

Atypical Behçet's Syndrome in a Patient with Myelodysplastic Syndrome

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Abstract

We report the case of a 67-year-old man with myelodysplastic syndrome (MDS), who presented with fever, painless penile and groin ulcers, as well as oral and esophageal ulcerations, all of which were exquisitely responsive to corticosteroids. Some cases of Behçet's syndrome and MDS have been reported in association with trisomy 8 and HLA B51, with the pathology varying from vasculitis to acute neutrophilic inflammation. Our patient with orogenital ulcers had neither trisomy 8 nor HLA B51. Also lacking were other features typical of Behçet's syndrome, such as uveitis, vasculitis, and central nervous system abnormalities. However, his response to corticosteroids on the initial presentation and subsequent episodes was dramatic. Esophageal ulcerations have not been described in Behçet's syndrome. In this respect, our patient was unique.

Key Words: Behçet's syndrome, myelodysplastic syndrome.

Introduction

NAMED AFTER THE TURKISH DERMATOLOGIST who first described it, Behçet's syndrome is characterized by recurrent orogenital ulcers, central nervous system abnormalities (CNS), arthritis, vasculitis and uveitis. The etiology of Behçet's syndrome is unknown. The course is prolonged and punctuated with remissions and exacerbations. The prevalence varies from 1:10,000 in Japan to 1:500,000 in North America and Europe. It is more common among young adults, more severe forms occurring in males than in females. Since the main pathologic lesion is vasculitis, and circulating autoantibodies to oral mucous membrane have been found in 50% of cases, it is suggested that Behçet's syndrome is an autoimmune disease (1). The ulcers may be shallow or deep, may occur singly or in crops, and are usually painful but heal without scars in approximately two weeks. The genital ulcers

resemble the oral ones. Clinical diagnostic criteria include recurrent oral ulceration plus two of the following: recurrent genital ulcers, eye lesions, skin lesions and pathergy test. Hypopyon uveitis is the hallmark of eye involvement in Behçet's syndrome, but occurs uncommonly. The arthritis of Behçet's syndrome is nondeforming and usually affects the knees and ankles. CNS involvement occurs more frequently in northern Europe and the United States (2).

Case Report

A 67-year-old black man presented with complaints of painless penile ulcers and bilateral groin ulcers of four days' duration. He had had myelomonocytic leukemia for six years, and suffered from hypertension, insulin-requiring diabetes mellitus (IRDM), and peptic ulcer disease. The patient noted the penile and groin ulcers incidentally while bathing. He denied pain, itching, oozing, or bleeding from the ulcers and had no cardiovascular, respiratory, urinary, or gastrointestinal complaints. He also denied fever, chills, anorexia, and loss of weight but claimed that little bumps appeared all over his body from time to time and disappeared on their own, sometimes breaking into small ulcers. The patient had been hospitalized for oral ulcers in 1992 and treated for arthritis

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of the acromioclavicular joints in 1993. He had a tubulocolonic adenoma removed in 1994 and had a left foot ulcer in 1996. He was taking captopril, isophane insulin suspension, sucralfate, and regular insulin and had received erythropoietin and granulocyte colony-stimulating factor (G-CSF) a year earlier for his myelodysplastic syndrome (MDS). He denied allergies, smoking, alcohol use, drug abuse, and sexually transmitted diseases. The family history was noncontributory.

The patient was a well-built man with mild pallor. His blood pressure was 110/85 mmHg, heart rate 84 beats per minute, temperature 98.8°F, and respiratory rate 16 per minute. Pupils were equal and reactive to light. Cardiovascular, pulmonary, neurological, abdominal, and rectal exams were unremarkable. There was no lymphadenopathy. A 5 cm x 4 cm ulcer was seen on the ventral surface of the penis near the root and a 1 cm diameter ulcer was present on the dorsum of the penis. Two 2 cm x 2 cm ulcers were present on the upper medial aspect of both thighs. The ulcers were well demarcated, without undermining, with indurated margins, mild oozing, and no slough. The patient's blood leucocyte count was 3600/mm³ (38% neutrophils, 28% lymphocytes and 34% monocytes), hemoglobin 8.3 g/dL, hematocrit 24.5%, mean corpuscular volume 102.8 fL and platelets 118,000/mm³. Routine blood chemistries, chest X-ray, and electrocardiogram were within normal limits.

