



Acute Precursor T Cell Lymphoblastic Leukemia Associated with Behcet's Disease: A Case Report

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Behcet's disease is an inflammatory disorder characterized by recurrent oral aphthous ulcers, genital ulcers, uveitis, and skin lesions. A few cases of hematologic disease in patients with Behcet's disease have been reported in the literature. However, acute precursor T cell lymphoblastic leukemia has never been described in association with Behcet's disease. We recently encountered a case of acute precursor T cell lymphoblastic leukemia in a 62-year-old

man with a prior diagnosis of Behcet's disease. The patient presented with febrile neutropenia and his bone marrow biopsy revealed acute precursor T cell lymphoblastic leukemia. He was scheduled to undergo therapeutic chemotherapy, but unfortunately he died from pneumonia prior to treatment.

Key Words. Behcet's disease, Acute precursor T cell lymphoblastic leukemia

Introduction

Behcet's disease is an inflammatory disorder of unknown cause that is characterized by recurrent oral aphthous ulcers, genital ulcers, uveitis, and skin lesions. Involvement of the gastrointestinal tract, central nervous system, and large vessels is less frequent (1).

Moderate anemia associated with chronic disease is common, and leukocytosis is seen in 15% of patients with Behcet's disease (2). However, cytopenia of multilineage is uncommon and Behcet's disease is rarely observed in association with leukemia or other hematologic disorders (3,4). There are some reports in the literature of patients with Behcet's disease associated with myelodysplastic syndrome (5,6).

To our knowledge, acute precursor T cell lymphoblastic leukemia has never been described in association with Behcet's disease. We recently encountered a patient who presented with Behcet's disease associated with acute precursor T cell lymphoblastic leukemia that was not attributable to other underlying causes. Here, we report this unique case of acute precursor T cell lymphoblastic leukemia in a man with Behcet's disease.

Case Report

A 62-year-old man was admitted to the hospital for evaluation of fever. The patient had been diagnosed with Behcet's disease about 4 years. Previously, he had recurrent oral and genital ulcers and erythema nodosum, and had suffered from arthritis in his right knee for 4 years. He also had Behcet's colitis and had been previously admitted for massive hematochezia and treated with arterial embolization (Figure 1). He had been treated with colchicine (1.2 mg/day for 4 years and thereafter dose reduction to 0.6 mg every other day for 4 months because of impaired renal function), corticosteroid, and mesalazine, and exhibited repeated fluctuation of symptoms. Upon presentation, the patient complained of acute onset of fever and chills and was admitted to the hospital via the emergency room.

On admission, his blood pressure was 150/90 mmHg, pulse rate was 138 rate/min, and body temperature was 38.4°C. He had an acute ill looking appearance, with anemic conjunctiva. Physical examination revealed multiple oral ulcers. His heart and lungs were normal and neither hepatosplenomegaly nor

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lymphadenopathy was noted. The peripheral blood count was as follows: hemoglobin level 11.2 g/dL, hematocrit 33.7%, platelets 7,000/mL, white blood cell count 3,100/mm³ (neutrophils 0.7%, lymphocytes 98.2%, monocytes 0.9%, basophils 0.2%, absolute neutrophil count 21), and erythrocyte sedimentation rate (ESR) 60 mm/hr. He already had anemia before admission due to multiple causes such as hematochezia for Behcet's colitis, chronic kidney disease. Before admission, leukocytosis was seen rather than neutropenia and platelet count was normal until 5 months previously, but thrombocytopenia had worsened progressively over the prior 2 months. Biochemical test was revealed that elevated level of blood urea nitrogen 34.1 mg/dL

and serum creatinine 2.08 mg/dL. Estimated glomerular filtration rate (GFR) calculated by Modification of Diet in Renal Disease (MDRD) equation was 34.56 mL/min/1.73 m² and the patient had already chronic kidney disease of stage 3 before admission. Other routine laboratory tests were unremarkable, except for an increased level of lactic dehydrogenase (LDH) 741 U/L (normal range 263~450) and C-reactive protein (CRP) 175.16 mg/L (normal range 0~5).

Peripheral blood smear revealed normocytic normochromic anemia, with 60% abnormal cells (Figure 2). Bone marrow biopsy was performed on posterior iliac crest to determine the cause of pancytopenia. On bone marrow aspiration, the most commonly observed cells were leukemic blasts with variable size, fine reticular chromatin pattern, irregular nuclei, and in-

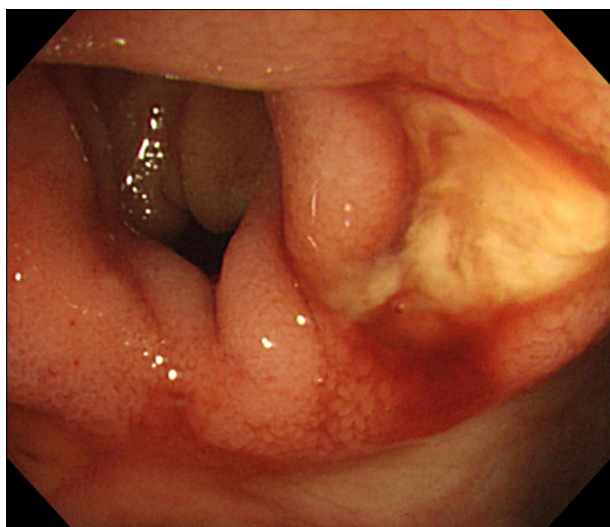


Figure 1. Endoscopic findings show a deep ulcer beneath the ileal opening.

