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APLAR GROUND ROUND CASE

Hairy cell leukemia presenting initially with symptoms of Behçet's disease

Mustafa Ferhat OKSUZ,[1] Belkis Nihan COSKUN,[1] Ayse Nur TUFAN,[1] Nurdan ORUCOGLU,[1] Ediz DALKILIC,[1] Hülya ÖZTÜRK NAZLIOĞLU[2] and Yavuz PEHLIVAN[1]

[1] *Departments of Rheumatology, and* [2] *Pathology, Faculty of Medicine, University of Uludag, Bursa, Turkey*

Abstract

Vasculitis is relatively uncommon in lymphoproliferative disease and may predate the diagnosis of lymphoproliferative disease. Many vasculitides have been associated with hairy cell leukemia (HCL), including polyarteritis nodosa (PAN) and leukocytoclastic vasculitis. We herein report a case whose initial presentation was like Behçet's disease (BD) (arthritis, oral and genital ulcerations, papulopustular skin lesions) in addition to pancytopenia, but turned out to have HCL. Because of the overlap between their symptoms, like oral ulcerations, skin lesions, arthritis and constitutional findings, HCL and BD may mimic each other. We should keep in mind other reasons for vasculitis such as lymphoproliferative disease, especially whose who have hematological abnormalities such as pancytopenia.

Key words: Behçet's disease, diagnosis, hairy cell leukemia.

INTRODUCTION

Hairy cell leukemia (HCL) is a rare B-cell lymphoproliferative disease, accounting for about 2–3% of all leukemias in adults. Many patients present with splenomegaly and pancytopenia. Other clinical manifestations include vasculitis and skin lesions. The skin lesions have been described in about 10–12% of patients.[1] Vasculitis is relatively uncommon in lymphoproliferative disease and may predate the diagnosis of lymphoproliferative disease. Many vasculitides and autoimmune diseases[2] have been associated with HCL, including polyarteritis nodosa (PAN), leukocytoclastic vasculitis, scleroderma, polymyositis and pyoderma gangrenosum. To our knowledge, there is only one previous report of Behçet's disease (BD) in the setting of HCL.[3]

We describe a patient whose initial presentation was like BD (artrhritis, oral and genital ulcerations, papulopustular skin lesions) in addition to pancytopenia, but turned out to have HCL.

Correspondence: Dr Yavuz Pehlivan, Department of Rheumatology, Uludag University, School of Medicine, Bursa TR16059, Turkey.
Email: drpehlivan@hotmail.com

CASE REPORT

A 46-year-old man with no clinically significant medical history was admitted to the rheumatology department because of a 4-week history of fatigue, weakness, subfebrile fever, painful swelling of joints, petechial and macular skin lesions in lower extremities and a 2-month history of recurrent aphthous oral ulcers.

Physical examination on admission revealed petechial and macular skin lesions in both lower extremities and oligoarthritis (both ankles and knees). There were no oral or genital ulcerations. Body temperature was about 37°C. No enlargement of the liver, spleen or peripheral lymph nodes was observed. The rest of the physical examination was normal. Laboratory tests showed leukopenia (white blood cells 3100/μL, 30% neutrophils and 21.5% monocytes), anemia (hemoglobin 11.1 g/dL), and thrombocytopenia (platelets 53 000/μL). Liver and kidney functions tests and electrolytes were normal. Erythrocyte sedimentation rate was 76 mm/h

and serum C-reactive protein was 5.51 mg/dL (normal < 0.5). Hepatitis A, B and C panels and HIV testing were negative. Rheumatoid factor, repeated blood cultures and procalcitonin were negative. Examinations of antinuclear antibodies (ANA), anti-neutrophil cytoplasmic antibodies and anti-cardiolipin antibodies were also negative. Pathergy test was negative and human leukocyte antigen (HLA)-B51 was positive. Routine chest X-ray was normal. Abdominal ultrasonography disclosed a normal liver and a slightly enlarged spleen (137 × 60 mm). Computed tomography (CT) scan of the chest and abdomen demonstrated enlarged para-aortic, aortacaval and subcarinal lymph nodes.

