Behcet disease in sub-Saharan Africa – a case report

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Abstract

Behcet disease (BD) is a chronic vasculitis that damages various organic systems. It is considered more prevalent in the areas surrounding the old silk trading routes, in the Middle East and Central Asia, and is rare in the Black race. Few cases have been reported in sub-Saharan Africa. Cardiac involvement is an unusual clinical manifestation of BD - about 1%, and acute pericarditis is one of the most common. We describe a case of a young Black male, from Guinea-Bissau, who presented mucocutaneous lesions, arthritis and precordialgia. The authors also carried out a literature review on cardiac involvement in BD.

Key words: Behcet disease; sub-Saharan Africa; acute pericarditis.

INTRODUCTION

Behcet's disease (BD) is a chronic, multisystemic, autoimmune vasculitis. The presence of recurrent oral ulcerations (a sine qua non condition for the diagnosis) is an internationally accepted[1] diagnostic criteria, together with two of the following: recurrent genital ulceration, eye lesions, skin lesions, and positive pathergy test (Table I). Other frequent clinical syndromes of this pathology are non-deforming oligoarticular arthritis, superficial or deep venous thrombosis, and a polymorphic variation affecting the central nervous system (Neuro-Behcet) and gastrointestinal tract.

The incidence peak is in the second and third decades of life, and there is no difference between the sexes, although the symptoms are more severe in male patients. The severity of the lesions decreases with age. The prevalence is higher in countries of the Mediterranean, Middle East and Far East. The etiology of BD remains unclear. The disease is characterized by systemic perivasculitis with early infiltration of neutrophils and fibrinoid necrosis. Circulating autoantibodies against endothelial α-enolase and anti-Saccharomyces cerevisiae antibodies (ASCA – which are characteristic of Crohn's disease) have recently been found in the late stage of the disease.[2] The close association with HLA-B51 alloantigen, and the fact that 1 in 10 patients has a relative with the disease, suggest a genetic basis for BD. However, it is thought that there might also be environmental influences.

CLINICAL CASE

Male patient aged 21 years, Black, born in Guinea-Bissau, without any known previous diseases, a non-smoker, and without drinking or drug habits. He had never traveled abroad until immigrating to Portugal, one year previously. The patient has had painful mouth ulcers for four years, which disappeared spontaneously after two to three weeks without any medication or therapeutic measure. These lesions have occurred more frequently in the past two years, and are accompanied by equally painful ulcerated skin lesions of the genitalia; painful, hot nodules in the limbs that ulcerated, leaving a scar; arthralgia and swelling of the joints of the lower limbs. These symptoms would disappear spontaneously. One week before admission, several ulcers reappeared in the mouth, and an ulcer occurred in the scrotum with the characteristics described above, accompanied by two nodules in the left leg and a nodule in the right forearm. Two days before admission, the patient had a sudden, sharp, persistent and continuous chest pain, without spreading, which worsened in the supine position and when inhaling deeply, but was relieved by bending forwards. The pain was accompanied by fever (the patient did not take his temperature), pal-

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TABLE I

Criteria for the diagnosis of Behcet's disease[1]

Recurrent mouth ulcers
+2 of the following:
Recurrent genital ulcers
Uveitis
Cutaneous lesions
Positive Pathergy test

pitations, sensation of tachycardia and arthralgia of the wrists and tibial-tarsal joints. Due to persistence and worsening of the symptoms, the patient visited the Emergency Unit of the Hospital de Santa Maria.

