 1. (Continued)

Author name, year	Demographic data/ Underlying conditionsrs	Clinical presentation	Nationality	Country	Lymphadenopathy (diffused / focal)	Leukocyte count (10^6/L)	Presence of CD markers	location of involvement	Misdiagnosis	EBV	Treatment	Outcome
Jeong et al, 2019	Case 1: M/ 81/ -	SExanthema/ Spleno-megaly	Korean	Korea	Focal	13725 (Eo=4200/ 30.6%)	Cervical LN= CD3+/ CD20+/ CD21+	LN	DRESS syndrome	Pos	-	Passed away
	Case 2: M/ 70/ -	Exanthema/ Spleno-megaly	Korean	Korea	Diffused (Detected by CT scan)	30232 (Eo=1300/ 4.3%)	Cervical LN= CD3+/ CD20+/ CD21+	LN	DRESS syndrome	Pos	-	Passed away
	Case 3: M/ 57/ -	Exanthema/ Spleno-megaly	Korean	Korea	Focal (Detected by CT scan)	16452 (Eo=6400/ 38.9%)	Cervical LN= CD3+/ CD20+/ CD21+	LN	DRESS syndrome	Pos	Chemotherapy	Passed away
	Case 4: M/ 69/ -	Exanthema/ Spleno-megaly	Korean	Korea	Diffused (Detected by CT scan)	22090 (Eo=3910/ 17.7%)	Cervical LN= CD3+/ CD20+/ CD21+	LN	DRESS syndrome	Pos	-	Passed away
Kanderi et al, 2020	F/ 87/ CAD, hyperlipidemia, COPD, pulmonary hypertension, gas-troesophageal reflux, hypothyroidism	lightheadedness/ dys-pnea/ cough/ weakness/ night sweats/ weight loss/ anorexia/ nausea/ edema/ mucosal dryness/ LAD	-	USA	Diffused	12800 (Neut= 9830/ 76.8%)	Cervical LN= CD20+, CD138+(scattered) and CD15+(scattered) on B cells/ CD23+ and CD5- on a small group of B cells/ CD3+, CD5+ and CD8+ on T cells/ CD10+, CD4+ and CD8+ on a small group of T cells/ CD10+, CD30+ and CD4+ on Atypical lymphoid cells/ CD21+	LN	-	Pos	Chemotherapy	-
Keefe et al, 2022	M/ 65/ Hepatitis B	Fever/weakness/rash/ery-thema/edema/ conjuncti-val injection/LAD	Filipino	USA	Diffused (Detected by CT/PET scan)	11600 (Eo=1070/ 9.2%)	Inguinal LN= CD3+/ CD4+/CD2+/CD5+/ CD7+/CD10+ Chest skin= CD3-/ CD5-	LN skin	DRESS syndrome	-	CHOP	Treated

Table 1. (Continued)

Author name, year	Demographic data/ Underlying conditionsrs	Clinical presentation	Nationality	Country	Lymphadenopathy (diffused / focal)	Leukocyte count (10^6/L)	Presence of CD markers	location of involvement	Misdiagnosis	EBV	Treatment	Outcome
Kraus et al, 2014	M/ 8/ heart transplant, ciliary dyskinesia, hypersensitivity pneumonitis	LAD/ lesions/ nerve palsy: Ptosis, diplopia/ rash/ neurologic deficits: limited eye movements, dilated pupil	-	USA	Diffused	13800 (Plasma cells= 6900/ 50%, Eo=1794/ 13%)	CSF and PB= CD3+(dim), CD4+(dim), CD2+(dim), CD5+(dim) and CD7(loss) on abnormal T cells PB= CD5+(bright) and CD10+ on abnormal T cells/ CD45+, CD19+ and CD38(bright) on plasmacytoid cells/ CD45+/ CD19+/ CD38+(bright) BM= CD45+, CD19+ and CD38(bright) on plasmacytoid cells/CD3+(dim),CD4+(dim) andCD7(loss) on abnormal T cell	LN CSF PB BM	Infectious/inflammatory neuritis, Sarcoidosis, Drug reaction	Neg	CEOP, methotrexate, cytarabine, hydrocortisone	Treated
Kuroda et al, 2021	M/ 61/ COPD, hypertension, hypercholesterolemia, prostatic hyperplasia, rheumatic heart disease	Rash/ dyspnea/ cough/ LAD/ pruritus	Caucasian	USA	Focal	leukocytosis on the first day of admission	Inguinal LN= CD3+/ CD10+	LN BM	COPD with community-acquired pneumonia/ Drug reaction/ autoimmune diseases: SLE, Sjögren's syndrome, dermatomyositis	Pos	CHEP-BV	Treated
Le Roy et al, 2019	F/ 55/ asthma	Weakness/ cough/ dyspnea	-	France	Diffused (Detected by CT/PET scan)	No leukocyte count was mentioned (Eo=2190)	CD4+/CD8+/ CD19+	LN BM	EGPA (Churg-Strauss syndrome)	-	Polychemotherapy/ bendamustine	Passed away

