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*Case Report*

# Peripheral blood involvement in angioimmunoblastic T-cell lymphoma: a case report and review of the literature

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**Abstract:** Angioimmunoblastic T-cell lymphoma (AITL) is an aggressive variant of peripheral T-cell lymphoma, occurring in elderly patients without any gender predisposition. It accounts for 1-2% of all non-Hodgkin lymphoma. Although characterized by some peculiar histological features, diagnosis of AITL can sometimes be challenging and a definite diagnosis requires a complete immunophenotypic and molecular workup. Peripheral Blood (PB) involvement in AITL has not been studied in detail and there is a paucity of published data about leukemic presentation of AITL. We present a case of a 38-year-old female diagnosed as AITL with PB involvement. Flow cytometric (FCM) examination of PB showed 40% abnormal lymphoid cells which were CD45+, CD4+, CD2+, cCD3+, CD5+, CD10+, CD16+ and TCRγδ restricted. PB involvement by AITL appears to be more common and under-reported. Nevertheless, detection of these tumoral T lymphocytes needs to be assessed in large case studies for assessing the true incidence of PB involvement. FCM analysis is an effective and reliable approach in the identification of leukemic phase of AITL and can lead to timely and effective intervention.

**Keywords:** Angioimmunoblastic T-cell lymphoma, peripheral blood involvement, review of literature

## Introduction

Over the last decade, new information on biology, diagnosis, prognosis, and therapeutic strategies for lymphoma has come to light. All of these contributed towards an update in 2016 WHO classification of lymphoid neoplasms [1]. The update proposed an umbrella category for nodal T-cell lymphomas with T follicular helper (TFH) phenotype under peripheral T-cell lymphomas (PTCL), which included angioimmunoblastic T-cell lymphoma (AITL), follicular T-cell lymphoma and nodal PTCL with TFH phenotype [1, 2]. AITL is now recognised as well-established subtype of PTCL [1, 3]. It occurs most commonly in elderly patients accounting for 1-2% of all non-Hodgkin lymphoma (NHL) and 15-30% of all cases of PTCL [1].

Patients typically present with generalised lymphadenopathy (LAP), hepatosplenomegaly, B symptoms, effusion/ascites and skin rash. Bone marrow (BM) involvement is common and has been variably described to be involved in nearly 70% cases [3]. Peripheral Blood (PB) involvement has not been studied in detail and there is a paucity of published data about the leukemic presentation of AITL. Although characterized by some peculiar histological features, diagnosis of AITL can sometimes be challenging and a definite diagnosis requires a complete immunophenotypic and molecular workup [3].

In this case, we highlight the leukemic presentation of AITL along with its clinical, laboratory, immunophenotypic profile and review the literature for case studies for these features.

## Case report

A 38-year-old woman suffering from intermittent fever and cervical LAP for 2 years was admitted to All India Institute of Medical

