Behçet's disease presenting as deep venous thrombosis and priapism

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ABSTRACT

Behçet's disease (BD) is a multi-system inflammatory disorder which may involve the vascular system. Currently, it is general practice to use the International Study Group (ISG) criteria for the diagnosis of BD. However, even though vascular involvement may be seen in one-fourth to one-half of BD patients, and occasionally is the presenting and only manifestation of BD, large vessel disease is not included among the ISG criteria. In this report we describe a patient who had deep venous thrombosis and priapism, but who does not fulfill ISG criteria for the diagnosis of BD.

Introduction

Behçet's disease (BD) is a systemic vasculitis of unknown etiology, characterized by recurrent oral and genital ulcers and uveitis. Cutaneous, articular, neurologic, intestinal, pulmonary, urogenital, or vascular manifestations have also been observed. It can affect vessels of all types and sizes. At present it is general practice to use the International Study Group (ISG) criteria for the diagnosis of BD (1), which does not include large vessel disease. However, such involvement may be seen in 1/4 to 1/2 of BD patients, and may occasionally be the presenting and only manifestation of BD, making the diagnosis difficult (2,3). We describe one such patient who came under our observation. He had systemic vasculopathy, including deep venous thrombosis and priapism that was highly characteristic of that seen in BD, but who did not fulfill ISG criteria for the diagnosis of BD.

Case report

A 48-year-old man was admitted to our hospital with recent onset oral ulcers, fever, oligoarthritis, erythema nodosum-like lesions, pain and swelling of the right lower extremity and the scrotum. His complaints had started 4 days after an upper respiratory tract infection, about 2 weeks previous to this hospitalization. He had pain especially of the right lower extremity that prevented him from walking. He was started on a course of antibiotics and nonsteroidal anti-inflammatory drugs, which had no effect on his symptoms. Physical examination revealed two minor aphtous lesions in the oral cavity. Respiratory, cardiac and abdominal examinations were normal. He had scrotal edema and tenderness, but no genital ulcers. Both ankles, the right elbow and knee were tender and swollen, and their motion was limited. The right lower extremity was tender, hyperemic and edematous. Homan's sign was positive. There were erythema nodosum-like lesions on both lower extremities and papulopustular eruptions on both hands. Ophthalmologic examination performed by an ophthalmologist was normal. A pathergy test was negative.

Laboratory findings revealed a erythrocyte sedimentation rate of 74 mm/hour. The white blood cell count showed leukocytosis (20.300/mm^3 with 94% neutrophils), the hematocrit value was 33.6%, the platelet count was 236.000/mm^3, and C-reactive protein was 169 mg/L. Urinalysis and renal function test results were normal. Antinuclear antibodies and antineutrophil cytoplasmic antibodies were not detected. Rheumatoid factor was negative. C3 and C4 complement levels were normal. HLA-B51 was negative. Testing for the primary causes of hypercoagulopathy, including antiphospholipid antibodies, lupus anticoagulant, protein C and S deficiency, and antithrombin III deficiency, yielded negative results. The serum homocysteine level was normal. A genetic study for thrombophylic pathology revealed factor V Leiden heterozygous mutation.

Upon admission the patient had spiking fevers. Cultures were taken and an empirical course of antibiotics started. No microorganisms were isolated from blood cultures. Doppler ultrasound examination of the lower extremities revealed bilateral thromboses of the external iliac, common iliac, superficial and deep femoral, popliteal and distal crural veins. Ultrasound examination of the scrotum revealed left testicular infarction. Low molecular weight heparin and aspirin 300 mg daily was started.

After one week, physical examination

revealed decreased breath sounds over the right lung. When computed tomography of the thorax showed an area of pulmonary infarction on the right lower lobe, prednisolone 80 mg/day was added to the therapy with a tentative diagnosis of systemic vasculitis, possibly BD. After 24 hours the fever had subsided, arthritis improved, and the performance status of the patient improved.