Table 1. (Continued)

Author name, year	Demographic data/ Underlying conditionsrs	Clinical presentation	Nationality	Country	Lymphadenopathy (diffused / focal)	Leukocyte count (10^6/L)	Presence of CD markers	location of involvement	Misdiagnosis	EBV	Treatment	Outcome
Mahajan et al, 2015	M/ 42/ -	Abscesses/pruritus/ weight loss/ poor appetite/weakness/pale skin/ ulcers/LAD/arthritis/ fever/ HSM	Indian	India	Diffused	55700 (Eosinophilia and lymphocytosis with no count)	LN= CD3+ and CD4+ on T cells/ CD31+ on endothelial cells/CD23+ on FDCs/ CD1a+/ CD20+/CD138+ on plasma cells	LN	Cutaneous T-cell lymphoma	-	CHOP	Treated
Mahesh et al, 2019	M/ 65/ -	Fever/weight loss/cough/ weakness/pruritus/paresthesia/ dyspnea/ skin lesions/HSM	Indian	India	Focal (Detected by CT scan)	No leukocyte count was mentioned (Eo=2910)	LN= CD3+/CD5+	LN	Secondary vasculitis, Mononeuritis multiplex	-	CHOP	Treated
Mangana et al, 2017	F/ 65/ Depression	Exanthema/weakness/ weight loss/arthralgia/ night sweats/edema/ LAD/splenomegaly	-	Switzerland	Focal	10650 (Eo=1200/ 11.2%)	Inguinal LN= CD23+ on FDCs/ CD3+/CD4+/ CD79a+ and CD20+ on B cells/ CD30+ on lymphoid blasts	LN PB	Parainfectious exanthema, DRESS syndrome	Pos	CHOP/ IGEV	Passed away
Merlio et al, 1991	M/ 36/ -	rash/ LAD	Caucasian	France	Diffused	26969 (Eo= 17800/ 66%)	Cervical LN= CD2+/ CD3+ (Predominant) / CD4+/ CD5+/ CD7+/ CD25+, CD30+ and CD22+ on large cells	LN	-	-	Chemothrapy	Treated
Mitsuhashi et al, 2011	M/ 70/ -	fever/ LAD	-	Japan	Diffused	No leukocyte count was mentioned (leukocytosis/ plasmacytosis)	-	LN	plasma cell leukemia	Pos	CHOP	Treated

Table 1. (Continued)

Author name, year	Demographic data/ Underlying conditionsrs	Clinical presentation	Nationality	Country	Lymphadenopathy (diffused / focal)	Leukocyte count (10^6/L)	Presence of CD markers	location of involvement	Misdiagnosis	EBV	Treatment	Outcome
Nakazono et al, 1991	M/ 14/ measles, mumps	LAD/ fever/ cough/ Tonsillar hypertrophy/ rash/ HSM/ Ascites/ pleural effusion	Japanese	Japan	Diffused	10900 (Eo=654/ 6%)	PB= CD3+, CD4+ and CD8+ on lymph cells Inguinal LN= CD5+ and CD3+ on lymphocytes Cervical and axillary LNs= CD4+/ CD3+/ CD8-/ CD1-/ CD38-/ CD57-/ CD14-/ CD30-	LN	reactive lymphadenitis, disseminated eosinophilic collagen disease	Neg	chemotherapy	Passed away
Pickard et al, 2020	M/ 76/ AITL	rash	-	UK	-	47910(Lymph= 38500/80.3%, Neut= 6540/13.6%)	PB= CD3+(weak)/ CD4+(weak)/CD8-/ CD7-/CD2-/CD5+/ CD10-/CD20(variable)/CD19-/ CD16-/ CD56-	PB LN	-	-	CHOP	Treated
Qubaja et al, 2009	M/ 62/ -	LAD/ rash/ edema/ weakness/ weight loss/ night sweat	French	France	Diffused (Detected by CT scan)	No leukocyte count was mentioned (Eo=2800)	Cervical LN= CD20+ on normal cells/ CD79a+/ CD3+ on neoplastic cells/ CD23+ on FDCs/ CD30+ Another group of cells= CD20-/ CD3+/ CD5+/CD2+/ CD4+/CD7+/ CD8-/CD56-/ CD57-/CD30-/ CD10+ on neoplastic cells/ CD21+ and CD23+ on FDCs	LN	-	Pos	ACVBP/ Holoxan-VP-16/ aracytin	Treated

Table 1. (Continued)

