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Behcet's Disease Associated with Myelodysplastic Syndrome : A Case Report

A rare case of Behcet's disease associated with myelodysplastic syndrome (MDS) is described. A 50-year-old Korean female suffering recurrent oral ulcer, genital ulcer, fatigue, arthralgia in both knees and fever was diagnosed as Behcet's disease. The findings of bone marrow aspirates were consistent with refractory anemia, a subtype of myelodysplastic syndrome. Chromosomal analysis of bone marrow cells revealed 46,XX,-8,-20,+der(8)t(8;20)(p23;p10),+der(8)t(8;20)(p23;q10)[30]. The chromosomal changes found in this patient were different from those of previous reports, which mostly revealed trisomy 8. If anemia, low reticulocyte count and dyspoietic cells are sustained in Behcet's disease, physicians should be alert to the possibility of MDS with aberration in chromosome 8 and perform a bone marrow study for the proper diagnosis and treatment of the disease. We presented a case of Behcet's disease associated with MDS, which is the first Korean case.

Key Words: *Myelodysplastic syndromes; Behcet's syndrome; Translocation (genetics); Chromosomes, human, pair 8*

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INTRODUCTION

Behcet's disease is a multisystem disorder presenting with recurrent oral and genital ulcerations as well as ocular lesions (1). Behcet's disease is rarely observed in association with leukemia and other hematologic disorders. About ten cases of Behcet's disease associated with myelodysplastic syndrome (MDS) have been reported, mostly in the Japanese patients (2). We present a case of Behcet's disease associated with MDS, which is the first Korean case.

CASE REPORT

A 50-year-old Korean female was admitted to evaluate recurrent oral and genital ulcer for ten years in May 1997. She complained of fatigue, arthralgia in both knees and fever. She had a history of dyspnea on exertion and chest discomfort. No hepatosplenomegaly or lymphadenopathy was found. Colonoscopic examination showed multiple ulcerations in terminal ileum and a biopsy specimen from ulcer lesion revealed nonspecific mucosal ulceration with vasculitis. No typical defined skin lesions were evident but a pathergy test was positive. The other laboratory test results were as follows: C-reactive protein 59.5 mg/L, erythrocyte sedimentation rate 51 mm/hr, rhematoid factor 10.11 IU/mL, C3 90.9 mg/dL, C4 31.9 mg/dL. The anti-nuclear antibody and anti-platelet antibody were negative. The patient was diagnosed as Behcet's disease according to the Criteria of International Study Group for Behcet's disease (1). Peripheral blood cell count was as follows: hemoglobin 6.3 g/dL, leukocytes 5.3×10^9/L (differential count: neutrophils 83%, lymphocytes 11%, monocytes 5%, eosinophils 1%), platelets 264×10^9/L. The level of corrected reticulocytes was 0.2%. The peripheral blood smear showed moderate anisocytosis and poikilocytosis without atypical cells including blast or leukemic cells. The anti-globulin test was negative. The results of iron studies were as follows: serum iron 20 μg/dL, serum total iron binding capacity 194 μg/dL, serum ferritin 66.1 ng/mL. She was treated for a period of one year with intermittent steroid therapy, but severe anemia continued and leukopenia (1.9×10^9/L) with thrombocytopenia (30×10^9/L) was developed. In September 1998, a bone marrow aspiration was performed. It revealed about 90% cellularity with 2% blasts, 27% erythroblasts, 3% promyelocytes, 12% myelocytes, 8% metamyelocytes, 10% band form neutrophils, 21% segmented neutrophils, 2% monocytes, 1% eosinophils and 14% lymphocytes. The iron staining preparation revealed increased amount of iron pigments in the par-