Bone marrow aspiration and biopsy was done in order to look for a possible hematological disease and also skin biopsy was performed. Afterwards, conservative therapy with diclofenac 75 mg twice daily and prednisone 10 mg/day was started but his symptoms did not alleviate. One week later, the patient complained of painful oral ulcers, papulopustular skin lesions on his back, and aphthous ulcers on the scrotum (Figs 1 and 2). In the skin biopsy, there was perivascular inflammation including neutrophils and lymphocytes and edema of the dermis which was consistent with active vasculitis. These findings indicated a BD flare and the patient was diagnosed with BD as he fulfilled the International Study Group of Behçet's Disease criteria (oral and genital ulcerations and skin lesions). A few days later, bone marrow biopsy revealed a patchy infiltrate of lymphocytes which had uniform small oval or round nuclei and abundant clear cytoplasms and a modarate degree of fibrosis. On immunohistochemical staining, CD20+, CD123+, tartrate-resistant acid phosphatase (TRAP)+CD79a+, CD23+, CD10+, CD5−, CD138−, CD43−, CD21−, kappa and lambda-were detected (Figs 3–5). Flow cytometric examination of the bone marrow cells revealed a monoclonal B lymphocyte population expressing CD19, CD20, CD 103, HLA-DR and CD11c surface antigens. Peripheral blood lymphocytes displayed TRAP positivity too. These findings were consistent with HCL as well.

The patient was transferred to the Hematology Department and started on cladribine and 30 mg/day prednisone. All of the patient's symptoms responded dramatically to this treatment and he was discharged for outpatient follow-up.

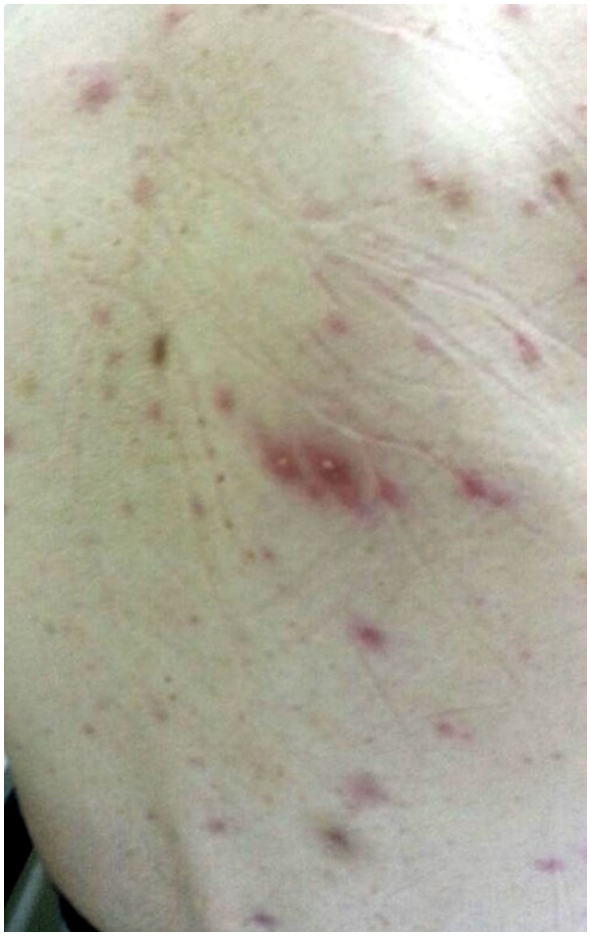

Figure 1 Papulopustular skin lesions on the patient's back.

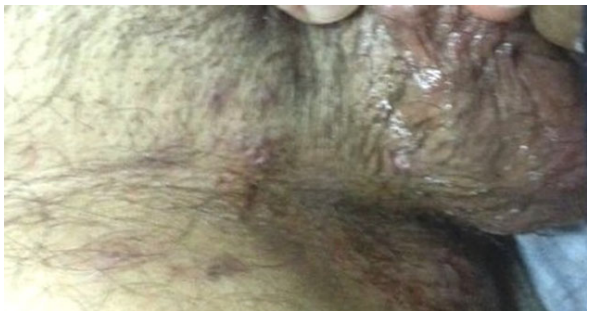

Figure 2 Aphthous ulcers on the scrotum.

DISCUSSION

In this case report, we have described a unique clinical manifestation of HCL presenting with artrhritis, orogenital ulcerations and papulopustular skin lesions along with HLA-B51 positivity mimicking BD. In our knowledge this is the first report of a patient whose initial presentation with BD led to the diagnosis of HCL.

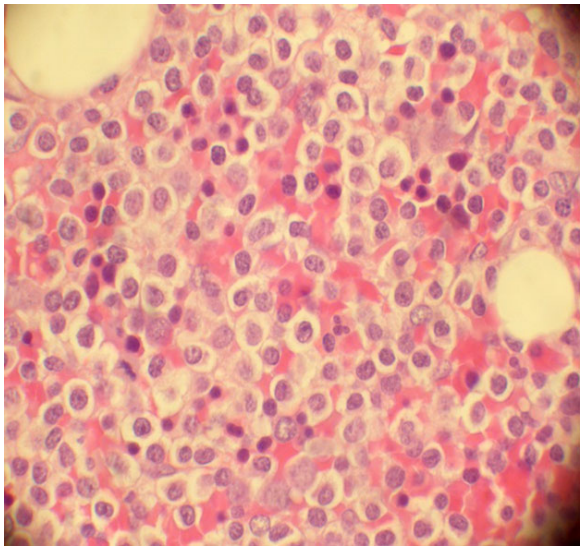

Figure 3 Interstitial infiltration of neoplastic lymphoid cells with characteristic clear cytoplasm and prominent erithrocyte extravasation (hematoxylin and eosin, ×1000).