Author name, year	Demographic data/ Underlying conditionsrs	Clinical presentation	Nationality	Country	Lymphadenopathy (diffused / focal)	Leukocyte count (10^6/L)	Presence of CD markers	location of involvement	Misdiagnosis	EBV	Treatment	Outcome
Renner et al, 2007	M/ 48/ -	edema/ Pruritus/ erythema	-	Germany	Diffused	No leukocyte count was mentioned (Eo= 25.5%)	LN and BM= CD3+/ CD5+/ CD7-	LN BM	Quincke's edema with chronic urticaria	Neg	vincristine/ CHOP/ ESHAP/ autologous stem cell transplantation	Treated
Roufosse et al, 2015	F/ 49/ anorexia nervosa, depression	Weakness/ Fever/ Angioedema/ weight gain/ myalgia/ stiffness/ night sweats/ Pruritus	Caucasian	Europe	Focal (Detected by FDG-PET/CT scan)	No leukocyte count was mentioned (Eo=15000)	Cervical LN= CD2+, CD3+, CD5+, CD10+, CD45RO+, CD4- and CD7- on atypical lymph cells/ CD20+,CD79a+ and CD30+ on large lymph cells/	LN	L-HES	Pos	R-CHOP	Passed away
Saillard et al, 2017	F/ 85/ -	LAD/ B symptoms/ Fever/ impaired consciousness	-	France	Diffused	No leukocyte count was mentioned (Mono=1400, Lymph=1800)	PB=CD2+, cCD3+, CD4+, CD5+, CD10+, sCD3-, CD7-, CD25- and CD56- on pathologic T cells	PB	-	Pos	5-azacytidine, vinblastine	Treated
Sasagawa et al, 1990	M/ 56/ -	fever/ ascites/ pleural effusion/ LAD	-	Japan	Diffused	No leukocyte count was mentioned (leukocytosis)	cervical LN= CD2+/ CD8+/ CD4-	LN	-	-	CHOP	Passed away
Schotte et al, 1992	F/ 13/ -	rash/ LAD/ HSM/ edema	-	Germany	Diffused	No leukocyte count was mentioned (eosinophilia)	-	LN skin	-	-	-	-
Tabata et al, 2017	-/ mid-70s/ -	weakness/ rash/ Poor appetite/ Splenomegaly/ LAD	-	Japan	Diffused	No leukocyte count was mentioned (Lymph= 10230)	LN=CD3+/ CD4+ BM= CD23+/ CD20+/ CD4+/ CD10+ pleural effusion and BM= CD2+/ CD3+/CD4+/CD5+/ CD10+/CD25+/ CD43+/CD45RO+/ CD7-/CD8-/CD19-/ CD20-/CD30-/ CD56-/CD57-	LN BM	IRIS	Pos	-	Passed away

Table 1. (Continued)

Author name, year	Demographic data/ Underlying conditionsrs	Clinical presentation	Nationality	Country	Lymphadenopathy (diffused / focal)	Leukocyte count (10^6/L)	Presence of CD markers	location of involvement	Misdiagnosis	EBV	Treatment	Outcome
Takeda et al, 1995	F/ 60/ pharyngeal tumor, Tonsillectomy	LAD/ rash	-	Japan	Diffused	8350 (Eo=2254/ 27%)	Cervical LN= CD45RO+/ CD20-	LN	-	-	E-CHOP, MA-COP, NEO-MA-COP	Passed away
Vasanawala et al, 2003	M/ 76/ Hypertension, diabetes, osteomyelitis	stiffness/ Ulcer/ plaque/ LAD	-	USA	Diffused (Detected by scan)	8100 (Neut=5103/ 63%, Lymph=729/ 9%, Eo=1782/ 22%)	Skin/axillary LN= CD3+(strong) and CD20- on atypical lymph cells/ CD21 and CD23 on FDCs	LN skin	Systemic infection	-	-	Passed away
Wakabayashi et al, 2018	F/ 68/ Hypertension, pulmonary adenocarcinoma, Epigastralgia, hepatitis B	Fever/ Rash/ Hepatomegaly	Japanese	Japan	Diffused	7590 (Neut=6945/ 91.5%, Lymph=387/ 5.1%, Mono=258/ 3.4%)	LN= CD3+/ CD5+/ CD10+ on T cell/ CD21+ on FDCs	LN PB	Hashimoto disease	Neg	Prednisolone, CEPP/ THPCOP/ GDP/ Sobuzoxane	Treated
Wawrzycki et al, 2021	M/ 68/COPD, diabetes, heart failure, hypertrophic cardiomyopathy, cardiac pacemaker implantation,P CI	Rash/ LAD/ Fever/ AP/ diarrhea/ lesions/ edema	-	Poland	Diffused (Detected by CT scan)	23600 (Eo=3960/ 16.7%)	Cervical LN= CD3+/ CD23+ Skin= CD3+/ CD4+	LN skin	Bacterial sepsis	-	-	Passed away
Wegerle et al, 1994	M/ 28/ -	LAD/ edema/ Exophthalmos	German	Germany	Diffused (Detected by ultrasonography)	No leukocyte count was mentioned (Eo=800)	-	LN	-	Neg	prednisolone, interferone α-2b	Treated
Yamamoto et al, 2005	M/ 72/ PSS	LAD/ HSM	Japanese	Japan	Diffused	22500 (Neut=15750/ 70%, Lymph=4950/ 22%, Mono=1350/ 6%, Eo=450/ 2%)	BM= CD19+ on B cells/ CD45+(strong), CD3+, CD4+ and CD8- Inguinal LN= CD20+ on blastic B cells/ CD3+ on T cells/ CD21+ on FDCs Minced LN= CD3+, CD4+ and CD8– on T cells/ CD10–, CD19+ and CD20+ on B cells	LN BM	DLBCL	Pos	CHOP / DeVIC	Passed away
Yoon et al, 2003	M/ 55/ -	exanthema/ weakness/ fever/ LAD/ HSM	Korean	Korea	Focal (Detected by CT scan)	No leukocyte count was mentioned (Lymphocytosis)	Skin/cervical LN= CD3+, CD4 equivocal, CD8-, CD20-, CD30- and CD68- on neoplastic lymphocytes	LN skin	Drug reaction	Pos/Neg	CHOP	Passed away