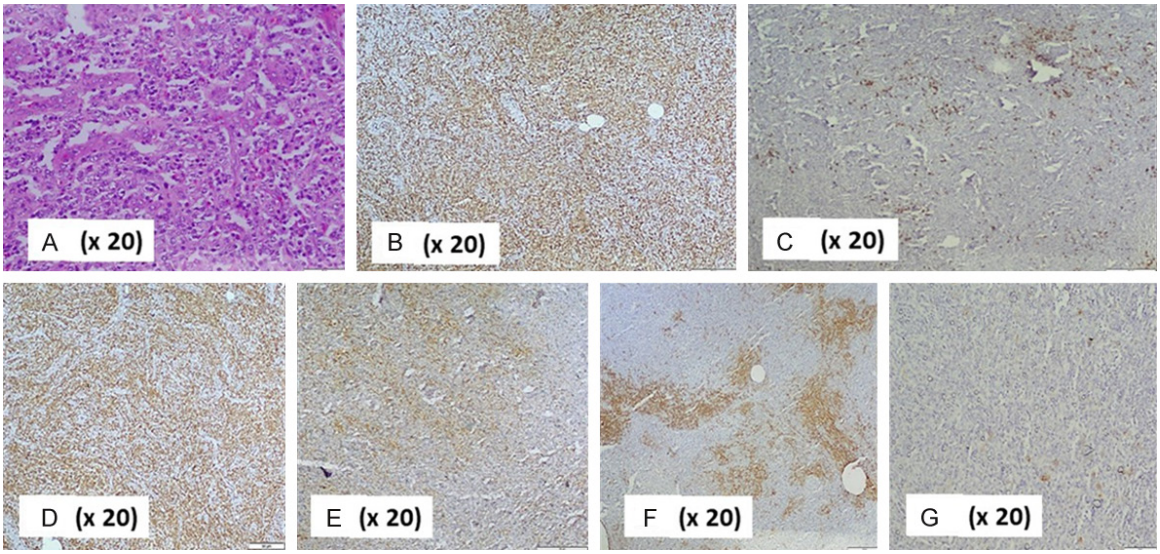


**Figure 1.** (A) Inguinal LN biopsy showing complete effacement of nodal architecture by polymorphous population of cells comprising of intermediate sized lymphoid cells admixed with eosinophils. There are many high endothelial venules (×20). Atypical cells are immunopositive for (B) CD3 (×20), (C) CD5 (×20), (D) CD20 (×20), (E) BCL6 (×20), (F) CD23 highlighting the meshwork of follicular dendritic cells (×20), (G) Large atypical cells immunopositive for CD30 (×20).

Sciences, New Delhi. She was diagnosed initially as tuberculosis at some other hospital and was given anti-tubercular treatment for 6 months. However, her symptoms worsened, and she developed pedal oedema, ascites, and respiratory failure. On CECT, she was found to have generalised LAP, splenomegaly, bilateral pleural effusion & ascites. Complete blood cell count revealed anemia and thrombocytopenia. Peripheral blood smear (PBS) showed thrombocytopenia with no abnormal lymphoid cells. Biopsy of inguinal lymph node (LN) revealed complete effacement of its architecture by polymorphous population including intermediate-sized lymphoid cells admixed with eosinophils. Many high endothelial venules were also seen. These atypical lymphoid cells were positive for CD3, CD5, CD20, and BCL6. Few large cells which were positive for CD30 and EBV-LMP were also seen. CD23 highlighting the meshwork of follicular dendritic cells outside follicles and around the vessels was also seen (**Figure 1A-F**). A diagnosis of AITL was given. BM was unremarkable. All procedures were done as part of routine work-up of the patient. Informed consent was taken before doing any procedure on the patient according to declaration of Helsinki. Owing to poor general physical condition, the patient was started on CHOP regimen at a reduced dose (60%). She had persistent fever, pancytopenia, and recurrent pleural effusion. She improved gradually after the first cycle of CHOP (60%) and was started on CEOP regimen at 75% dose for 2$^{nd}$ cycle. After this second cycle her condition improved further and was discharged in stable condition.

Few months later, she again developed fever, splenomegaly, pleural effusion, and ascites. Overall features were compatible with progressive disease. PBS showed around 18% abnormal lymphoid cells (**Figure 2A-D**). Flow cytometry (FCM) of PB showed 40% abnormal lymphoid cells which were CD45+, CD4+, CD2+, cytoplasmic CD3+, CD5+, CD10+, CD16+ and TCRγδ restricted. CD8 was positive in a subset of cells. The cells were negative for sCD3, CD7, CD8, CD56, CD19, CD22, CD20 and CD38 (**Figure 3**). BM aspirate was diluted with the preponderance of eosinophils and its precursors (**Figure 2E**, **2F**). However, BM biopsy showed near-total replacement of hematopoietic elements by atypical lymphoid cells along with an increase in eosinophils and its precursors (**Figure 2G**, **2H**). The patient was then started on ICE (Ifosamide, Carboplatin, Etoposide) chemotherapy at 50% dose. Post ICE there was a reduction in atypical lymphoid cells to 7% in PBS from baseline. The patient developed persistent severe pancytopenia which failed to recover even after chemotherapy and supportive treatment. The general condition of

