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ORIGINAL ARTICLE

Aggressive Angioimmunoblastic T Cell Lymphomas (AITL) with Soft Tissue Extranodal Mass Varied Histopathological Patterns with Peripheral Blood, Bone Marrow, and Splenic Involvement and Review of Literature

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Abstract Angioimmunoblastic T cell lymphoma (AITL) is a peripheral T cell non-Hodgkin lymphoma with an aggressive fatal course and it has varied clinical presentation with an uncommon presentation when they present as soft tissue masses or when there is spill in the peripheral blood or there are composite lymphomas that are rare presentations. Common presentations include lymphadenopathy, fever and systemic symptoms, hemolytic anemias, skin rashes, and rheumatoid arthritis. The classical histopathology is absence of follicles in lymph nodes with presence of high endothelial venules and the tumor cells of small to medium-sized lymphocytes with pale cytoplasm mixed with reactive T cells. On immunohistochemistry, the cells are positive for CD3, CD4, CD10, BCL2, and CXCL13. In this observational study, the clinicopathologic presentation and the immunohistochemical profile of five cases who initially presented with a soft tissue mass which is an extremely rare presentation of this rare type of non-Hodgkin lymphoma that was diagnosed at our center with peripheral blood and bone marrow involvement and the clinicopathologic presentation, immunohistochemical profile, and response to treatment on follow-up are correlated with the literature review. One case had a fulminant and aggressive course and was fatal within 2 months of diagnosis. The rest of the four cases are on regular chemotherapy and follow-up. Our five cases had presented with soft tissue masses, two in the axillary regio,n two in the hand, and one in the scapular region with an extranodal presentation, and there was associated lymphadenopathy which developed subsequently with classic histomorphology and immunohistochemical findings. The age range was 46–54 years and all five cases were males. Three cases were with anemia (hemoglobin range 6.5–8.0 mg/dl) and all five cases were having peripheral blood plasmacytosis. Histopathology was classic with paracortical involvement with polymorphous population of cells with neoplastic lymphocytes of small and large sizes with numerous arborizing blood vessels which correspond to high endothelial venules. Microscopically, three architectural patterns; pattern I was seen in three cases (60%) and then pattern II and III in one case each (20% each). Immunohistochemistry revealed CD4+, CD8−, CXCL13+, CD10+, BCL6+, CD19, CD20, CD1a, Tdt, CD21, and CD23+ in follicular dendritic cells. AITL is a rare and aggressive non-Hodgkin lymphoma with varied clinical presentation with classic histomorphology with various patterns which may cause diagnostic dilemma and immunophenotypic findings, and prompt and early diagnosis is mandatory for institution of therapy.

Keywords Angioimmunoblastic lymphoma · Non-Hodgkin lymphoma

Introduction

Angioimmunoblastic T cell lymphoma (AITL) is a peripheral T cell lymphoma described first by Forster and Moeschlin in 1954 [1]. AITL has become increasingly recognized with the advent of immunophenotypic, cytogenetic, and molecular evidence of T cell monoclonality. AITL represents 18% of T cell lymphomas and they may emerge as a spectrum of benign

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to malignant transformation. This is a disease of adults of middle age with rapid onset and varied clinical presentations like lymphadenopathy, weight loss, anemia, pruritus, arthralgia, cough. Histologically, lymph node architecture is effaced with proliferation of high endothelial venules with a polymorphous population of lymphoid cells and presence or absence of follicles depending on the histopathological pattern I, II, or III. The neoplastic T cells are positive for CD2, CD3, CD4, CD10, CXCL-13, PD1, and BCL-6. AITL is associated with autoimmune hemolytic anemia, rheumatoid factor, antismooth muscle antibodies and hypergammaglobulinemia. AITL is an aggressive disease and the aim of the present study is to better characterize the diagnostic and clinical aspects of AITL for prompt and urgent therapy.

Methods

We analyzed five cases of AITL in this observational study, diagnosed on the basis of biopsy of lymph nodal and soft tissue mass. Clinical history, age, gender, symptoms of fever malaise, site of involvement (nodal or extra nodal), stage of disease, complete blood cell counts, lactate dehydrogenase (LDH), beta-2 microglobulin, and serum proteins were recorded. Serological markers of immunodeficiency and viral markers were done later. Hematoxylin and Eosin (H&E) sections were studied. Immunohistochemistry was performed on formalin-fixed, paraffin-embedded serial tissue sections and was performed using prediluted Dako antibodies against CD2, CD3, CD4, CD5, CD7, CD8, CD30, CD19, CD20, CD79a, PAX-5, ALK1, PD-1, and CXCL13. To assess the T and B cell clonality, polymerase chain reaction (PCR) for T cell receptor gamma and IgH heavy chain (IGH) was performed on formalin-fixed, paraffin-embedded whole tissue sections.