3.6. Quality Appraisal

To evaluate the quality of included studies, the Joanna Briggs Institute (JBI) checklist consisting of eight items, was applied. It was individually filled by two authors. The checklist was prepared based on 8 questions along with 4 rating scales including Yes, No, Unclear, and Not applicable. The total score ranged from 0 to 8; "Yes" got 1 point and others got none. Studies with scores ≥6 were taken into account for high quality, and less than 3 were considered as high-bias risk articles. Studies between these ranges, (≥3 to 5) were assessed as medium risk of bias and quality. The probable mismatches were resolved by a third author.

3.7. Synthesis of the results

As long as there was heterogeneity between studies and low case numbers, more analysis was not possible; therefore, we narratively reported the results and tabulated and classified them into several items available in **Table 1**.

4. Results

4.1. Literature Search

At the outset of the search process, 129 articles from PubMed, Scopus, Science Direct, and Web of Science databases were identified. 19 articles were added from other sources. After removing duplicates, 127 articles remained, and by scanning titles and abstracts, 69 articles that came up to our inclusion standards, remained. In conformity with eligibility criteria, the full texts of articles were properly evaluated. At last, 41 studies with 46 cases were included and 28 studies were excluded. (**Figure 3**)

4.2. Quality Assessment

According to the JBI quality evaluation tool, our included studies achieved scores ranging from 4 to 8. The studies' mean score was 6.8. About 80.4% of all articles were in a high-quality group, while 19.5% formed medium-quality groups. None of the studies were among the low-quality group.

4.3. Study Characteristics and Demographic Data

The characteristics of the conducted studies were described in **Table 1**. Although the age of our included cases ranged from 8 to 87, the highest rate of AITL occurred in elderly ones. About 70.4% were above 55 years of age. 75.5% were male. Among all the cases, 18 of them had underlying conditions, the most prevalent diseases were heart disease (5 cases), respiratory disease (4 cases), hypertension (4 cases), hepatitis B (2 cases), and diabetes (2 cases). Across all the cases, the most reported were from Asia (43.4%), Europe (30.4%), and the USA (23.9%). Among European countries, the reports were predominantly from France (42.8%). Also, Among the Asian countries, the reports were from East Asia for the most (85%).

4.4. Clinical Presentation

The most presented symptom at the time of admission was lymphadenopathy (65.2%). Dermatological conditions such as rash, pruritus, lesions, erythema, exanthema, petechiae, and abscess were presented in 24 patients. According to the collected data, high proportions of lymphadenopathies were in diffused forms (76.7%). About 37.2% of lymphadenopathy diagnoses were accompanied by different types of scans including CT and PET scans. One of the most mentioned complaints by cases was B symptoms (56.5%); among these symptoms, the fever had the highest incidence (73%) in comparison with weight loss (34.6%) and night sweats (23%). Other clinical manifestations such as weakness (12 cases), edema (10 cases), hepatosplenomegaly (9 cases), and dyspnea (5 cases) were less common.

4.5. Diagnosis (WBC count, EBV)

In about 27 cases, leukocyte count was mentioned, ranging from 3.9×10^9/L to 55.7×10^9/L. Eosinophilia was the most prevalent condition with 60.8% and eosinophils had a wide range of 2% to 79.6%. In 8 cases, lymphocytosis was observed. Half of the cases with eosinophilia presented B symptoms. Dermatological conditions were also seen in 75% of patients with eosinophilia. Involvement of peripheral blood, bone marrow, pleura, skin, and CSF were seen in some cases. In cases that EBV tests had been carried out, 80% were EBV positive (of course some of them didn't specify EBV test results).

