Clinical Case Report

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Concomitant T-cell prolymphocytic leukemia and visceral leishmaniasis

A case report

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Abstract

Rationale: T-cell prolymphocytic leukaemia (T-PLL) is a rare aggressive lymphoid disease featured by a significant increased lymphocyte count and obvious hepatosplenomegaly with poor prognosis. The concomitant presentation of T-PLL and visceral leishmaniasis (VL) has not previously been reported.

Patient concerns: The patient initially suffered from anorexia, skin pigmentation, fever and hepatosplenomegaly. Bone marrow smear described leishmania and antibody test was positive. VL was diagnosed and he was given antimony gluconate therapy. His symptoms recurred.

Diagnosis: A combination of serological rk39 test, morphologic evaluation and immunophenotyping by flow cytometry finally supported the diagnosis of concomitant VL and T-PLL.

Outcomes: Amphotericin B was used for the treatment of VL first and a referral for treating T-PLL after recovery from VL was suggested. Unfortunately, the patient requested to be discharged. Telephone follow-up indicated that he died a few days after leaving the hospital.

Lessons: Due to the rarity of the disease combination, the pathogenesis association of T-PLL and VL is unclear. However, a duly diagnosis is crucial for treatment. In immunosuppressed patients due to malignancies and treatment, VL should be considered as an opportunistic infection. In VL infections, the clinical manifestations mimicking hematological malignancies may cover up the underlying disease. Under such conditions, a complete work-up based on laboratory test is necessary to achieve a correct diagnosis.

Abbreviations: LD = *Leishmania donovani*, T-PLL = T-cell prolymphocytic leukaemia, VL = visceral leishmaniasis.

Keywords: diagnosis, immunophenotype, morphology, T-cell prolymphocytic leukemia, visceral leishmaniasis

1. Introduction

T-cell prolymphocytic leukemia (T-PLL) is a rare, aggressive hematologic disease in post-thymic stage. About 15% of patients may follow an "indolent" clinical course for as long as several years, but rapid disease progression cannot be avoided once it occurs.[1] Accurate diagnosis is mainly based on complete blood cell count and differentiation, cell morphology evaluation, and immunophenotyping. Examination of a peripheral blood film is a key diagnostic test and often provides the first clue to the diagnosis.[2] Leishmaniasis is an endemic zoonosis caused by pathogens including *Leishmania donovani* (LD) and *L. infantum*, with infection transmitted by sand flies.[3] Depending on the pathogen species, leishmaniasis is further divided into cutaneous leishmaniasis, visceral leishmaniasis (VL), and mucocutaneous leishmaniasis. It is estimated that approximately 0.5 million people worldwide develop VL every year.[4] Misdiagnosis may lead to a delay in the administration of proper treatment, resulting in fatal consequences.[5] Although T-PLL and leishmaniasis are extensively studied disease entities, concurrent presentation of T-PLL and VL has never been reported.

Here we describe such an unprecedented case that presented with manifestations mimicking VL and T-PLL in which T-PLL was masked. Finally, a combination of serological antibody testing, blood and bone marrow cell morphology and immunophenotyping, and immunohistochemistry staining revealed the coexistence of LD bodies and an abnormal population of clonal lymphocytes.

2. Case report

A 50-year-old male patient presented to a local hospital because of anorexia, fever, weight loss, and skin darkening in the previous 7 months. A complete blood count showed pancytopenia and a few atypical lymphocytes. Bone marrow examination revealed

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LD bodies. The patient had traveled 7 months earlier to Xinjiang Province, China, a known VL endemic area. He was diagnosed of VL infection, treated with 2 courses of sodium antimony gluconate therapy, and subsequently discharged. Three months later his symptoms recurred, along with intermittent fever and hepatosplenomegaly. The patient was referred to West China Hospital for further treatment.

