Relapsed angioimmunoblastic T-cell lymphoma with large pericardial effusion

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ABSTRACT

T-cell lymphomas comprise 10% to 15% of all lymphoid malignancies and affect precursor or mature T cells; the latter are referred to as peripheral T-cell lymphomas. We present a case of a subtype, angioimmunoblastic T-cell lymphoma, in which a patient previously treated with chemotherapy and autologous stem cell transplant relapsed with B symptoms and large pericardial/pleural effusions. Recurrent lymphoma was confirmed on pericardial tissue biopsy. Treatment was trialed with lenalidomide and the effusions resolved. Five months later she died from septic shock and multiorgan failure. Our case highlights the need for rapid evaluation of B symptoms and/or new effusions in patients with a known history of angioimmunoblastic T-cell lymphoma.

KEYWORDS AITCL; AITL; angioimmunoblastic T-cell lymphoma; malignant effusion; pericardial effusion

T-cell lymphomas comprise 10% to 15% of all lymphoid malignancies and can be further categorized based on the maturity of the affected T cells.¹

Peripheral T-cell lymphoma primarily affects more mature T cells and has many subtypes, including angioimmunoblastic T-cell lymphoma (AITCL).^{1,2} We report a case of relapsed AITCL that presented with B symptoms and large pericardial/pleural effusions.

CASE REPORT

A 74-year-old white woman presented with an autoimmune hemolytic anemia initially controlled with steroids and splenectomy. Imaging and pathology were negative for lymphoma. The anemia recurred and cyclophosphamide with rituximab achieved complete response. Two years later, she developed AITCL, stage IIIB, diagnosed on lymph node biopsy, and was treated with etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin. Three months later, she relapsed with cutaneous disease, which was treated with brentuximab followed by autologous stem cell transplant (ASCT). Three months after ASCT, she had intermittent cutaneous disease treated with romidepsin for 18 months until she was admitted with 3 weeks of fevers, night

sweats, rash, cough, and dyspnea which failed to improve with antibiotics and diuretics. Physical exam was remarkable for hypotension, tachycardia, tachypnea, jugular venous distension, 2+ pitting edema, diminished breath sounds, bibasilar crackles, and axillary lymphadenopathy.

Electrocardiogram (*Figure 1a*) showed low voltage and atrial fibrillation. Chest radiograph (*Figure 1c*) and computed tomography (*Figure 1d*) showed bilateral pleural effusions, moderate pericardial effusion, and axillary, supraclavicular, and mediastinal lymphadenopathy. Echocardiogram (*Figure 1b*) showed a hyperdynamic left ventricle with an ejection fraction of 75% and a large, circumferential, pericardial effusion with collapse of the right ventricle in diastole. Intravenous fluids improved the hypotension and tachycardia, avoiding clinical tamponade.

Pericardiocentesis was complicated by hemodynamic instability following removal of 50 cc of pericardial fluid. Thoracoscopy, pericardial window, and bilateral thoracenteses yielded an additional 250 cc of serosanguinous pericardial fluid and 3000 cc of serous pleural fluid. Cytology was remarkable for an aberrant T-cell immunophenotype. Pericardial biopsy showed thickening, chronic inflammation, congestion, atypical lymphocytes clustered around blood vessels, and CD3/CD10 coexpression on immunohistochemistry (*Figures 2*). Flow

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Figure 1. (a) Electrocardiogram with low voltage—especially in leads III, aVL, aVF, and V3—and rate-controlled atrial fibrillation. (b) Parasternal long-axis echocardiographic view of large circumferential pericardial (asterisks) and pleural effusions (delta). (c) Portable anteroposterior chest radiograph with bilateral pleural effusions (deltas). (d) Noncontrast spiral chest computed tomography with moderate to large pericardial effusion (asterisks), large bilateral pleural effusions (deltas), and scattered lymphadenopathy (arrows). Ao indicates ascending aorta; LA, left atrium; LV, left ventricle; RV, right ventricle.

Figure 2. (a) Pericardial tissue immunohistochemistry with CD3 positivity (T cells). (b) Pericardial tissue immunohistochemistry with CD10 positivity denoting follicular helper T cells, the origin cells of angioimmunoblastic T-cell lymphoma.

cytometry detected a 59% atypical T-cell population consistent with the history of AITCL.

Lenalidomide was started and there was no recurrence of pericardial effusion. Over the next 5 months, the patient developed hypercalcemia, *Clostridium difficile* diarrhea, disseminated intravascular coagulation, and thrombocytopenia and died from septic shock and multiorgan failure.

DISCUSSION

AITCL comprises 1% to 2% of all non-Hodgkin lymphomas and up to 18.5% of peripheral T-cell lymphomas.^{3,4}

The median age of onset of AITCL is 65 years.^{3,4} Its presentation includes classic lymphoma-related symptoms such as generalized lymphadenopathy, fevers, night sweats, weight loss, ascites, pleural effusion, arthralgias, and hepatosplenomegaly.^{3,4} Skin lesions are a common extranodal manifestation and can include macular or papular rashes, plaques, or nodules.^{4–6} Laboratory studies commonly elucidate autoimmune phenomena associated with AITCL, such as hemolytic anemia, cold agglutinins, and circulating immune complexes.⁵ Our patient's clinical course noted a majority of these clinical manifestations and autoimmune comorbidities,

including a hemolytic anemia 2 years before her diagnosis of lymphoma.

One unusual feature of our patient's course was pericardial disease. Pericardial involvement leading to effusion and tamponade is rare in AITCL and has only been reported as the presenting finding in two cases.^{7,8} Lymphomas overall, most commonly diffuse large B cell, follicular, and Burkitt, are a common source of cardiac metastasis through hematogenous spread and preferentially deposit as focal tumors within the subepicardial adipose tissue.^{9–11}

AITCL is diagnosed via biopsy of involved tissue.^{12,13} Affected lymph nodes show complete effacement with polymorphous T cells, characteristic sparing of the subcapsular sinus, and arborization and proliferation of endothelial venules.¹² Immunohistochemistry can be positive for a variety of T-cell-specific markers; CD10, CXCL13, PD-1, and BCL-6 are the most specific for AITCL.^{12,14} Our patient had an aberrant T-cell phenotype in the pericardial fluid and CD10 positivity in the pericardial biopsy. CXCL13 and PD-1 were positive at the time of initial diagnosis and on skin biopsies at relapse.

AITCL is preferentially treated with high-dose chemotherapy, most commonly anthracycline-based regimens, followed by ASCT.^{3,4,12,15} Brentuximab, romidepsin, and lenalidomide have also shown efficacy, with the latter two agents used in recurrent disease after ASCT.^{3–5,15,16}

The prognosis of AITCL is poor, with a median 5-year survival of approximately 32%.^{3,4} The combination of chemotherapy and ASCT has an overall survival of 67% and 59% at 2 and 4 years, respectively, double that of chemotherapy alone.^{4,14} Recurrence after ASCT is up to 50% at 2 years.^{2,15} Our case demonstrates the need for rapid evaluation of B symptoms in patients with a known history of AITCL given the high rate of mortality from recurrent disease.

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