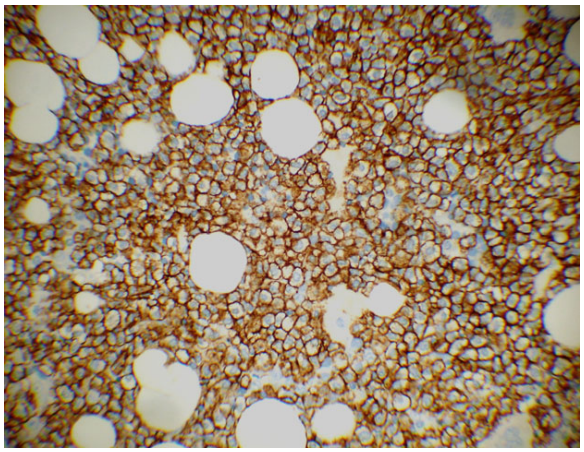

Figure 4 CD20 expression on neoplastic lymphoid cells (CD20, ×400).

The association between HCL and vasculitis was first described by Hughes *et al.*[4] in 1979 and was supported by subsequent reports.[5–7] The vasculitis can precede, occur concurrently with, or follow the diagnosis of HCL.[8] The mechanism of the association between vasculitis and HCL has been assumed in some studies, but there is no evidence including a specific etiology. The pathogenesis of the vasculitis is not known, but possible mechanisms include immune complex injury,

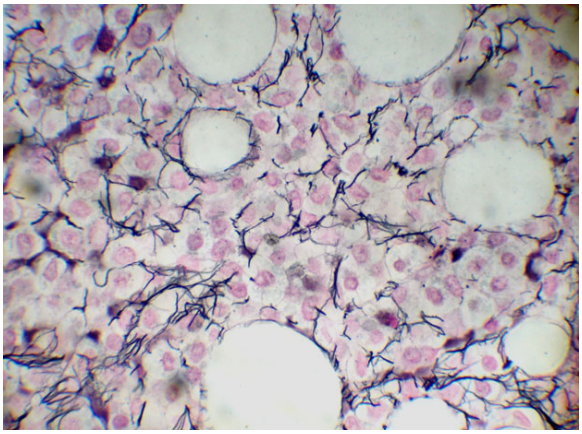

Figure 5 İncreased bone marrow stromal reticulin network (reticulin, ×1000).

autoantibodies to hairy cells cross-reacting with endothelial cells, or direct effect of hairy cells on the vessel wall.[7] Production of cytokines with the inclusion of tumor necrosis factor-α, transforming growth factor-β and various local paracrine growth factors by leukemic cells may contribute to the latter. The presence of malignancies in patients with vasculitis has been estimated to be about 4.5–8.0%, hematological neoplasms being the most frequently observed.[1] There is a well-recognized relation between HCL and PAN.[9] HCL can manifest as paraneoplastic vasculitis, either a leukocytoclastic vasculitis or PAN. Both HCL and PAN are rare diseases and their concurrent association exceeds what would be expected by chance alone.[10] Furthermore, there is direct evidence linking the two conditions with histopathology showing direct invasion of the vessel wall by leukemic cells.[10] In a literature review of 42 cases of vasculitis associated with HCL, 21 cases were consistent with PAN (with four cases demonstrating vessel wall infiltration by the leukemic cells). To our knowledge there is only one previous report of BD in the setting of HCL.[3] In this patient the clinical picture of BD developed in the setting of HCL. However, our patient's initial presentation was like BD. BD is characterized by recurrent oral ulcers, genital ulcers, uveitis and skin lesions. Pancytopenia is an extremely rare presentation of BD. Some studies[11,12] have identified a relationship between myelodysplastic syndrome and BD, especially intestinal BD.

This patient emphasizes considering HCL in the differential diagnosis in patients with vasculitis, especially BD, when atypical findings like cytopenias exist. HCL may remain obscure and undiagnosed for long periods

because of its slow nature and patients with HCL may develop different clinical pictures of vasculitis. Because of the overlap between their symptoms like oral ulcerations, skin lesions, arthritis and constitutional findings, HCL and BD may mimic each other. This means that rheumatologists should be familiar with this entity.

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