



Case Report

Behcet's disease in acquired immune deficiency syndrome



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ARTICLE INFO

Article history:

Received 18 October 2015

Received in revised form 14 November 2015

Accepted 21 November 2015

Keywords:

HIV

AIDS

Behcets

ABSTRACT

HIV/AIDS patients often present with orogenital ulcers. In the immunocompromised patient diagnosis of these ulcers pose a challenge, as there is a myriad of etiologies. We present a case of an HIV/AIDS patient with recurrent orogenital aphthosis that was confirmed to have concomitant diagnosis of Behcet's disease. Proper awareness of the causes of these ulcers is essential for prompt and effective treatment. While rare causes may be at the bottom of a differential list in an immunocompetent host, when HIV/AIDS is involved these rare causes often percolate to the top.

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Introduction

Behcet's disease is a rare chronic immune-mediated small-vessel systemic vasculitis that is characterized by a triad of oral ulcers, genital ulcers and ocular manifestations [1]. There is evidence to suggest that infection (viral or bacterial), as well as genetic and environmental factors, play a role in this disease. However, the pathophysiology of the diseases has not been clearly identified and it may be the final step due to a variety of different stimuli. Behcet's disease is rarely reported in HIV/AIDS patient [2–5]. We present such a case.

Case report

A 41 year old male, with a past medical history of HIV with no recent CD4 count, was admitted with a several month history of fatigue, night sweats, anorexia, painful swallowing with ulcers over the upper lip, and painful draining ulcers in inter-gluteal fold. On physical exam, these ulcers were noted to have a purulent discharge, with erythema of the surrounding skin. He was also found to have painful pretibial nodules and oral thrush. Chest examination included normal breath sounds and regular heart sounds. The abdominal examination was non-tender and soft with normal bowel sounds. The initial impression was cutaneous herpes involving perianal skin and lips, with a bacterial superinfection. Odynophagia

was attributed to possible candidal esophagitis versus herpes esophagitis. Accordingly, treatment with acyclovir, fluconazole, vancomycin and piperacillin/tazobactam was initiated.

Serologies for FTA-ABS for syphilis were found to be positive, with an RPR titer of 1:4, and weekly treatment for latent syphilis with benzathine penicillin was started for duration of three weeks. Empiric treatment for *Lymphogranuloma venereum* (LGV) was begun with doxycycline. CD4 count was 78, and therefore, prophylaxis for PCP was initiated with atovaquone, as the patient had an allergy to trimethoprim/sulfamethoxazole. At this time HAART therapy was initiated as well. Eventually serologies for *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, LGV serology, and acid fast smear for TB were negative.

Our patient's condition improved with antibiotics and the patient was discharged with antiretroviral therapy and scheduled for a follow up as outpatient. Two months later the patient was readmitted with perianal ulcers, and multiple painful oral ulcers. The largest ulcer was measured at 10 mm × 7 mm in diameter; at this time a differential diagnosis of ulcers secondary to an HSV infection and oral thrush was considered. The patient was noncompliant with the antiretroviral medications since discharge from the hospital. His CD4 count at this time was less than 20, HAART medications were resumed during at admission. The patient was started on fluconazole for possible candidal esophagitis, acyclovir for cutaneous herpes, and primary antimicrobial prophylaxis for pneumocystosis and toxoplasmosis. Upper endoscopy was done, and showed a large 5 cm deep ulcer in the lower esophagus.

The patient went for colonoscopy that showed active GI bleed from the descending colon. Patient had technetium-labeled red

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blood cell bleeding scan which was negative. Angiography was performed which did not reveal any actively bleeding vessel but during the procedure the patient developed massive lower gastrointestinal bleeding, requiring 20 units of transfused blood. He underwent subtotal colectomy with ileostomy and a PEG tube was placed for feeding.