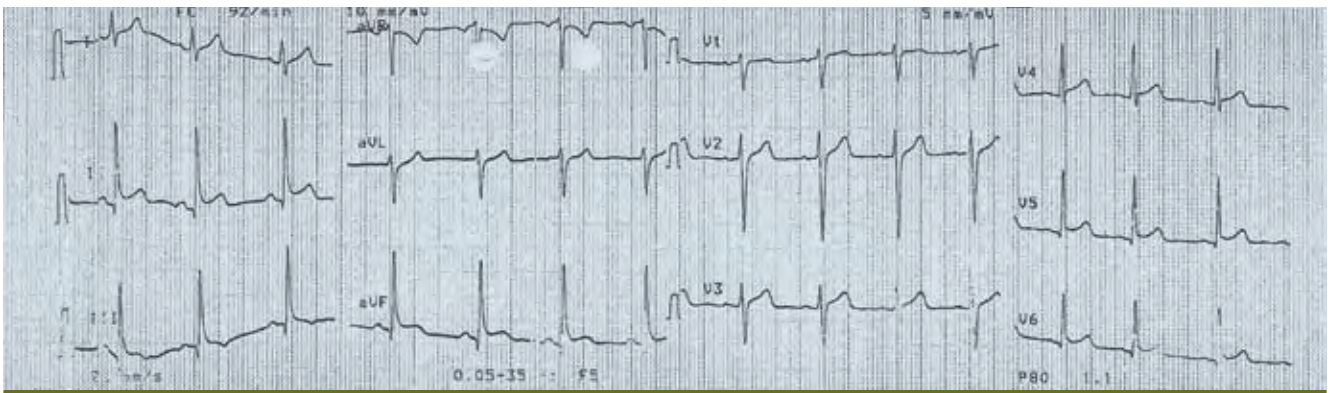
In the Emergency Unit, the patient was afebrile, eupneic while breathing room air, with 98% peripheral saturation and tachycardia (HR = 110 bpm), normotensive. Ulcers of varying sizes, and painful to touch, were observed in the buccal mucosa, inner lower lip and side of the tongue. On pulmonary auscultation, vesicular murmur was sustained and symmetrical, with no adventitious sounds. On cardiac auscultation, S1 + S2 were rhythmic, no murmur or extra-sounds were heard; abdomen was flat, loose and depressible, bowel sounds present, painless on surface and deep palpation; no masses or organomegalies were palpable. Cicatricial skin lesions were observed on the limbs, particularly the lower limbs, and there were two subcutaneous, hard, hot, painful nodules of 2.5cm diameter maximum in the left leg and right forearm with the same characteristics. The patient's wrists and ankles were swollen and hot. There were no signs of venous thrombosis. The patient also had an ulcerated lesion on the scrotum measuring 1 cm, which was painful to the touch. There were no adenomegalies. Chest x-ray in the posteroanterior profile view showed no alterations in the lung fields, clear costophrenic sinuses, and a cardiothoracic ratio of 50%. Electrocardiogram (Fig. 1) showed sinus rhythm, 110 bpm heart rate (HR), ST segment elevation with superior concavity in leads DII, DIII, aVF and V4-V6. The results of the analyses were as follows:

Chromatographic separation resulted in a profile that was the same as the normal levels; HbA2 = 3.2%; HbF <1.0%. The sickling test with reducing agent was negative. MM + 2D echocardiogram did not reveal morpho-structural alterations, valve disease or pericardial effusion.

DISCUSSION

The diagnosis of acute pericarditis in the case analyzed is based on the clinical symptoms, laboratory data and electrocardiogram analysis.

The hypothesis of acute pericarditis secondary to the autoimmune disease is supported by the association of mucocutaneous lesions and arthritis and the symptoms of acute pericarditis. The diagnosis of BD in our clinical case is established by the presence of three clinical criteria - orogenital ulcers and painful, recurrent subcutaneous nodular lesions - and by the exclusion of other autoimmune pathology in the laboratory tests.



12-lead electrocardiogram analysis of the patient admitted to the emergency unit.