Results

Our five cases had presented with soft tissue masses, two in the axillary region, two in the hand, and one in the scapular region with extranodal presentation and associated lymphadenopathy that developed subsequently, and the biopsy of the mass was diagnostic with classic histomorphology and immunohistochemical findings. The age range was 46–54 years and all five cases were males. Three cases were with anemia (hemoglobin range 6.5–8.0 mg/dl) and all five cases were having peripheral blood plasmacytosis with bone marrow involvement. Histopathology was classic with paracortical involvement with polymorphous population of cells with neoplastic lymphocytes of small and large size with numerous arborizing blood vessels which correspond to high endothelial venules. Microscopically, three architectural patterns; pattern I was seen in three cases (60%) and then pattern II (20%) and pattern III (20%). Immunohistochemistry revealed CD4+, CD8−, CXCL13+, CD10+, BCL6+, CD19, CD20, CD1a−, Tdt−, CD21, and CD23+ in follicular dendritic cells. Bone marrow aspirate in five patients revealed plasmacytosis with spill in peripheral blood. In the May-Giemsa-stained smear, specimens of the bone marrow, small-to-medium-sized atypical lymphoid cells were seen. Subsequently, bone marrow biopsy confirmed involvement with AITL with neoplastic lymphocytes that were immunohistochemically positive for CD4, CD10, CXCL13, and BCL2. One of our cases had a second composite lymphoma developing after 1 month of diagnosis that was a diffuse large B cell lymphoma which responded to treatment and is on follow-up on combination chemotherapy.

Discussion

In 2001, the WHO classification of tumors of hematopoietic and lymphoid tissues listed AITL as a peripheral T cell lymphoma [1]. Massimo et al. studied 243 patients of AITL and concluded that it is a rare clinicopathologic entity with an aggressive course and dismal outcome [2]. In 1974, Frizzera et al. [3] described AITL as a reactive lymphoproliferative disorder of T lymphocytes.

Our five cases had presented with two soft tissue masses in axillary region, two in the hand, and one in the scapular region with extranodal presentation and associated lymphadenopathy with classic histomorphology (Fig. 1) and immunohistochemical findings (Figs. 2, 3, 4, 5, 6). The age range was 46–54 years and all five cases were males. Three cases were with anemia (hemoglobin range 6.5–8.0 mg/dl) and

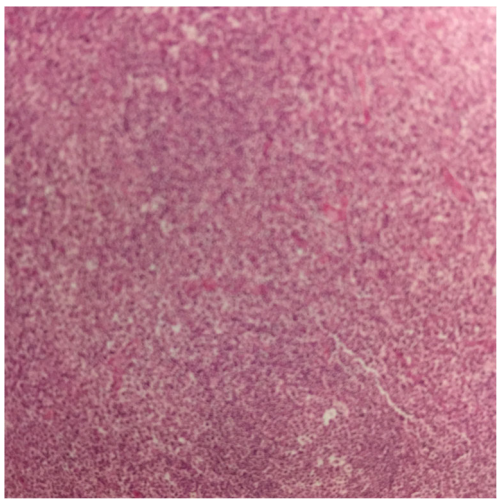

Fig. 1 Microphotograph of angioimmunoblastic T cell lymphoma with medium to large tumor cells consisting of polymorphous population of cells

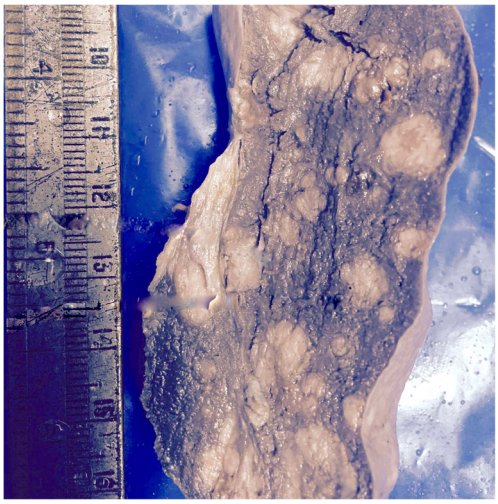

Fig. 2 Gross involvement of the spleen by angioimmunoblastic lymphoma

all five cases were having peripheral blood plasmacytosis with bone marrow involvement.