4.6. Immunophenotypic characterization of AITL

Most of the cases were positive for CD3 (76%) and CD4 (50%). CD10 was expressed in 16 cases, it was majorly expressed in lymph nodes (58.3%) in comparison with peripheral blood and bone marrow (total of 29.1%). CD8, CD7, CD45, CD30, and CD56 had low percentages with 20%, 17.5% (for both CD45

and CD7), 15%, and 10% expression, respectively. CD3 had the highest frequency amongst lymph nodes expressed CD markers.

4.7 Treatment and outcomes

Among different available medications and methods for treating AITL, chemotherapy had been used the most. Based on the available data CHOP was the most commonly used chemotherapy (16 cases) which had led to about 56.2% survivability. The treatment process finished unsuccessfully in most of the patients and only 46.3% were reported to get survived. Among the cases which were in trouble with a definitive diagnosis, 62.5% of them passed away.

5. Discussion

Most of the reviewed cases were in their 60s. In agreement with our data, other studies also mentioned that the AITL occurs the most in elderly patients with a median age of 69 (13). The reason was suggested previously; a linkage between growth rates of mutations namely TET2 (80%) and DNMT3A (20% to 38%), and increasing age, may lead to hematologic malignancies. However, RHOA G17V was reported to have no relation with age or sex (14, 15). In contrast with the previous studies, which reported similar ooccurrencesof AITL between men and women (2), in our systematic review, an absolute male predominance among AITL patients with leukocytosis was observed. Horesh N et al. discussed the probable effects of gender in Non-Hodgkin lymphomas (NHL); it was indicated that the higher estrogen levels in women might perform a protective duty by inhibiting lymphoid cells proliferation and reducing IL-6 cytokine which is produced immediately after inflammations (16, 17). However, more studies should be done concerning AITL development and the gender of patients.

Considering the countries that reported AITL cases with leukocytosis in this systematic review, a predominance of cases was observed to be from Asia, particularly East Asia. According to previous studies, AITL was more prevalent in Europe than in Asia and the United States (13). It is indicated that the low commonness of AITL in Asia could be associated with increased NK/T-cell and adult T-cell lymphoma. Due to this problem, Chiba S et al. suggested considering adult T-cell lymphoma influence on lower AITL rates among peripheral T-cell lymphomas (18, 19).

Skin manifestations should be considered as an alarm in patients with AITL. In a high percentage of cases, misdiagnosis and missed diagnosis played crucial roles in patients' death. We can say that physicians should consider the possibility of encountering DRESS syndrome and drug reactions. Jeong J et al. compared 5 AITL patients that primarily were thought to have DRESS syndrome. The main differences were: 1) more generalized lymphadenopathy, 2) more prevalence of splenomegaly, 3) lower hepatic enzymes, 4) shorter latency, and finally, 5) poor prognosis in AITL patients (20).

Heart involvement as an underlying condition should not be ignored. It could be manifested as congestive heart failure (21), coronary artery disease (22), rheumatic heart disease (23), and hypertrophic cardiomyopathy (11). Delayed diagnosis of heart disease in cases with hypereosinophilia, may lead to a patient's death (24).

Lymphadenopathy was highly presented in our cases. Additionally, it was an apparent marker commonly presented by AITL patients (25). In our study, about one-third of lymphadenopathies, whether diffused or focal, were identified along with scans and medical imaging. It notes body scanners' requirement to avoid ignorance of lymphadenopathy at physical examination.

In this literature, most of the EBV+ patients showed cutaneous AITL. Some studies suggested a hypothesis on the role of EBV in the pathogenesis of AITL (13). Lee W J et al. assessed the association between EBV+ skin specimens of AITL patients and clinicopathologic outcomes; about 45.2% of cases with skin involvement were positive for EBV through in situ hybridization. It was shown that EBV might increase tumor function via immune cytokines modification in AITL patients (26). These data revealed a relationship between EBV and skin manifestations in AITL cases.

In the case we mentioned as a report, significant features were leukocytosis and lymphocytosis of 25875 cells per microliter of blood. In parallel with our case report, Pickard K et al. presented a relapsed AITL case with 38560 lymphocytes per microliter. By contrast, some studies explained AITL peripheral blood with lymphopenia (27, 28). Generally, lymphocytosis is a rare condition among AITL patients that demands more consideration.