On admission, his clinical appearance was normal except for facial expressions indicative of chronic disease, with palpable bilateral anterior, posterior cervical, and supraclavicular lymph nodes that were enlarged to soybean size. The laboratory workup was notable for anemia and leukocytosis (RBC 3.05×10^{12}/L, hemoglobin 88 g/L, WBC 28.97×10^{9}/L, lymphocytes 58%). Lactate dehydrogenase levels were slightly elevated (279 IU/L). An immunochromatographic rk39 strip test (InSure; InBios International Inc., Seattle, WA) showed a positive result. Examination of a peripheral blood smear identified a population of atypical lymphocytes described as having coarse chromatin, dark blue-staining cytoplasm, and a few cells with petal-shaped nuclei; some cells displayed multiple nucleoli or "warty" protuberances at the outer edge of the cytoplasm (Fig. 1A). Examination of a bone marrow smear revealed 30.5% abnormal lymphocytes with the above morphology and scattered LD bodies (Fig. 1B). Lymphocytic infiltration was identified by bone marrow flow cytometry as including 30% abnormal T lymphocytes co-expressing CD2, CD3, CD5, CD7, and CD8, with restricted expression of T-cell receptor (TCR) vβ23 and negative for CD4, CD16 and CD56 (Fig. 2). Histopathology of bone marrow biopsy showed amastigotes, as well as scattered or small focal infiltration by suspected lymphocytes and plasma cells. Further immunohistochemistry staining indicated that these cells were CD20(−), CD3ε(+), CD2(+), CD5(+), CD7(+), CD4 (−), CD8(+), CD56(−) (Fig. 3). The karyotype of bone marrow cells was normal as 46, XY.

Considering the results of blood tests, bone marrow examinations, and previous investigations, the patient was finally diagnosed with concomitant T-PLL and VL. Amphotericin B was used for the treatment of VL.[6] Our hematology department suggested a referral for treating T-PLL after recovery from VL. Unfortunately, the patient requested to be discharged. Telephone follow-up indicated that he died a few days after leaving the hospital.

3. Discussion

T-PLL malignant cells are medium-sized immature lymphocytes with visible or invisible nucleoli. Most malignant cells originate from TCRαβ type and $CD4^{+}$ T lymphocytes. In a few cases, malignant cells are $CD4^{+}CD8^{+}$, which is uncommon in other types of mature T cell tumors,[2,7,8] as presented in this case. Considering a very small percentage of all lymphoid malignancies that T-PLL accounts for, clinicians may sometimes make an incorrect diagnosis.

Currently, the gold standard for VL diagnosis is the presence of amastigotes in tissues like bone marrow, lymph nodes, the spleen, and skin.[9] Monocyte and macrophage hyperplasia is substantial in the bone marrow of VL patients, in which LD bodies are found; granulocyte nucleus maturation is delayed and the total proliferation is less active. The erythoid cell nuclear-cytoplasmic ratio is disproportional and the proliferation is active. Some metarubricytes show a binuclear, multinuclear, or deformed nucleus. The megakaryocytes may proliferate normally or inactively with scattered and reduced number of platelets. Reticular cells, or degenerated cells, may increase significantly. In the initial disease period of VL, small lymphocytes usually account for <70% of the total number of lymphocytes. In the recovery stage, the low lymphocyte count can gradually increase to above 80%. Conformational diagnosis can be made using recombinant protein antigen (rk39) and PCR. Leishmaniasis should be considered if the clinical appearance and epidemiologic background together support the diagnosis.

A review of the literature failed to identify previous reports of simultaneous or sequential occurrence of VL and T-PLL. Patients with VL and hematological and lymphoid malignancies usually show resembling clinical symptoms including fever, hepatosplenomegaly, and pancytopenia. Such mimicking of manifestations is of great challenge to the diagnosis of concomitant VL and lymphoma. Furthermore, concurrent presentation with lymphoid or hematological malignancies may result in leishmaniasis manifestations being considered atypical [10] or asymptomatic,[11] which adds to the difficulty of a correct diagnosis. As shown in this case, the initial workup at the local hospital was incompatible with clinical standards for the diagnosis of either disease. Treatment with sodium antimony gluconate failed to reduce the enlarged spleen and lymph nodes or the fever. At the same time, the examination of peripheral blood