Lachenal et al. [4] analyzed 77 patients with angioimmunoblastic T cell lymphoma. There were 43 men and 34 women; the median age was 64.5 years (range, 30–91 yrs.). Average time between the first symptoms of the disease and diagnosis was 3.6 months. At diagnosis, peripheral nodes were present in all but one patient and were generalized in 90% of cases. Constitutional symptoms were reported in 77% of cases and spleen enlargement in 51%. A cutaneous eruption—morbilliform, urticarial, or more polymorphic—was present in 45% of patients; in one third of them, the eruption occurred after drug administration. Other clinical manifestations included pleuritis (22%); arthralgia or arthritis (17%); ear, nose, and throat involvement (14%); central or peripheral neurologic manifestations (10%); and ascites (5%). Most patients presented with advanced disease at diagnosis (bone marrow involvement in 60% of cases).

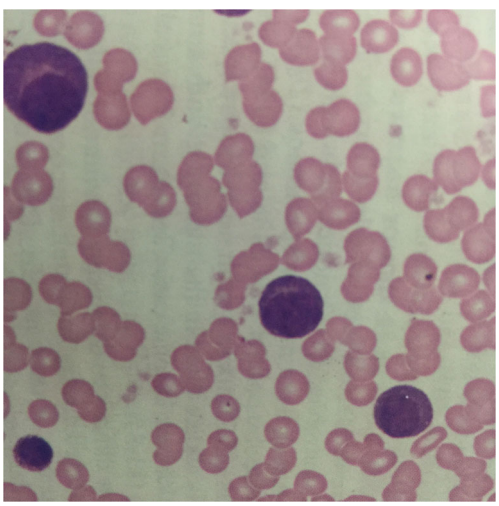

Fig. 3 Peripheral blood smear with large plasmacytoid cells

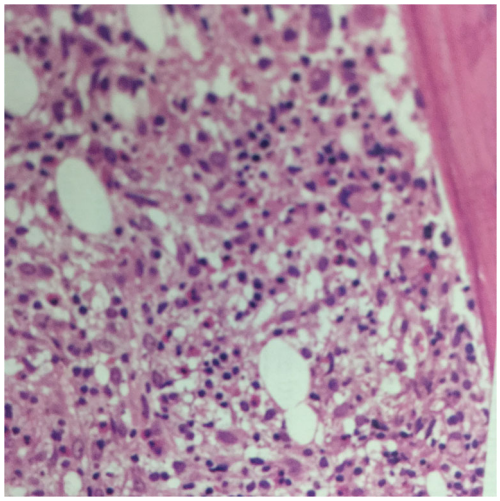

Fig. 4 Bone marrow biopsy with plasmacytoid tumor cells of AITL

The main laboratory abnormalities were elevated lactate dehydrogenase levels (71%), inflammatory syndrome (67%), hypergammaglobulinemia (50%), anemia (51%), and lymphopenia (52%). Autoimmune hemolytic anemia was present at diagnosis in 19% of patients and thrombocytopenic purpura in 7%.

In our study, all the five cases were immunopositive for CD10. Attygale et al. studied in 30 cases of AITL that the neoplastic T cells in angioimmunoblastic lymphoma express CD10 [5]. CD10 is a phenotypic marker that specifically identifies the tumor cells in 90% of AITL and distinguishes it from peripheral T cell lymphoma. This finding provides an objective criterion for accurate and early diagnosis of AITL.

In our study, all the five cases were immunopositive for CXCL13. Dupuis et al. studied in 29 cases of AITL that the neoplastic T cells in angioimmunoblastic lymphoma express CXCL13 [6, 7] and postulated that AITL derives from follicular helper T cells and pathological insights are gained to

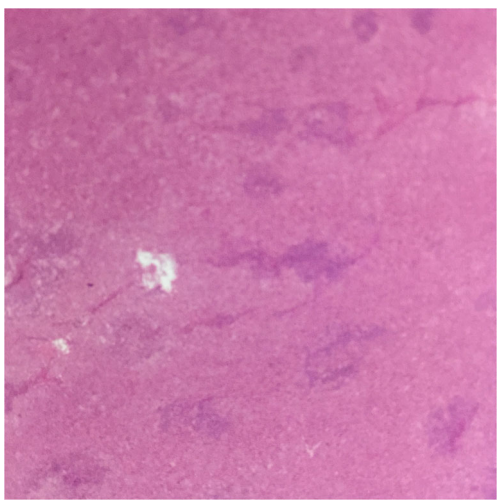

Fig. 5 Pattern I of AILT with hyperplastic follicles with polymorphous pattern

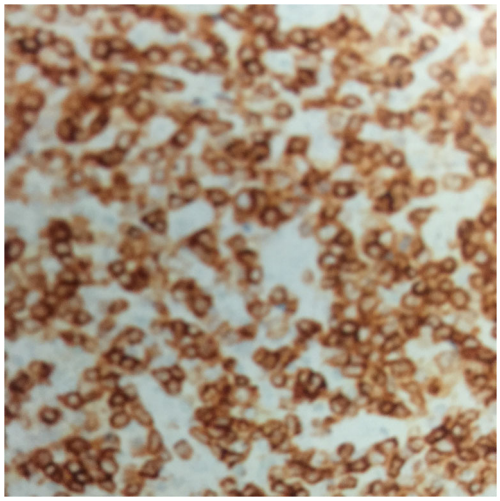

Fig. 6 Tumor cells immunopositive for CD10

understand the disease origin and helps in early and prompt diagnosis.