Flow cytometry results provided valuable data in classifying hematopoietic neoplasms and assisted in the diagnostic procedure (29). CD markers also

played crucial roles in the diagnosis of AITL. Our case had three distinctive features: CD3, CD10, and CD7 expressions. CD3 and CD10 were highly expressed. The same was present in most of our reviewed cases. CD3 has an essential role in the detection of lymphomas. Our studied case showed a bright expression (nearly 100%). Likewise, in this systematic study high expression of CD3 was shown in lymph nodes. However, abnormal expression and loss of CD3 were stated in some cases (30, 31). Baseggio L et al. were the first who reported blood involvement with CD10+ T cells (32). Also, others mentioned this fact after them (33). This systematic review also confirmed the importance of CD10, but this marker was majorly expressed in lymph nodes. CD7 is a pan T cell marker that is used in the detection of abnormal T cells. CD7 was expressed in our 57-year-old Iranian case. However, resulting from the reviewed cases, low CD7 rates were also observed. We can highlight CD7 as a contradictory marker known to have downregulation in many studies (5, 6, 18, 34-36). More attention to this marker is needed in further studies. The loss of sCD3 and CD16 was seen in all studies. In accordance with these findings, Jain G et al. conducted a review that revealed sCD3 as the most absent T cell surface marker. Contrary to our data, she reported a CD16+ case, meaning future researchers should pay more attention to these rare expressions (5). CD56 is a marker for NK lymphomas. Four CD56 positive cases were present in our systematic review. In like manner, Hori H et al. presented a rare AITL case with CD56+ (9). Keeping the rare CD expressions in view, immunophenotyping results are the essentials of AITL diagnosis.

The first-line treatment in many cases of AITL is polychemotherapy, usually accompanied by an autologous stem-cell transplant (37). Our review demonstrated that CHOP (Cyclophosphamide, Doxorubicin, Oncovin, and Prednisone) is the main combination chemotherapy. Cyclophosphamide is an alkylating agent which hampers tumor promotion by making crosslinks in DNA strands (38). Doxorubicin induces apoptosis and prevents cell maturation via binding to DNA enzymes (39). Oncovin stops cellular division by binding to tubulin protein (40). Ultimately, Prednisone as a corticosteroid regulates inflammation (41). In relapsed AITL, hypomethylating agents and histone deacetylase inhibitors like 5-azacytidine and romidepsin are preferred (42). Yoon SE et al. also indicated the 5-azacytidine's usefulness in 15 patients with relapsed refractory AITL(43). Further analysis of peripheral blood by immunophenotypic methods will shed light on AITL's hidden secrets.

6. Conclusion

In this systematic review and case report, we at first introduced our AITL case with leukocytosis and lymphocytosis and then carried out a systematic search to compare the characteristics of all AITL cases with leukocytosis as long as the latter (leukocytosis) is a rare finding in T-cell angioimmunoblastic lymphadenopathies. So, as it happened to us, the simultaneous occurrence of these two complications may lead to a missed diagnosis as long as there is no available systematic review that investigates a throughout characteristic of AITL patients with leukocytosis. Unfortunately, AITL itself usually occurs in various manifestations which makes the diagnosis more difficult. Pathologic examination has been used for better diagnosis, but this method is majorly performed in the late stages. In some cases, no malignancy was seen despite performing a biopsy in the early stages. Lymph node biopsy is relatively painful. Moreover, no palpable lymph node was available in some cases, thus adding to the difficulty of identifying the source of the lymphadenopathy. Clinical manifestations were also helpful but not specific. CD markers play a crucial role in distinguishing the subtypes of lymphomas, but an unusual expression of some CD markers, as we observed in our reported case, reduces the accuracy of these markers. In conclusion, to gain a better insight into AITL diagnosis, all the above-mentioned methods should get in uuse Also, by comparing the new cases with this systematic review, better and simpler diagnoses, treatments and outcomes may be achieved.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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References