FIG. 1

TABLE II

Routine Tests

Hemoglobin (g/dL)	14.1	CRP (mg/dL)	18.1 (↑)	LDH (U/L)	238
Hematocrit (%)	42.7	ESR (mm)	50 (↑)	AST (U/L)	13
Leukocytes (x109/L)	7.770	INR	1.13	ALT (U/L)	13
Neutrophils (%)	66	Fibrinogen (mg/dL)	340	Total bilirubin (mg/dL)	0.2
Eosinophils (%)	1.6	Urea (mg/dL)	20	hTSH (uU/mL)	2.01
Basophils (%)	1.5	Creatinine (mg/dL)	0.9	FT4 (ng/dL)	1.25
Lymphocytes (%)	18.9	Na+ (mmol/L)	139	CK (ug/L)	78
Monocytes (%)	12	K+ (mmol/L)	4.8	CK-MB (ug/L)	1.8
Platelets (x109/L)	304	Uric acid (mg/dL)	6.6	Troponin T (ug/L)	< 0.03

TABLE III

Serologies

VDRL	Negative	Anti-HTLV I e II	negative
Anti-HIV 1 and 2	Negative	Anti-Parvovirus	negative
HB-Ag	Negative	Anti-Coxsackievirus A and B	negative
Anti-HBs	Positive	Anti-Echovirus	negative
HBe-Ag	Negative	Anti-Adenovirus	negative
Anti-HCV	Negative	Anti Herpes Simplex Virus 1 and 2	negative
Anti-Epstein-Barr Virus	Negative	Hemoculture under aerobic conditions	negative

TABLE IV

Autoimmune analyses

C3 (g/L)	1.43	Ac Anticardiolipin	negative
C4 (g/L)	0.30	Lupus anticoagulant	negative
Circulating immune complexes (ug/mL)	0.8	Ac. Anticytoplasm (MPO)	negative
Ac. Antinuclear antibodies (ANA)	negative	Ac. Anticytoplasm (c-ANCA)	negative
ANA profile	negative	Ac. Anti-histone (UI/ml)	< 40
RF test (UI/mL)	< 8.7	Ac. Anti-LKM	negative
Ac. Anti DS-DNA (UI/ml)	< 20	Ac. Anti-smooth muscle antibody (ASMA);	negative
Ac antiphospholipid	negative	Ac. Anti-mitochondrial antibody (AMA);	negative
HLA Genotyping Class 1	A03/A23; B15/B58; Cw02/Cw03		

BD rarely occurs among Black individuals, with rare cases being described in sub-Saharan Africa. In 1991, a case of a patient from Uganda with BD and HIV infection was described;[3] in 1994, five cases of Black individuals with BD in South Africa with predominantly mucocutaneous lesions were described. In 1997, the first case of a patient with BD in West Africa was described; the patient had genital ulceration and suffered from a severe and rare complication of intestinal involvement in BD – ileal perforation.[5] In 2003, a group of Senegalese researchers published studies of 17 cases of Black patients with BD over a period of 26 years.[6] The prevalence of each clinical manifestation was similar to those of the countries where the incidence of the disease is higher [mucocutaneous lesions (94.11%), eye lesions (58.82%), neurological lesions (47.05%), articular lesions (47.05%), vascular lesions (35.29%) and digestive lesions (11.76%)]. The clinical manifestation of BD in the patients from the sub-Saharan Africa does not differ significantly from the typical manifestation of the disease elsewhere in the world.

The cardiovascular involvement in BD, identified in 1946, is peculiar because it occurs in young patients without risk factors for this nosological entity. Two case studies involving 3153 and 2147 patients with

BD published in 1996 and 1997 respectively, concluded that cardiac involvement occurs in less than 1% of pacients.[7,8] However, this manifestation of BD is likely to be underestimated; according to Lakhanpal's[9] systematic study of autopsies from 1961 to 1976 in Japan, 17% of 170 corpses observed had cardiac involvement.

In 2003, the Center for Cardiothoracic Surgery of Istanbul published a retrospective analysis of cardiac lesions that have been attributed to BD in the last six decades.[10] Several forms of pericardiopathy [myopericarditis, recurrent acute pericarditis, constrictive pericarditis], coronariopathy [coronary disease with acute myocardial infarction or silent myocardial ischemia, coronary arteritis, coronary artery aneurysm] endocardiopathy [granulomatous endocarditis, aortic insufficiency, mitral valve prolapse, endomyocardial fibrosis], alterations in cardiac electrical conduction (complete auriculo-ventricular block), ventricular arrhythmias and amyloidosis were reported.