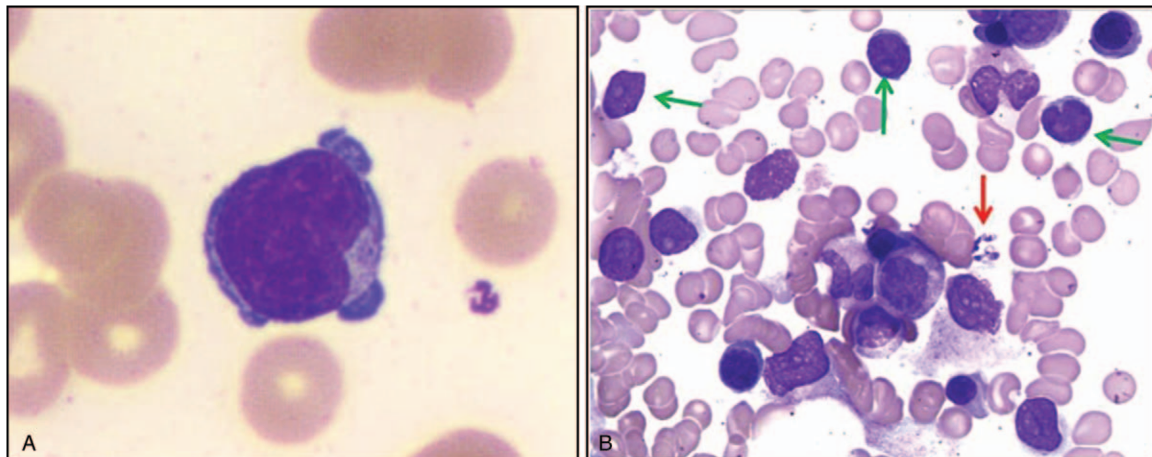

Figure 1. Morphology of the infiltrated lymphocytes in (A) peripheral blood: coarse nuclear chromatin, petal-like nuclei, intensely basophilic agranular cytoplasm with cytoplasmic protrusions. (B) Bone marrow: visible LD bodies (red arrow) and the infiltrated lymphocytes (green arrow). LD=*Leishmania donovani*.

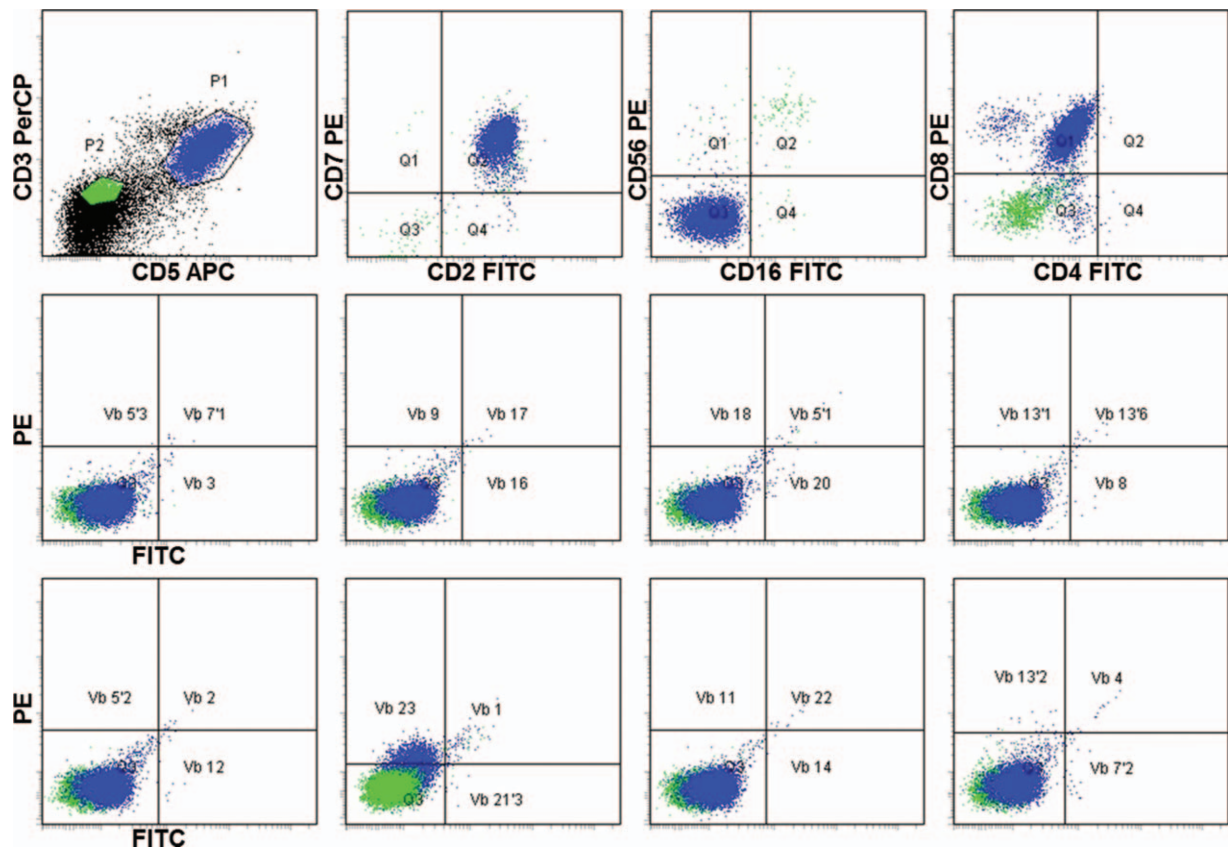

Figure 2. Immunophenotyping of bone marrow flow cytometry: T lymphocytes gated by CD3-PerCP and CD5-APC (blue), co-expressing CD2, CD7, CD8, and restrictively expressing TCRvβ23.