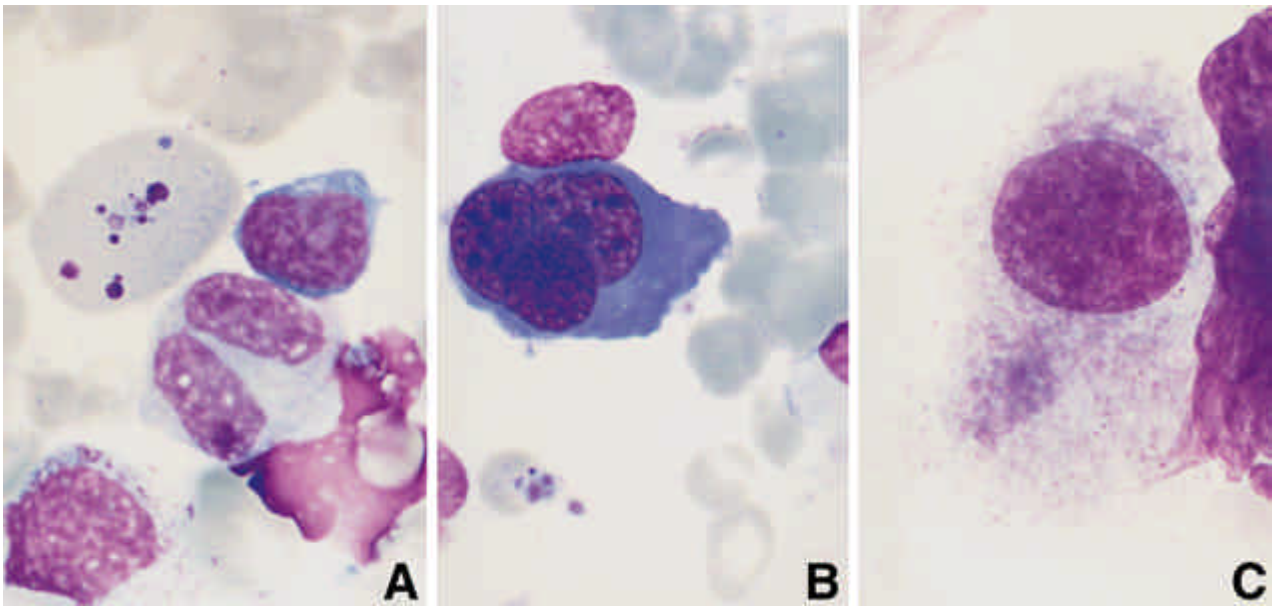

Fig. 1. Bone marrow aspiration (Wright stain, ×1,000) showing trilineage dysplasia. **A:** Pseudo-Pelger polymorph, **B:** multinucleate erythroblast, **C:** atypical mononuclear megakaryocyte.

ticles but revealed no ringed sideroblasts. Numerous dysplastic features were found in the three lineages (Fig. 1). Refractory anemia, a subtype of myelodysplastic syndrome was diagnosed according to the FAB (French-American-British) classification (3). Chromosomal analysis of bone marrow cells revealed 46,XX,-8,-20,+der(8)t(8;20)(p23;p10),+der(8)t(8;20)(p23;q10)[30]. Her human leukocyte antigen (HLA) type was A11, 24; B27, 54; Cw1. She was treated with anti-inflammatory agents and corticosteroids (prednisolone). After three months, the second bone marrow aspirate was performed. It revealed similar findings to those found in the previous bone marrow. Until February 1999, cytopenia and her symptoms had been sustained.

DISCUSSION

Behcet's disease has rarely been reported in association with therapy-unrelated MDS. Previously, ten patients in Japan and one in Spain with Behcet's disease and MDS have been reported (4-11). In this presentation, one case of Behcet's disease with MDS in a 50-year-old Korean female was reported which is the first case in Korea. Hematological and bone marrow findings in our patient were consistent with the diagnosis of refractory anemia, a subgroup of MDS, and she was also diagnosed as Behcet's disease, based on the clinical findings of oral and genital ulcer and eye lesion. In cytogenetic study, chromosomal analysis of bone marrow cells revealed 46,XX,-8,-20,+der(8)t(8;20)(p23;p10),+der(8)t(8;20)(p23;q10)[30]. The chromosomal changes were different from those of previous reports, which mostly revealed trisomy 8. The reported incidence of trisomy 8 was shown to be only 10-20% among untreated MDS patients with chromosomal anomalies (12-15) and 10-30% in de novo acute myeloid leukemia with chromosomal aberrations (16-19). Ohno et al. (2) suggested that trisomy 8 might predispose to Behcet's disease in a subgroup of MDS because the percentage of trisomy 8 in patients with MDS and Behcet's disease was higher than in those patients with MDS alone. They suggested that increased reactive oxygen species production by activated neutrophils due to one or more serum factors would play an important role in the association MDS with Behcet's disease and these serum factors might be increased in a subgroup of MDS patients with trisomy 8 (2). On the other hand, Yano et al. (20) described that immunological defect and/or the hypersensitivity to infection observed in MDS patients with chromosomal abnormality, especially trisomy 8, might be involved in the etiology of Behcet's disease. In the present case, MDS was diagnosed about one year after the diagnosis of Behcet's disease, and the disease was assumed to have developed concurrently with MDS based on the findings of continuous presence of pancytopenia and reticulocytopenia from the first visit. Therefore, we suppose that aberration in chromosome 8 including translocation or deletion instead of trisomy may also predispose to Behcet's disease in MDS patients.

Cytopenia in Behcets disease may be considered to be arising from a variety of causes, including autoimmune

phenomena, hypersplenism, and therapy with chemotherapeutic and other agents (21). In addition, normal or only slightly reduced neutrophil count, possibly due to neutrophil hyperfunction in spite of sustained anemia, may contribute to delay in bone marrow study. In this case, the cause of anemia was considered to be combined effects of autoimmunity and ulcer bleeding. Behcet's disease occurs with a high prevalence in the Far East, including Korea and Japan (20, 22). Therefore, if anemia, low reticulocyte count and dyspoietic cells are sustained in Behcet's disease, physicians should be alert to the possibility of MDS with aberration in chromosome 8 and perform a bone marrow study for the proper diagnosis and treatment of the disease.

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