Involvement of the endocardium may be limited to heart valves or may extend to the ventricle. It manifests, particularly, as symptoms of acute or subacute aseptic endocarditis with valvular insufficiency, particularly the aortic, but may also affect the mitral or tricuspid valves. The mechanism responsible for the aortic insufficiency may be valvular prolapse or perforation, pseudoaneurysm of the sinus of Valsalva, or annular dilatation, secondary to aortitis or aortic aneurysm. The association of mitral valve prolapse (MVP) with BD was first described in China by Shen in 1985. Later, Morelli[11] compared the prevalence of cardiac alterations in a group of patients with BD with a group of healthy subjects through echocardiography MM + 2D + Doppler. MVP was observed in 50%, and proximal aortic dilatation in 30% of the patients. It was concluded that there was a higher incidence of these two pathologies in BD.

Endomyocardial fibrosis is a rarer clinical manifestation, involving the endocardium in BD, with only nine cases reported between 1977 and 1999[12]. The manifestation varies from an echocardiographic finding (thickened hyperechoic endocardium, reducing the ventricular area, particularly in the apical region) to heart failure. Although it can affect both ventricles, the right ventricle endocardium is mostly affected. Anatomopathological examination of the endomyocardium reveals dense fibrous connective tissue, sometimes intensely calcified, as a result of an inflammatory perivasculitis. When the fibrosis extends to the valves, insufficiency in the mitral or tricuspid valves occurs. Pulmonary thromboembolism is the most serious complication of endomyocardial fibrosis, due to its association with right intraventricular thrombogenesis.

It has been suggested that chronic inflammation is likely to be the etiology of electrical cardiac conduction alterations in BD, making specialized conduction pathways dysfunctional. The intensity of auriculo-ventricular block and the point of origin in the conduction system are varied. In BD, there is a higher incidence of ventricular arrhythmia. However, accurate information on the arrhythmogenic mechanisms in this pathology is needed. The most likely process is a greater gap in the QT interval ($QT_{maximum} - QT_{minimum}$), regardless of the heart rate.

The incidence of each cardiac manifestation is not clearly established. According to Wechsler[12], acute pericarditis is the most frequent cardiac manifestation of BD, accounting for over 40% of cases in the author's case studies. It may evolve to myopericarditis and can be associated with other cardiac disorders. Coronariopathy is the second most frequent manifestation, representing one third of the cases in the author's case studies. Unlike pericarditis, coronary involvement rarely corresponds to the initial manifestation, and is most often the result of acute myocardial infarction. Other possible clinical manifestations are angina and silent ischemia. The coronary lesions are usually single-vessel and proximal. The mortality rate for these patients is about 20% and is often due to congestive heart failure or acute myocardial infarction.[13]

In acute pericarditis, non-steroid anti-inflammatory agents (NSAIDs) are recommended for the relief of symptoms.

In the clinical case analyzed here, due to the final diagnosis of acute pericarditis in the context of active autoimmune disease – Behcet's disease - the following therapy was administered: prednisolone 40mg/day per os, colchicine 2mg/day per os, and naproxen 500mg/day per os. During hospitalization, the patient remained afebrile and normotensive; the clinical manifestations of pericarditis regressed, with resolution of the analytical parameters of inflammation. A progressive regression of mucocutaneous lesions and tibial-tarsal arthritis were also observed.

CONCLUSION

Behcet's disease is rare in Black individuals, particularly those from the sub-Saharan Africa, but it occurs in similar form to that seen in patients who live in regions with higher prevalence. Cardiac involvement is very unusual in the cases studies in which the incidence of BD is the highest. It is assumed, therefore, that this clinical manifestation will be equally rare among Black individuals. Among all forms of cardiac involvement in BD, acute pericarditis is one of those with the highest relative frequency. ■

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