Follow-up of the cases in our study showed 04 of them were on chemotherapy and on regular follow-up at 6 months; however, one patient died at 2 months time after diagnosis and autopsy revealed splenic involvement. (Fig. 2) Pangalis et al. studied 41 patients of AITL in which 27 patients with combination chemotherapy had median survival up to 51 months and had better response than the other patients [8].

Awareness of the histopathological patterns (Figs. 1, 4 and 5) is relevant as they can be observed in a diverse number of morphological mimics of AITL. Our three cases had hyperplastic follicles with expanded paracortex (pattern I). Accurate recognition of pattern 1 is challenging and phenotypic and morphologic characterization is mandatory; otherwise, a diagnostic miss costs a life. Pattern III (diffuse with absent follicles) was seen in one case, and one case with pattern II with burnt-out follicles which mimics the abortive follicles of Castleman's disease [9–11].

One of our cases had a second lymphoma developing after 1 month of diagnosis that was a diffuse large B cell lymphoma. Due to immunodeficiency associated with AITL, second lymphomas also occur and diffuse large B cell lymphoma is the commonest type that was seen in one of our cases [12].

Histopathologically, diagnosis of AITL is difficult and challenging due to various patterns and immunohistochemistry resolves the issue with CD10 and CXCR13 positivity and prompt and early diagnosis is mandatory for institution of therapy with combination chemotherapy to improve survival as evidenced in literature.

References

1. Jaffe ES, Ralfkiaer E (2001) Angioimmunoblastic T-cell lymphoma. In: Jaffe ES, Harris NL, Stein H et al (eds) World Health Organization classification of tumors. Pathology and genetics of tumors of hematopoietic and lymphoid tissues. IARC Press, Lyon, pp 225–226
2. Federico M, Rudiger T, Bellei M, Nathwani BN, Luminari S, Coiffier B et al (2013) Clinicopathologic characteristics of angioimmunoblastic T-cell lymphoma: analysis of the International Peripheral T-cell Lymphoma Project. J Clin Oncol 31(2):240–246
3. Frizzera G, Moran EM, Rappaport H (1974) Angio-immunoblastic lymphadenopathy with dysproteinaemia. Lancet 1:1070–1073
4. Lachenal F, Berger F, Ghesquires H et al (2007) Angioimmunoblastic lymphoma. Clinical and laboratory features at diagnosis in 77 patients. Medicine 86:282–292
5. Attygale A, Al Jehani R, Diss TC et al (2002) Neoplastic T cells in angio-immunoblastic lymphoma express CD10. Blood 99:627–633
6. Dupuis J, Boye K, Martin N et al (2006) Expression of CXCL13 by neoplastic cells in angio-immunoblastic T cell lymphoma (AITL):a new diagnostic marker providing evidence that AITL derives from follicular helper T cells. Am J Surg Pathol 86:490–494
7. Dunleavy K, Wilson WH, Jaffe ES (2007) Angio-immunoblastic lymphoma. Pathological insights and clinical implications. Curr Opin Hematol 14:348–353
8. Pangalis GA, Moran EM, Nathwani BN, Zelman RJ, Kim H et al (1983) Angioimmunoblastic lymphoma. Long-term follow-up study. Cancer 52:318–321
9. Iannitto E, Ferreri AJ, Minardi V, Tripodo C, Kreipe HH (2007) Angio-immunoblastic lymphoma. Crit Rev Oncol Hematol 68: 264–271
10. de Leval L, Gisselbrecht C, Gaulard P (2010) Advances in the understanding and management of angio-immunoblastic lymphoma. Br J Hematol 148:673–689
11. Rodriguez-Justo M, Attygale AD, Munson P, Roncador G, Marafioti T, Piris MA (2009) Angio-immunoblastic lymphoma with hyperplastic germinal centers: a neoplasia with origin in the outer zone of the germinal center? Clinicopathological and immunohistological study of 10 cases with follicular T cell markers. Mod Pathol 22:753–761
12. Suefuji N, Niino D, Arakawa F, Karube K, Kimura Y, Kiyasu J et al (2012) Clinicopathological analysis of a composite lymphoma containing both T and B cell lymphomas. Pathol Int 62:690–698