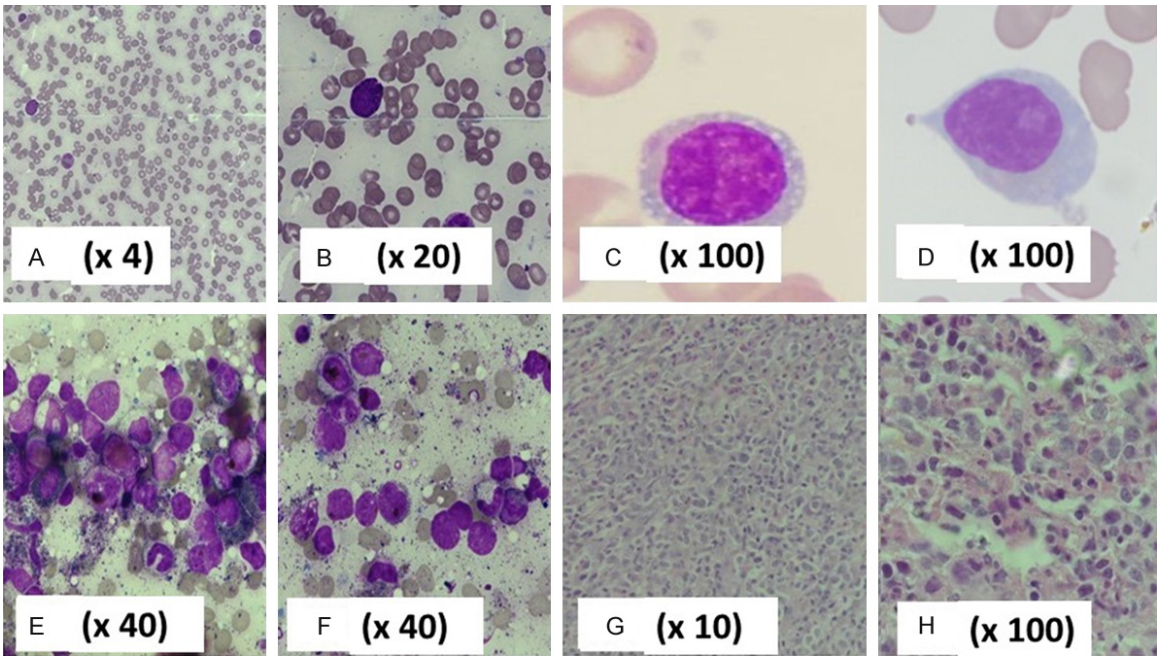


**Figure 2.** A-D. PBS showed 18% abnormal lymphoid cells (×4; ×20; ×100; ×100). E, F. Bone marrow aspirate and touch imprint smears were diluted with preponderance of eosinophils and its precursors (×40). G, H. BM biopsy showed near total replacement of hematopoietic elements by atypical lymphoid cells along with increase in eosinophils and its precursors (×10; ×100).

the patient deteriorated further. She was started on oral metronomic therapy with supportive care. The patient finally succumbed to her illness owing to progressive disease.

## Discussion and review of literature

AITL has been classified as a subset of PTCL in the WHO 2016 classification of lymphoid neoplasms, under Nodal T-cell lymphomas with T follicular helper phenotype (TFH) [1]. Tumours belonging to this category should express a minimum of 2 or 3 TFH-related antigens, i.e. CD279/PD-1, CD10, BCL6, CXCL13, ICOS, SLAM-associated protein, and CXCR95 [1, 2]. Owing to the rarity of this disease, published data about biological, clinical, immunophenotypic features and their impact on prognosis is limited.

AITL has a peculiar geographical relation, being more common in Europe (28.7%) than in Asia (17.9%) [3]. EBV has a close but paradoxical relationship in AITL where the B cells demonstrate active viral infection, sparing the malignant T cells. AITL has a very high ratio of case reports to the incidence of diagnosis when compared to other NHL subtypes. This may be attributed to the spectrum of peculiar and at times non-specific symptoms and presentations which takes months for a diagnosis to be rendered [3].

*Clinical features (**Table 1**)*

AITL mostly affects elderly population (median age, 57-68 years) with slight male preponderance in some studies [3-15]. B symptoms (fever, weight loss and drenching night sweats) and LAP remain the most common complaints and physical findings of these patients. Around 46% of patients present with more than one extra-nodal site involvement [13]. Hepatomegaly and splenomegaly occur at variable frequencies with some studies reporting the incidence of splenomegaly in upto 70% patients [5-7, 11]. Skin manifestations ranging from rash to urticaria and even nodular tumors are common in AITL. Other less common non-specific findings such as pleuritis, arthralgia, neurological manifestations, ascites, and respiratory symptoms due to lung involvement have also been described [6, 9]. Most patients are known to present with advanced disease [3]. Studies have reported that as many as 60-100% cases present with Ann Arbor stage III/IV [5, 9, 11, 13, 15].