On the 10th day after admission, the patient developed priapism. Penile Doppler ultrasound examination revealed low flow in both of the cavernosal arteries. Despite the prompt administration of appropriate therapies: topical agents, thrombolytic therapy with tPA, 1000 mg monthly iv pulse cyclophosphamide, and an increase in the daily steroid to 100 mg, penis necrosis developed. Upon formation of a demarcation line along the distal 2/3 of the penile shaft (Fig. 1), resection of the distal 3/4 of the penis was performed. Histopathological analysis of the penectomy material revealed complete hemorrhagic infarct of both the penile body and the corpus cavernosum. A small intact area in the penile shaft included a few middle-sized arteries with thrombotic obliteration. Histopathological examination of the erythema nodosum-like lesions showed lymphocytic vasculitis. The patient received intravenous 1000 mg monthly pulse cyclophosphamide for a total of 6 months. After this treatment 2 mg/kg/day azathioprine was begun. He is currently free of all presenting symptoms after 15 months of this therapy.

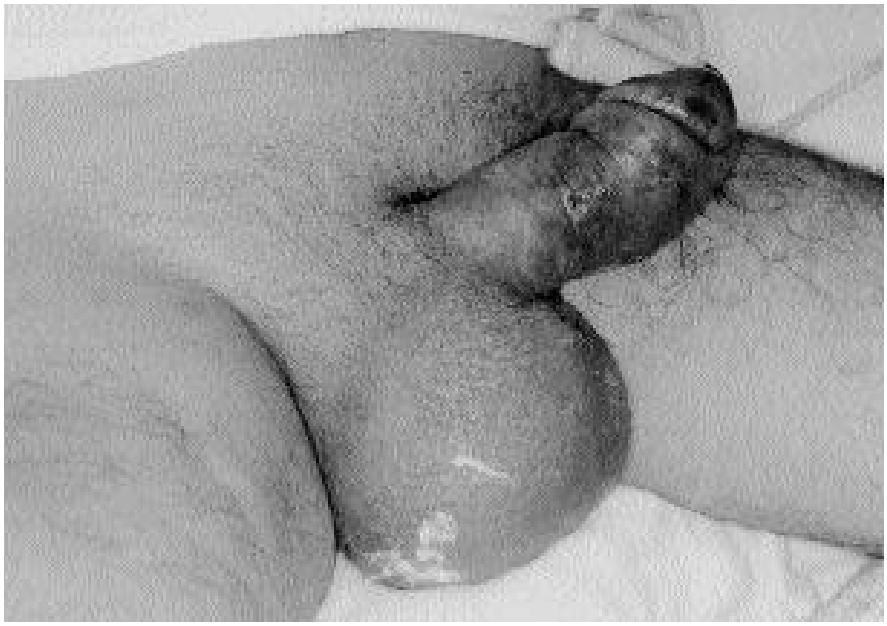

Fig. 1. Anecrosis on the distal 2/3 of the penile shaft.

Discussion

We describe a patient who does not fulfill ISG criteria for the diagnosis of BD, but for whom no other diagnosis can be suggested. He had fever, recent onset oral ulceration, oligoarthritis and erythema nodosum-like skin lesions. He also exhibited extensive venous thromboses, pulmonary and testicular infarction and developed priapism resulting from arteritis confirmed by histopathological examination. With these findings, a form of vasculitis involving both the arteries and veins had to be considered. Among the vasculitides (4), the possibility of classical polyarteritis nodosa was evaluated in the differential diagnosis but excluded because of the presence of bilateral deep vein thromboses. Microscopic polyangiitis affects the small arterioles, venules, and capillaries with resulting nephritis and alveolitis. However, he had a normal urinalysis, and ANCA was found to be negative. Behçet's disease is distinctive among the vasculitides in that it can affect all types and sizes of vessels. Accordingly, we considered BD as the most likely diagnosis in this case.