Biopsy of esophagus showed mild acute and chronic inflammation. Biopsy from duodenum, stomach and esophagus was negative for fungal elements, HSV1, HSV2, and CMV PCR. Colon biopsy showed punched out ulcers, associated with monocytic inflammation, vasculitis with thrombi, mural necrosis with histiocytes and lymphocytes in the vascular wall. A diagnosis of Behcet's disease, along with Behcet's colitis was made based on the histopathology findings and the correlating clinical history. Subsequently treatment with colchicine twice a day was initiated for mucocutaneous manifestations of Behcet's disease until resolution of symptoms.

Discussion

Behcet's disease is a rare disease that is characterized by recurrent oral aphthae and any of several systemic manifestations, including genital aphthae, ocular disease, skin lesions, gastrointestinal disease, neurologic disease, vascular disease, and arthritis. Most clinical manifestations of Behcet's disease are believed to be due to vasculitis. The disease is remarkable for its ability to involve blood vessels of all sizes (small, medium, and large) on both the arterial and venous sides of the circulation [6]. Our patient had orogenital ulcers, which initially responded well to antiretroviral and antibacterial treatment. However, through non-compliance with his antimicrobials, and worsening control of his HIV he developed a recurrence of his orogenital ulcers, with ulcers and colitis found during endoscopy and colonoscopy. The cause of Behcet's disease is unknown, but viral agents or autoimmune mechanisms are currently suggested as possible important factors in pathogenesis. Genome wide association studies have identified HLA-B51 to be associated most strongly with disease susceptibility [7]. Although the mechanism is still not clear to how this allele contributes to pathogenesis in Behcet's disease, it is hypothesized that it plays a role in presentation of CD8+ T cells. Arterial disease in Behcet's disease is most commonly a small vessel vasculitis, but medium and large vessel involvement may occur. Large vessel vascular involvement occurs in approximately one-third of patients with Behcet's disease. In these patients, perivascular and endovascular inflammation may lead to hemorrhage, stenosis, aneurysm formation, thrombus formation in both arteries and veins, and varices.

One of the earliest reports of Behcet's disease occurring in an HIV infected individual was by Buskila and colleagues in 1991 [8]. The pathophysiology of Behcet's disease in HIV patients is still unclear; however it is proposed that the disturbances in the immune system caused by HIV virus may result in susceptibility to autoimmune disease and vasculitis [9]. Considering the growing number of cases with HIV infection and Behcet's disease an association seems probable. This case highlights the immune

deregulation caused by HIV infection and the pathogenesis of Behcet's disease. Given the rarity of this presentation more knowledge on pathogenesis, management and evolution of these two diseases is needed. Most of the reports involve HIV infected individuals who have not yet been treated with antiretrovirals or have been poorly treated with low CD4 cell counts and high HIV viral loads. Importantly, a number of reports documented that effective antiretroviral therapy produced a remission of the signs and symptoms of Behcet's disease [3,4,9]. The response of HIV infection to antiretroviral treatment is measured by the drop in HIV viral load (virological effect) and a subsequent rise in the number of circulating CD4 cells (immunological effect). As Behcet's disease is thought to be immunological in origin, it might be thought that, in the cases of the disease associated with HIV infection, the rise in the number of circulating CD4 cells might be responsible for the remission of Behcet's disease. A 1997 report [10] investigated an individual with idiopathic CD4 T-lymphocytopenia (CD4 cell count 10) with a Behcet's disease-like illness but no other cases have been reported to our knowledge. Mercie et al. [11] observed a relationship between Behcet's disease activity an increased viral load. In addition, Cicalini et al. [9] have postulated that induction of Behcet's disease in HIV-associated cases might be a direct effect of viral replication or through HIV-induction of autoimmune mechanisms. More recently, a case of Behcet's disease has been reported after acute HIV infection [12] when the CD4 count was not low, further suggesting that, if there is a true relationship, HIV replication itself could be the relevant HIV parameter causing immune dysregulation.

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