1. Mehrpouri M, Pourbagheri-Sigaroodi A, Bashash D. The contributory roles of histone deacetylases (HDACs) in hematopoiesis regulation and possibilities for pharmacologic interventions in hematologic malignancies. International Immunopharmacology. 2021;100:108114.
2. Adam MNM, Adam MNM, Idris AAA, Ali ASM, Khalid IO. A rare diagnostic case of angioimmunoblastic T-cell lymphoma: https://doi. org/10.52152/spr/2022.165. Science Progress and Research (SPR). 2022;2(1):414-8.
3. Shin WY, Bang HI, Kim J-A, Kim J, Park R. Angioimmunoblastic T-Cell Lymphoma with Polyclonal Proliferation of Plasma Cells: A Cautionary Note for Flow Cytometry Interpretations. Korean Journal of Clinical Laboratory Science. 2022;54(1):68-72.
4. Alaggio R, Amador C, Anagnostopoulos I, Attygalle AD, Araujo IBdO, Berti E, Bhagat G, Borges AM, Boyer D, Calaminici M. The 5th edition of the World Health Organization classification of haematolymphoid tumours: lymphoid neoplasms. Leukemia. 2022;36(7):1720-48.
5. Jain G, Kumar C, Malhotra A, Mallick SR, Bakhshi S, Chopra A. Peripheral blood involvement in angioimmunoblastic T-cell lymphoma: A case report and review of the literature. American Journal of Blood Research. 2020;10(5):257.
6. Xie Y, Jaffe ES. How I diagnose angioimmunoblastic T-cell lymphoma. American Journal of Clinical Pathology. 2021;156(1):1-14.
7. Džeko Škugor N, Perić Z, Vrhovac R, Radić-Krišto D, Kardum-Skelin I, Jakšić B. Diffuse Large B-cell Lymphoma in Patient after Treatment of angioimmunoblastic T-cell Lymphoma. Collegium antropologicum. 2010;34(1):241-5.
8. Ferran M, Gallardo F, Baena V, Ferrer A, Florensa L, Pujol RM. The 'deck chair sign'in specific cutaneous involvement by angioimmunoblastic T cell lymphoma. Dermatology. 2006;213(1):50-2.
9. Hori H, Tanaka Y, Nakayama R, Nohgawa M. CD56-positive Angioimmunoblastic T-cell Lymphoma Complicated by Chylothorax. Internal Medicine. 2022;61(5):729-33.
10. Swarup S, Kopel J, Thein KZ, Tarafdar K, Swarup K, Thirumala S, Quick DP. Sequential Complications of Hypercalcemia, Necrotizing Granulomatous Vasculitis, and Aplastic Anemia Occurring in One Patient with Angioimmunoblastic T-cell Lymphoma. The American journal of the medical sciences. 2021;361(3):375-82.
11. Wawrzycki B, Prystupa A, Szumiło J, Panasiuk L, Krasowska D. Fever, rash, and eosinophilia–early signs of angioimmunoblastic T-cell lymphoma. Annals of Agricultural and Environmental Medicine. 2021;28(3):525.
12. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann T, Mulrow CD, Shamseer L, Moher D. Mapping of reporting guidance for systematic reviews and meta-analyses generated a comprehensive item bank for future reporting guidelines. Journal of clinical epidemiology. 2020;118:60-8.
13. Mohammed Saleh MF, Kotb A, Abdallah GE, Muhsen IN, El Fakih R, Aljurf M. Recent Advances in Diagnosis and Therapy of Angioimmunoblastic T Cell Lymphoma. Current Oncology. 2021;28(6):5480-98.
14. McBride AB, Porcu P. The rise of a new "great teacher". Blood, The Journal of the American Society of Hematology. 2021;138(3):205-6.
15. Nguyen PN, Tran NT, Nguyen TP, Ngo TN, Van Lai D, Deel CD, Hassell LA, Vuong HG. Clinicopathological Implications of RHOA Mutations in Angioimmunoblastic T-Cell Lymphoma: A Meta-analysis: RHOA mutations in AITL. Clinical Lymphoma Myeloma and Leukemia. 2021;21(7):431-8.
16. Horesh N, Horowitz NA. Does gender matter in non-Hodgkin lymphoma? Differences in epidemiology, clinical behavior, and therapy. Rambam Maimonides medical journal. 2014;5(4).
17. Tanaka T, Narazaki M, Kishimoto T. IL-6 in inflammation, immunity, and disease. Cold Spring Harbor perspectives in biology. 2014;6(10):a016295.
18. Chiba S, Sakata-Yanagimoto M. Advances in understanding of angioimmunoblastic T-cell lymphoma. Leukemia. 2020;34(10):2592-606.
19. Lunning MA, Vose JM. Angioimmunoblastic T-cell lymphoma: the many-faced lymphoma. Blood, The Journal of the American Society of Hematology. 2017;129(9):1095-102.
20. Jeong J, Yu JE, Choi YD, Kim SK, Yoon W, Koh Y-I. Differentiation of angioimmunoblastic T-cell lymphoma from DRESS syndrome. The Journal of Allergy and Clinical Immunology: In Practice. 2019;7(5):1684-6. e1.
21. Burns EA, Anand K, Chung B, Shah S, Randhawa JK, Pingali SR. The development of T-cell malignancies in patients with pre-existing myeloproliferative neoplasms: a report of three cases. ecancermedicalscience. 2020;14.
22. Kanderi T, Goel S, Shrimanker I, Nookala VK, Singh P. Angioimmunoblastic T-cell Lymphoma: An Unusual Case in an Octogenarian. Cureus. 2020;12(2).
23. Kuroda K, Tambe A, Iftikhar R, Nat AS, Basnet A. A Case of Angioimmunoblastic T-cell Lymphoma That Mimics As Autoimmune Diseases and Infections. Cureus. 2021;13(7).
24. Genovesi-Ebert A, Lombardi M, Capochiani E, Simi U, Savoia MT, Baldini U, Digiorgio A, Carluccio M, Di Santo D, Galli M. Heart involvement in T cell lymphoma through hypereosinophilic syndrome: a common complication of a rare condition. Journal of Cardiovascular Magnetic Resonance. 2005;7(2):495-9.
25. Yabe M, Dogan A, Horwitz SM, Moskowitz AJ. Angioimmunoblastic T-cell lymphoma. T-Cell and NK-Cell Lymphomas. 2019:99-126.
26. Lee WJ, Won KH, Choi JW, Won CH, Chang SE, Choi JH, Lee MW. Cutaneous angioimmunoblastic T-cell lymphoma: Epstein-Barr virus positivity and its effects on clinicopathologic features. Journal of the American Academy of Dermatology. 2019;81(4):989-97.
27. Ahsanuddin AN, Brynes RK, Li S. Peripheral blood polyclonal plasmacytosis mimicking plasma cell leukemia in patients with angioimmunoblastic T-cell lymphoma: report of 3 cases and review of the literature. International Journal Of Clinical and Experimental Pathology. 2011;4(4):416.
28. Mourad N, Mounier N, Brière J, Raffoux E, Delmer A, Feller A, Meijer CJ, Emile J-F, Bouabdallah R, Bosly A. Clinical, biologic, and pathologic features in 157 patients with angioimmunoblastic T-cell lymphoma treated within the Groupe d'Etude des Lymphomes de l'Adulte (GELA) trials. Blood, The Journal of the American Society of Hematology. 2008;111(9):4463-70.
29. Gabali A. Flow cytometry, molecular analysis, and other special techniques (in Serous Fluid Cytopathology). CytoJournal. 2022;19.