The patient was treated with ceftriaxone, ticlopidine, and acyclovir. On day 5 he became febrile, and on day 8 he developed oral ulcers. Direct laryngoscopy showed vesicles on the epiglottis, larynx, and posterior uvula. The differential diagnoses included Sweet's syndrome, pyoderma gangrenosum, and Fournier's gangrene. He remained febrile (103°–106°F) while receiving antibiotics. Blood cultures, Venereal Disease Research Laboratory (VDRL) test for syphilis, orogenital, bacterial, fungal, and viral cultures were negative. Gallium scan and chest X-ray were normal. Oral and penile ulcers were biopsied and showed chronic, active inflammation with no vasculitis. Bone marrow biopsy showed chronic myelomonocytic leukemia with no evidence of transformation. Erythropoietin was given and antibiotics and acyclovir were discontinued due to lack of improvement in the ulcers and fever. The patient developed extreme odynophagia and drooled saliva copiously. His hematocrit decreased to 17%. Since the patient refused blood

transfusion, the dose of erythropoietin was increased from 5000 units subcutaneously to 10,000 units three times weekly for 20 days. In addition, peripheral parenteral nutrition was commenced because the patient could not eat. On the 18th day of hospitalization, oral steroids were given. Within 48 hours, the patient became afebrile, and the orogenital ulcers showed signs of improvement. However, inability to swallow persisted. Upper gastrointestinal endoscopy showed extensive severe ulceration from 20–35 cm. Esophageal biopsy was read as unremarkable squamous epithelium. Within a week of steroid therapy, the ulcers and the odynophagia were markedly improved. The patient began eating, and steroids were tapered gradually. On the 50th day of hospitalization, the patient was discharged afebrile and able to eat normally. The oral and genital ulcers had healed.

Discussion

In rare cases, Behçet's syndrome has been reported in association with myelodysplastic syndrome (3), hepatitis C (4), acute necrotizing myositis (5), Sweet's syndrome (6), and anti-cardiolipin antibody syndrome (7). Primary findings include recurrent orogenital ulcers, uveitis, seronegative arthritis, CNS abnormalities, vasculitis, erythema nodosum, superficial and deep thrombophlebitis, ulcerative skin lesions and a positive pathergy test. Arthritis occurs in two-thirds of patients, and ocular involvement is usually fulminant, resulting in blindness. CNS involvement encompasses cranial nerve palsies, convulsions, encephalitis, mental disturbances, spinal cord lesions and even death. Ten to thirty-seven percent of patients have occlusion of major blood vessels and aneurysms. Seven to thirty-seven percent have thrombosis of superior and inferior vena cava (8). Pulmonary vascular involvement causes severe hemoptysis and is the cause of death in 39% of patients. Rare cases of endomyocardial fibrosis in Behçet's disease (9) and a case of abdominal aortic aneurysm with lumbar vertebral erosion have been described. Concomitant MDS with Behçet's syndrome has been described with trisomy 8 (3) and HLA B51 (10). The pathology in Behçet's syndrome is characterized by vasculitis and/or acute neutrophilic inflammation.

Although it is usually chronic, with remissions and exacerbations, Behçet's syndrome is characterized by rapid response to steroids.

Also beneficial are azathioprine, chlorambucil, and cyclosporine. While clinically meeting criteria for Behçet's syndrome, the pathology in our patient was not characteristic. The occurrence of Behçet's syndrome with MDS is unexplained. In Behçet's syndrome, there is increased production of reactive oxygen species (ROS) by neutrophils, whereas MDS is characterized by decreased production of ROS by neutrophils. In a study of ten patients with MDS and Behçet's syndrome (11), the production of ROS by neutrophils was investigated by luminol-enhanced chemiluminescence assay (CL). Of the ten patients, nine underwent cytogenetic analysis of bone marrow and seven had trisomy 8. Neutrophils taken from the patients during the active phase of Behçet's syndrome demonstrated an increased CL response. The authors concluded that trisomy 8 predisposes to Behçet's syndrome in patients with MDS. Cytogenetic analysis of our patient on two different occasions did not reveal trisomy 8. A strong association has also been shown between Behçet's syndrome and HLA B51 in ethnic groups extending from the Middle East to Japan. HLA typing of our patient was negative for HLA B51. Esophageal ulcers have not been described in Behçet's syndrome. In this respect, our patient is unique.

A trial of corticosteroids was given to our patient after all cultures for bacteria, viruses, and fungi proved negative. The patient had a dramatic response, with resolution of all signs and symptoms. The use of corticosteroids should be considered in patients with a clinical picture of Behçet's syndrome even if the pathology is inconclusive. In a study conducted by the University of Istanbul (12), thalidomide was effective in resistant cases of Behçet's syn-

drome. Although banned globally because of its teratogenic effects, this drug may have important therapeutic uses.

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