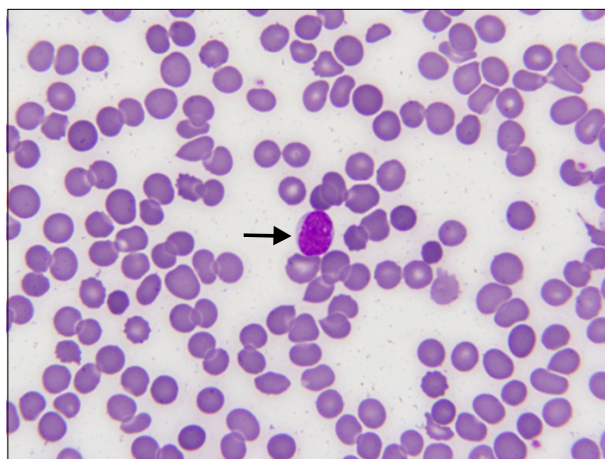


Figure 2. Peripheral blood smear shows abnormal cell (arrow) (H&E stain, $\times 1,000$).

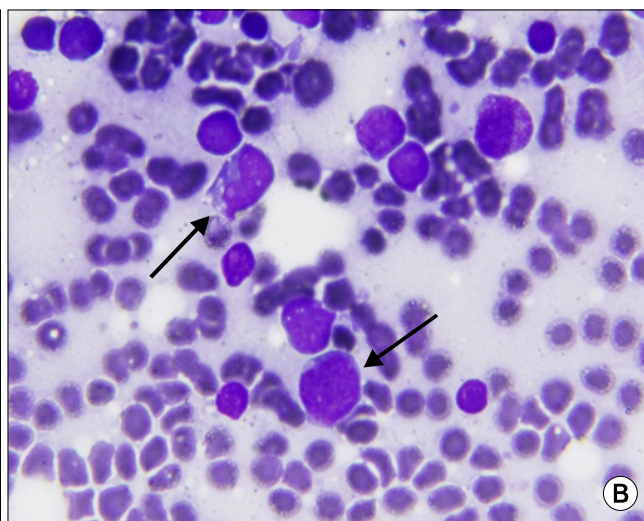
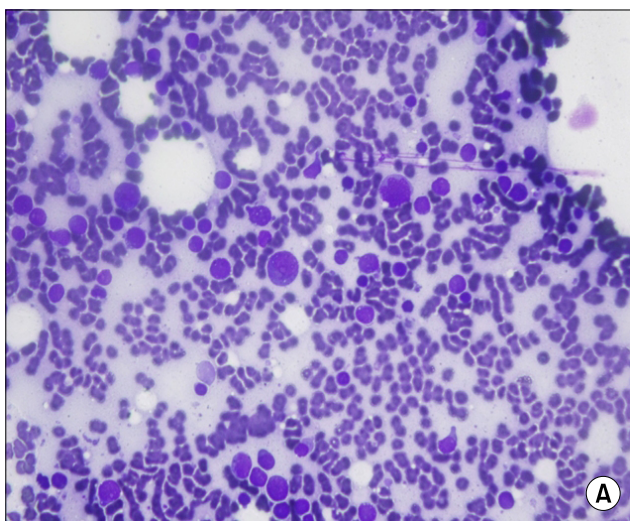


Figure 3. Bone marrow aspiration shows leukemic blasts with variable size (A, H&E stain, $\times 400$). Leukemic blasts show irregular nuclei, and indistinct nucleoli (arrows) (B, H&E stain, $\times 1,000$).

distinct nucleoli, accounting for up to 72.8% of marrow absolute neutrophil counts (Figure 3). Erythroid and granulocytic precursors were markedly decreased in number. The estimated myeloid to erythroid (M:E) ratio was 26.6:1. Megakaryocytes were occasionally observed without dysplasia. The immunophenotype of the neoplastic cells was positive for characteristics of T lymphoid precursors with ectopic expression of CD33, CD117, and cCD79a, which was suggestive of precursor T cell lymphoblastic leukemia. A chromosome study revealed the karyotype 46,XY,der(12)t(1;12)(q21;p13),15ps+[12]/46,XY,add(3)(p25),del(6)(q13)x2,15ps+,der(?17)t(13;17)(q14;q23),add(18)(p11.3),add(21)(q22)[5]/46,XY,15ps+[7].