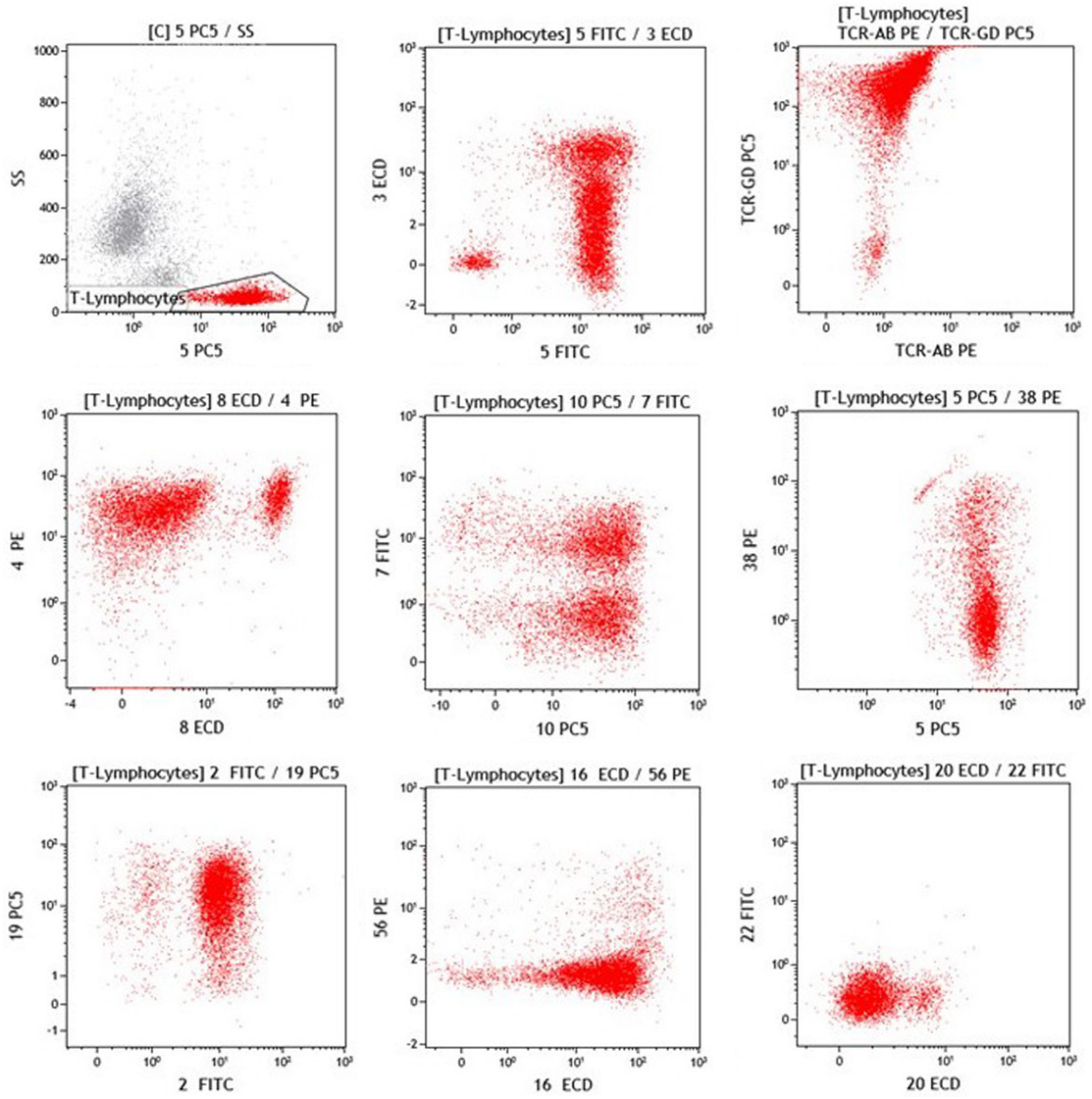


**Figure 3.** Flow cytometric (FCM) examination of peripheral blood showed 40% abnormal lymphoid cells which were cCD3+, CD4+, CD5+, CD10+, CD16+ and TCR gamma/delta restricted. The cells were negative for CD7, CD8, CD56, CD19, CD22, CD20, TCR alpha/beta and CD38.