One of the diagnostic difficulties presented by BD is the variability of the disease manifestations in different patients. Behçet's disease is commonly diagnosed in a patient presenting with recurrent oral ulcerations when two or more of the following co-exist: recurrent genital ulcerations, eye and skin lesions, or a positive pathergy test (1). However, some cases may initially present with only a few findings. Therefore, application of the ISG criteria for a proper diagnosis may be insufficient. Although sensitivity rates as high as 95% have been reported (5), Calamia *et al.* state that the ISG criteria had a diagnostic sensitivity of 75.6% in their patients (6).

Large vessel involvement is observed in 25-50% of patients with BD (2, 3). There is an ongoing debate regarding whether or not to include large vessel involvement as a major criterion. There are case reports of patients who presented with life-threatening large vessel complications but no oral ulcerations and who did not fulfill the ISG criteria for the diagnosis of BD (7-9). Although the sensitivity of vessel involvement is reported to be low, the specificity of subcutaneous thrombophlebitis, deep vein thrombosis, and arterial occlusion and/or aneurysm is found to be higher than eye lesions, pathergy testing and most skin lesions (1). Calamia *et al*. have suggested that large vessel involvement be added as a criterion since in practice many clinicians use these criteria for diagnostic purposes. Although the addition of vascular involvement will not affect the classification of patients, it would be valuable in the diagnosis of the atypical patient with early vessel involvement (10). Silman and Gul reiterate the point that the ISG criteria were devised for classification purposes and were not intended to be used as strict diagnostic criteria (11). They recommend that decisions be made on a patient-to-patient basis, during the clinical practice.

One interesting point regarding our patient is that, to the best of our knowl-

edge, he represents only the second case of BD associated with priapism due to vasculitis. Moalla *et al.* (12) reported the first case, which involved a 38-year-old Tunisian man whose main symptomatology was a 3-year history of oral ulcers, pseudofolliculitis, a positive pathergy test, and arthralgia. The diagnosis in his case was BD with priapism caused by thrombophlebitis of the cavernous body. In contrast to our case, he fulfilled the ISG criteria for BD and did not have deep vein thromboses and vasculitis. In our patient, priapism led to penile necrosis due to arteritis, whereas the previous case involved thrombophlebitis only, with no necrosis.

Priapism can be defined as a state of prolonged engorgement or erection of the penis, not related to sexual desire or stimulation. The clinical presentation may vary with the underlying etiology and can best be thought of as a spectrum of diseases. Among the causes of priapism, idiopathic cases, infections, tumours, perineal or genital injuries, epilepsy, drugs such as psychotropic and antidepressant agents, hydralazine, guanetidine and androgens, cocaine abuse, heavy alcohol intake, hematological dyscrasias, and brain and spinal cord injury are well-known (13). Among the various causative factors are conditions or drugs that obstruct or reduce the venous outflow (low flow) or alternatively produce high arterial inflow (high flow), overcoming the draining ability of the outflow channels. In all cases, the delicate balance between the arterial inflow and venous drainage that normally exists is altered, resulting in prolonged periods of tumescence (14).

The possibility of an underlying vasculitis should be considered in the differential diagnosis of the causes of priapism. Vasculitis is likely to cause priapism of the low flow type (15). This constitutes a true urologic emergency classically marked by acidotic corporal sinusoids, penile venous outflow obstruction, and pain. If untreated, this form of priapism can lead to corporal fibrosis, infection and permanent loss of erectile function. However, although treated promptly and aggressively, we observed an unexpected and hitherto unreported complication – penile necrosis – in our patient. Although Lakhanpal *et al.* reported that priapism due to vasculitis should respond to corticosteroids (15), steroids and immunosuppressive and thrombolytic treatment were not enough in our case. Since medical therapy failed, partial penectomy had to be performed. However, our patient is currently free of all presenting symptoms in the 15th month of this therapy.

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