30. Loghavi S, Wang SA, Jeffrey Medeiros L, Jorgensen JL, Li X, Xu-Monette ZY, Miranda RN, Young KH. Immunophenotypic and diagnostic characterization of angioimmunoblastic T-cell lymphoma by advanced flow cytometric technology. Leukemia & lymphoma. 2016;57(12):2804-12.
31. Satoh T, Kayano H, Takahashi N, Tsukasaki K, Yasuda M. Diagnostic utility of the aberrant immunohistochemical expression of CD3 molecules for peripheral T-cell lymphomas. Annals of Diagnostic Pathology. 2022;60:152013.
32. Baseggio L, Berger F, Morel D, Delfau-Larue M, Goedert G, Salles G, Magaud J, Felman P. Identification of circulating CD10 positive T cells in angioimmunoblastic T-cell lymphoma. Leukemia. 2006;20(2):296-303.
33. Patel BK, Basu D, Kar R, Dubashi B. Immunophenotyping of Nodal Peripheral T-cell Lymphomas and its Association with Epstein-Barr Virus. Iranian Journal of Blood and Cancer. 2019;11(3):101-8.
34. Chen N, Amber S. Eosinophilia and Cutaneous Involvement in Angioimmunoblastic T-Cell Lymphoma. Journal of Allergy and Clinical Immunology. 2016;137(2, Supplement):AB169-AB70.
35. Hapgood G, Mottok A, Slack GW, Gascoyne RD, Steidl C, Savage KJ, Weng AP. Flow Cytometric Characterization of 129 Cases of Peripheral T Cell Lymphoma Not Otherwise Specified (PTCL NOS) and Angioimmunoblastic T Cell Lymphoma (AITL). Blood. 2015;126(23):2667.
36. Satou A, Takahara T, Tsuzuki T. Pathological and Molecular Features of Nodal Peripheral T-Cell Lymphomas. Diagnostics. 2022;12(8):2001.
37. Bahmani F, Azadpour S, Pourbagheri-Sigaroodi A, Bashash D. Plant-derived natural compounds as promising anticancer agents in hematological malignancies. Iranian Journal of Blood and Cancer. 2022;14(3):57-70.
38. SAHU S, DONGRE N. A Review on Analytical Method Development and Validation of Cyclophosphamide.
39. Tacar O, Sriamornsak P, Dass CR. Doxorubicin: an update on anticancer molecular action, toxicity and novel drug delivery systems. Journal of pharmacy and pharmacology. 2013;65(2):157-70.
40. Avendano C, Menendez JC. Anticancer drugs targeting tubulin and Microtubules. Medicinal Chemistry of Anticancer Drugs Elsevier, Boulevard. 2015:359-87.
41. Puckett Y, Gabbar A, Bokhari AA. Prednisone. 2018.
42. Moskowitz AJ. Practical treatment approach for angioimmunoblastic T-cell lymphoma. Journal of oncology practice. 2019;15(3):137-43.
43. Yoon SE, Cho J, Kim YJ, Kim SJ, Kim WS. Real-World Efficacy of 5-Azacytidine as Salvage Chemotherapy for Angioimmunoblastic T-cell Lymphoma. Clinical Lymphoma Myeloma and Leukemia. 2022;22(11):e972-e80.