*Laboratory parameters in AITL (**Table 2**)*

Anemia (33-100%) and elevated LDH levels (25-90%) were the most common deranged laboratory parameters in AITL [3, 5-15]. Thrombocytopenia was also a relatively common feature, being reported in 20-50% of cases. AITL can act as an immune activator and can lead to autoimmune phenomena, such as cold agglutinins, haemolytic anemia, circulating immune complexes, rheumatoid factor, and anti-smooth muscle antibodies. Hypergammaglobulinemia is present in approximately 50% of patients and is polyclonal [13]. Other immunological dysregulation associated are hypogammaglobulinemia, monoclonal serum immunoglobulin, and hypoalbuminemia [13]. Lymphopenia has been reported in 52-66% of cases [13]. Leucocytosis is less frequent [15].

*Morphology*

Histologically, there is partial or complete effacement of LN architecture by abnormal lymphoid cells in AITL, which are typically small to medium-sized with round nucleus, irregular

**Table 1.** Clinical and demographic features in AITL at diagnosis

| Clinical parameter | Baseggio et al., 2011 [6] (n=28) | Lachenal et al., 2007 [10] (n=77) | Dobay et al., 2017 [8] (n=94) | Cho et al., 2009 [7] (n=33) | Loghavi et al., 2016 [12] (n=38) | Singh et al., 2014 [14] (n=17) | Baseggio et al., 2006 [5] (n=12) | Mourad et al., 2008 [13] (n=157) | Federico et al., 2013 [9] (n=243) | Tokunaga et al., 2012 [15] (n=207) | Li et al., 2017 [11] (n=52) | Bal et al., 2010 [4] (n=17)$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Median age (range) in years | 62 (40-91) | 64.5 (30-91) | 67.8# | 58.5 (with BM involvement); 56 (without BM involvement)# | 59 (29-81) | 57 (34-78) | 58 (38-82) | 62# | 65 (20-86) | 67 (34-91) | 62 (40-83) | 57 (28-82) |
| Male:female ratio | 1.15:1 | 1.26:1 | 1.29:1 | 2.8:1 (with BM involvement) and 4:1 (without BM involvement)# | 1:1.11 | 1.83:1 | 1:1 | 1.53:1 | 1:3 | 1.83:1 | 2:1 | 2.4:1 |
| B symptoms (%) | 10.71 | 77 | - | 66 | 54 | - | 25 | 72 | - | 60 | 65 | 70 |
| Performance status > 1 (%) | - | 40 | 53 | - | | - | - | 50 | 37 | 36 | 48 | - |
| Advanced stage (III/IV) (%) | - | 92 | 99 | - | 95 | 100 | - | 81 | 89 | 90 | 90 | 60 |
| LAP (%) | 100 | 90 | - | 91 | 68 | - | 67 | 100 | 76 | - | - | 60 |
| Hepatomegaly (%) | - | 51 | - | 50 | 45* | - | - | 25 | 35 | 9 | 12 | 50 |
| Splenomegaly (%) | 39.28 | 26 | - | 59 | 45* | - | 25 | 55 | 26 | 7 | 48 | 70 |
| Skin lesions (%) | 21.42 | 45 | - | 31 | 42 | - | 25 | 30 | 21 | 7 | 29 | 10 |

#Age range not mentioned. *Information about hepatomegaly and splenomegaly not given separately, incidence of hepatosplenomegaly mentioned in the study [8]. $Detailed clinical information was available in 10/17 patients. AITL Angioimmunoblastic T-cell leukemia; BM bone marrow.

nuclear margins and pale chromatin [2]. Expanded follicular dendritic network and prominent proliferation of high endothelial venules are some of the other characteristic features of AITL. Neoplastic cells account for only a fraction of the infiltrate and are admixed with infiltration by accessory cells such as reactive small lymphocytes, reactive CD8 T cells along with few macrophages, eosinophils and mast cells. Some large Reed-Sternberg like lymphoid B cells are also seen that are often EBV infected (66-91%) [2]. The morphology can overlap with some reactive disorders like autoimmune diseases, reactive lymphoid hyperplasia, hence, AITL cannot often be diagnosed based on morphology alone. Supplementation by additional immunological data either by IHC or immunophenotyping (IPT) is essential.

*PB and BM involvement (**Table 2**)*

BM can be involved in as many as 50-86% of cases of AITL [3-15]. Patients with BM involvement have higher frequencies of hepatosplenomegaly and pleural effusion [7]. BM involvement has been often found to be associated with bone marrow plasmacytosis, hypercellular marrow, and eosinophilia.