The patient was diagnosed with acute precursor T cell lymphoblastic leukemia and therapeutic chemotherapy was planned, but unfortunately he died from infection during treatment for pneumonia prior to chemotherapy. The cause of his death was sepsis due to hospital acquired pneumonia.

Discussion

Behcet's disease is an inflammatory disorder that is clinically characterized by recurrent oral ulcers, genital ulcers, and uveitis and pathologically exhibits chronic vasculitis and acute neutrophilic inflammation. In addition, any of several systemic manifestations may also be present, including skin lesions, arthritis, neurologic disease, and gastrointestinal disease (7).

It is rare that Behcet's disease is observed in association with hematologic disorders. But there are some reports in the literature of patients with Behcet's disease associated with hematologic malignancy of myeloid lineage like myelodysplastic syndrome, acute myeloid leukemia, chronic myeloid leukemia (5,6,8). To our knowledge, acute precursor T cell lymphoblastic leukemia has never been described in association with Behcet's disease.

In some literatures about report of Behcet's disease associated with hematologic malignancy, it is assumed that the development of hematologic malignancy in Behcet's disease is related to dysregulation of the immune system and use of immunosuppressive drugs (5,6). Possible mechanisms are impaired immune activity against viruses or immunosurveillance of neoplastic cells, DNA damage and disruption of DNA repair mechanisms, and the upregulation of cytokines that can promote tumor progression (including transforming growth factor β 1, interleukin-10, vascular endothelial growth factor) (9). But there are no proven mechanisms that related to development of hematologic malignancy in Behcet's disease and there are no common reported mechanisms between Behcet's disease and acute lymphoblastic leukemia with regard to the development.

There is a literature about autoimmune diseases associated with leukemia in Sweden of 402,462 autoimmune disease patients. Among them, 1,128 leukemia patients were diagnosed and there was no case with Behcet's disease associated with acute lymphoblastic leukemia. Some autoimmune diseases such as rheumatoid arthritis, type 1 DM, systemic sclerosis were associated with increased standardized incidence ratio (SIR) and hazard ratio (HR) in acute lymphoblastic leukemia, significantly (8). It might be related to dysregulation of the immune mechanism in autoimmune disease with regard to the development of acute lymphoblastic leukemia.

Acute lymphoblastic leukemia (ALL) is a malignant disorder that originates in a single B- or T-lymphocyte progenitor. Proliferation and accumulation of blast cells in the marrow result in the suppression of normal hematopoiesis and subsequent development of anemia, thrombocytopenia, and neutropenia. Initiation and progression of ALL are driven by successive mutations that alter cellular functions, including an enhanced ability for self-renewal, subversion of the control of normal proliferation, a block in differentiation, and increased resistance to death signals. Acquired genetic abnormalities are a hallmark of ALL (10). An abnormal karyotype is found in approximately 50% of acute T cell lymphoblastic leukemia cases. Cryptic deletions leading to the loss of tumor suppressor genes occur, the most common of which are deletions at chromosome 6q and 9p21 (11). In case of this patient, there was a chromosomal deletion of 6q.

Acute lymphoblastic leukemia in adults is a relatively rare neoplasm and the age-adjusted incidence rate of ALL was 1.6 per 100,000 men and women per year in the United States (10). In adults, ALL represents about 15% of leukemias and acute T cell lymphoblastic leukemia compromise approximately 25% of cases of adult ALL. There was no reported case of Behcet's disease associated with ALL to our knowledge, and it might be related to lower incidence rate of ALL rather than myelodysplastic syndrome, acute myeloid leukemia, and chronic myeloid leukemia.

There is a case in the literature of acute promyelocytic leukemia in a patient with Behcet's disease who had received long-term treatment with colchicine. The authors suggest that long-term colchicine therapy may play a role in the pathogenesis of acute promyelocytic leukemia. Colchicine has been reported to be a spindle poison that induces aneuploidy and polyploidy in various cells and organisms (12). In addition, it can modulate T-cell function and acts as an anticytokine agent. However, for the present case it is unlikely that colchicine is related to development of ALL because of usual dosage for mucosal involvement for less than 5 years (longer than

10 years in that reported case).

Considering that the pathophysiology of Behcet's disease is chronic recurrent inflammation, it might be that recurrent inflammation and an impaired immune system influence the development of acute precursor T cell lymphoblastic leukemia. Considering the low incidence of acute precursor T cell lymphoblastic leukemia and given the rarity of association of Behcet's disease and acute precursor T cell lymphoblastic leukemia, it is possible that acute precursor T cell lymphoblastic leukemia developed independently in this patient with Behcet's disease.

To our knowledge, it is first case report of acute precursor T cell lymphoblastic leukemia with Behcet's disease. Therefore, there is a limitation to assume that there is an association with Behcet's disease and acute precursor T cell lymphoblastic leukemia.

This association is needed to be investigated in more studies and a greater number of cases.

Summary

A few cases of hematologic disease in patients with Behcet's disease have been reported in the literature. However, to our knowledge, the case presented here is the first report of acute precursor T cell lymphoblastic leukemia in association with Behcet's disease.

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