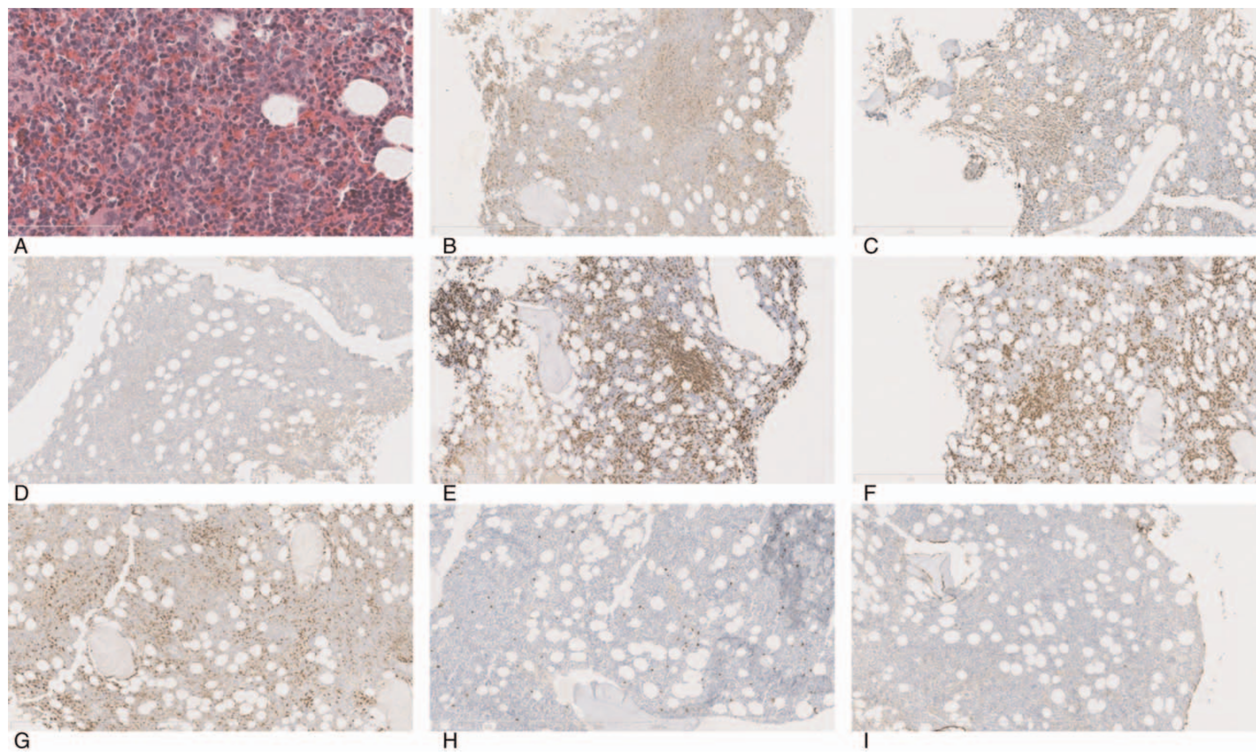

Figure 3. Histopathology features and immunohistochemistry (IHC) of the partial bone marrow biopsy. (A) Scattered or grouped distribution of histiocytes; amastigotes visualized inside the cytoplasm or stroma of the histiocytes; scattered or focal distribution of lymphocytes and plasma cells (hematoxylin and eosin, ×400). Representative images show positive expression for CD2 (B) CD3ε (C) CD5 (E) CD7 (F) CD8 (G) and negative expression for CD4 (D) CD20 (H), and CD56 (I) (×100). IHC = immunohistochemistry.

revealed a population of atypical lymphocytes. Differential identification and correct description of such cells in a routine complete blood cell count was critical to the diagnosis of T-PLL in this case.

To the best of our knowledge, this is the first report of a patient with concurrent VL and T-PLL, which will broaden the knowledge of VL presented with hematological malignancies. Laboratory professionals and clinicians should be alert to the differential diagnosis of VL in endemic areas and among patients with a travel history to these areas. Owing to malignancies and treatment, VL should be considered as an opportunistic infection in immunosuppressed patients. Conversely, in VL infections, clinical manifestations resembling hematological malignancies may mask the underlying disease. Under such conditions, a complete workup based on laboratory testing is needed for a correct diagnosis.

Author contributions

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