Peripheral Blood involvement by AITL has been variably reported by various studies and is not well documented. One study concluded that PB involvement is found exclusively in all patients with BM involvement [7]. Bassegio et al., 2006 found PB involvement in all cases where PB sample was available [5]. Singh et al., 2014 studied 17 cases of AITL, all of which showed PB involvement by malignant T lymphocytes [14]. Loghavi et al., 2016 found malignant T cells in the peripheral bloodstream in 78% of their cases [12]. Other studies have neither documented occurrence of PB involvement in AITL nor evaluated PB for its involvement.

The median range of neoplastic cells in PB is around 8.5-23% [12, 16]. Most PBS reveal a polymorphic lymphoid population containing only a minority of atypical lymphoid cells and many other cells making up the majority such as small lymphocytes, large granular lymphocytes, lympho-plasmacytic cells or plasma cells. Lymphocytosis is a rare finding with only few studies reporting 90% atypical lymphocytes in PBS [3].

*Immunophenotype (IPT) of AITL (**Table 3**)*

Multiparameter FCM can identify the distinct population of aberrant T cells in cases of AITL. The immunophenotypic profile of lymphoma cells varies according to site of involvement [12]. Knowledge of this variability is essential to reach a definitive diagnosis [12]. CD10 expression by neoplastic T cells is seen in 80-90% of cases of AITL and is a very specific marker for diagnosing AITL by FCM [5]. Definition of a cut-off to identify CD10 positivity is essential as few cases of reactive hyperplasia, follicular lymphoma or marginal lymphoma may also harbour benign T cells showing positivity for CD10 [6]. CD10 expression by > 5% by CD4/CD5 positive T cells is taken to be positive.

Gene expression profiling has indicated TFH origin of AITL, and hence, neoplastic T cells are positive for CXCL13, BCL6, PD-1, and ICOS. However, while the latter two can be detected by FCM also, the first two markers are not routinely available for IPT and are to be used as markers by IHC [14].

Malignant T cells also express CD2, CD4, CD5 and CD45. They lack CD8, CD56, and have dim to negative expression of surface CD3 (sCD3). sCD3 is the most frequently downregulated/absent T antigen in AITL (60% to 100%) (**Table 3**). The complete loss of sCD3 is more common in BM and PB samples compared with LN specimens [12]. Singh et al., 2014 studied sCD3-/CD4+ circulating T cells in PB of AITL patients versus patients with other CD4+ lymphomas and concluded that the combination of sCD3-/CD4+ immunophenotype has a 94% predictive value for the diagnosis of AITL [14]. Our case also showed expression of CD16 and TCRγδ in neoplastic T cells which have not been reported previously. CD4 and CD8 were also positive in a subset of cells in contrast to literature which demonstrate AITL cells to be CD8 negative (**Table 3**).

Among case studies, CD2 and CD5 were the least commonly down-regulated antigens reported to be absent in only two studies [5, 12]. However, CD7 may be absent in upto 28-67% of cases [2, 17]. Since circulating lymphoma cells have tendency to downregulate a number of surface molecules, particularly, CD3 and CD7, the most suitable markers used for gating these cells on FCM is a combination of CD4

**Table 2.** Laboratory features at diagnosis in AITL

| Lab feature | Baseggio et al., 2011 [6] | Lachenal et al., 2007 [10] | Dobay et al., 2017 [8] | Cho et al., 2009 [7] | Loghavi et al., 2014 [12] | Baseggio et al., 2006 [5] | Mourad et al., 2008 [13] | Federico et al., 2013 [9] | Tokunaga et al., 2012 [15] | Li et al., 2017 [11] | Bal et al., 2010 [4] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Anemia (%) | 86 | 51 | 66 | 44 | 29 | 100 | 65 | 33 | 61 | 73 | 80 |
| Thrombo-cytopenia (%) | - | 20 | - | 31 | 6 | - | 20 | 25 | 34 | 53 | 30 |
| Positive DAT (%) | 10.71 | 58 | 45 | 75 | - | - | 33 | 36 | 46 | 33 | - |
| Hyper-gamma-globulinemia (%) | 59 | 51 | 48 | - | 41 | 50 | 50 | 30 | 54 | - | 100 |
| Hypereosinophilia (%) | 10.71 | 33 | - | 34 | - | - | 32 | - | - | - | - |
| PB involvement (%) | 93.75 | 33 | - | 28 | 42 | 100 | - | - | - | - | 0 |
| BM involvement (%) | 85 | 60 | - | 70 | 63 | 82 | 47 | 28 | 29 | 50 | 60 |
| LDH elevation (%) | - | 71 | - | 84 | - | - | 66 | 60 | 75 | 75 | 90 |

AITL Angioimmunoblastic T-cell leukemia; BM bone marrow; PB peripheral blood; DAT direct antiglobulin test; LDH lactate dehydrogenase.

**Table 3.** Immunophenotypic characterization of AITL in peripheral blood by flow cytometry

| Antigen | Baseggio et al., 2011 [6] | Loghavi et al., 2016 [12] | Singh et al., 2014 [14] | Baseggio et al., 2006 [5] | Current case |
|---|---|---|---|---|---|
| Surface CD3 | Complete loss in 47% | Complete loss (81.3%); partial loss/decreased intensity (18.8%) | Negative | Complete/partial loss | Partial loss |
| CD4 | Positive | Positive | Positive | Positive; negative in 1 case | Positive |
| CD5 | Positive | Positive | Positive | Positive | Positive |
| CD8 | ND | Negative | Negative | Negative | Positive in a subset |
| CD10 | Positive in 80% | Positive | Positive | Positive | Positive |
| CD2 | Positive | Positive | Positive | Positive | Positive |
| CD7 | Dim positive/positive | Complete/partial loss | Negative | Dim positive | Partial loss |
| CD52 | ND | Positive | ND | ND | ND |
| TCRαβ | ND | Complete loss/decreased intensity | ND | ND | Negative |
| TCRγδ | ND | ND | ND | ND | Positive |
| ICOS | Positive in 47% | ND | ND | ND | ND |
| PD1 | Positive | ND | ND | ND | ND |
| CD16 | ND | ND | Negative | ND | Positive |
| CD56 | ND | ND | Negative | ND | Negative |
| CD57 | ND | ND | Negative | ND | Negative |

ND-not done.

and CD5 [10]. CD30 as a marker has not been studied extensively in AITL. It is expressed in only 20% of cases of AITL and has recently become relevant for therapeutic reasons [2].

*Prognosis*

The overall prognosis of AITL patients is poor with median survival of less than 3 years with long-term survival approaching 30% [18]. The factors included for prognostification of AITL include age > 60 years, performance status > 2, extranodal sites > 1, presence of B symptoms and thrombocytopenia [18].

## Conclusion

Our case highlights the frequent presence of circulating lymphoma cells in AITL. These cells can be readily missed if we are relying on morphology alone. Immunophenotyping of PB sample by multiparameter FCM should be done in every case of AITL to assess its true incidence, its link with BM involvement, and its impact on patient outcome. Our case also underscores the need to have knowledge about various aberrancies in the expression pattern of various surface markers so as to make timely definitive diagnosis.

## Disclosure of conflict of interest

None.

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## References

[1] Swerdlow SH, Campo E, Pileri SA, Harris NL, Stein H, Siebert R, Advani R, Ghielmini M, Salles GA, Zelenetz AD and Jaffe ES. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood 2016; 127: 2375-2390.

[2] Fujisawa M, Chiba S and Sakata-Yanagimoto M. Recent progress in the understanding of angioimmunoblastic T-cell lymphoma. J Clin Exp Hematop 2017; 57: 109-119.

[3] Lunning MA and Vose JM. Angioimmunoblastic T-cell lymphoma: the many-faced lymphoma. Blood 2017; 129: 1095-1102.

[4] Bal M, Gujral S, Gandhi J, Shet T, Epari S and Subramanian PG. Angioimmunoblastic T-cell lymphoma: a critical analysis of clinical, morphologic and immunophenotypic features. Indian J Pathol Microbiol 2010; 53: 640-645.

[5] Baseggio L, Berger F, Morel D, Delfau-Larue MH, Goedert G, Salles G, Magaud JP and Felman P. Identification of circulating CD10 positive T cells in angioimmunoblastic T-cell lymphoma. Leukemia 2006; 20: 296-303.

[6] Baseggio L, Traverse-Glehen A, Berger F, Ffrench M, Jallades L, Morel D, Goedert G, Magaud JP, Salles G and Felman P. CD10 and ICOS expression by multiparametric flow cytometry in angioimmunoblastic T-cell lymphoma. Mod Pathol 2011; 24: 993-1003.

[7] Cho YU, Chi HS, Park CJ, Jang S, Seo EJ and Huh J. Distinct features of angioimmunoblastic T-cell lymphoma with bone marrow involvement. Am J Clin Pathol 2009; 131: 640-646.

[8] Dobay MP, Lemonnier F, Missiaglia E, Bastard C, Vallois D, Jais JP, Scourzic L, Dupuy A, Fataccioli V, Pujals A, Parrens M, Le Bras F, Rousset T, Picquenot JM, Martin N, Haioun C, Delarue R, Bernard OA, Delorenzi M, de Leval L and Gaulard P. Integrative clinicopathological and molecular analyses of angioimmunoblastic T-cell lymphoma and other nodal lymphomas of follicular helper T-cell origin. Haematologica 2017; 102: e148-e151.

[9] Federico M, Rudiger T, Bellei M, Nathwani BN, Luminari S, Coiffier B, Harris NL, Jaffe ES, Pileri SA, Savage KJ, Weisenburger DD, Armitage JO, Mounier N and Vose JM. Clinicopathologic characteristics of angioimmunoblastic T-cell lymphoma: analysis of the international peripheral T-cell lymphoma project. J Clin Oncol 2013; 31: 240-246.

[10] Lachenal F, Berger F, Ghesquières H, Biron P, Hot A, Callet-Bauchu E, Chassagne C, Coiffier B, Durieu I, Rousset H and Salles G. Angioimmunoblastic T-cell lymphoma: clinical and laboratory features at diagnosis in 77 patients. Medicine (Baltimore) 2007; 86: 282-292.

[11] Li Y, Yang C, Mao L, Wang J, Li C and Qian W. Clinical characteristics of angioimmunoblastic T-cell lymphoma in China and C-reactive protein as an independent prognostic factor. Medicine (Baltimore) 2017; 96: e8091.

[12] Loghavi S, Wang SA, Medeiros LJ, Jorgensen JL, Li X, Xu-Monette ZY, Miranda RN and Young KH. Immunophenotypic and diagnostic characterization of angioimmunoblastic T-cell lymphoma by advanced flow cytometric technology. Leuk Lymphoma 2016; 57: 2804-2812.

[13] Mourad N, Mounier N, Brière J, Raffoux E, Delmer A, Feller A, Meijer CJ, Emile JF, Bouabdallah R, Bosly A, Diebold J, Haioun C, Coiffier B, Gisselbrecht C and Gaulard P. Clinical, bio-

logic, 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 2008; 111: 4463-4470.

[14] Singh A, Schabath R, Ratei R, Stroux A, Klemke CD, Nebe T, Flörcken A, van Lessen A, Anagnostopoulos I, Dörken B, Ludwig WD, Pezzutto A and Westermann J. Peripheral blood sCD3-CD4+ T cells: a useful diagnostic tool in angioimmunoblastic T cell lymphoma. Hematol Oncol 2014; 32: 16-21.

[15] Tokunaga T, Shimada K, Yamamoto K, Chihara D, Ichihashi T, Oshima R, Tanimoto M, Iwasaki T, Isoda A, Sakai A, Kobayashi H, Kitamura K, Matsue K, Taniwaki M, Tamashima S, Saburi Y, Masunari T, Naoe T, Nakamura S and Kinoshita T. Retrospective analysis of prognostic factors for angioimmunoblastic T-cell lymphoma: a multicenter cooperative study in Japan. Blood 2012; 119: 2837-2843.

[16] Chen W, Kesler MV, Karandikar NJ, McKenna RW and Kroft SH. Flow cytometric features of angioimmunoblastic T-cell lymphoma. Cytometry B Clin Cytom 2006; 70: 142-148.

[17] Alikhan M, Song JY, Sohani AR, Moroch J, Plonquet A, Duffield AS, Borowitz MJ, Jiang L, Bueso-Ramos C, Inamdar K, Menon MP, Gurbuxani S, Chan E, Smith SM, Nicolae A, Jaffe ES, Gaulard P and Venkataraman G. Peripheral T-cell lymphomas of follicular helper T-cell type frequently display an aberrant CD3(-/dim) CD4(+) population by flow cytometry: an important clue to the diagnosis of a Hodgkin lymphoma mimic. Mod Pathol 2016; 29: 1173-1182.

[18] Mosalpuria K, Bociek RG and Vose JM. Angioimmunoblastic T-cell lymphoma management. Semin Hematol 2014; 51: 52-58.