Behcet’s Disease: The Darker side!

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Abstract
Behcet’s disease (BD) is a chronic inflammatory disease affecting blood vessels throughout the body mainly veins and clinically characterized by oro-genital aphthae, ophthalmologic involvement, cutaneous lesions, articular, neurological involvement and less commonly by gastrointestinal manifestations which may have dreadful complications. Here we report a case of 58 year male with gastrointestinal complications of BD and a rapidly worsening course.

Introduction
Behcet’s disease (BD) was first defined in 1937 by Hulusi Behcet,¹ a Turkish dermatologist, as a triad of recurrent aphthous stomatitis, genital aphthae and relapsing uveitis. It is a chronic autoimmune disorder characterized by inflammation of blood vessels throughout the body. Diagnostic criteria for BD were defined by the international study group for BD in 1990. It has multiorgan involvement with oro-genital aphthae, cutaneous, articular, neurological and gastro-intestinal involvement. Of these, gastrointestinal manifestations of the disease has poor prognosis leading to massive bleeding and perforation and needs surgical intervention along with medical management. Typical lesions are giant oval shaped punched out ulcers in ileocaecal area. Corticosteroids form the cornerstone of management along with immunomodulator and immunosuppressive therapy. Azathioprine, Colchicine, Chlorambucil, Cyclophosphamide, cyclosporine are the agents commonly used. The efficacy of anti-TNF alpha monoclonal antibodies in intestinal BD was first reported in 2001. Infliximab and adalimumab have been used successfully for the same.

Case Report
58 year male, non-diabetic, non-hypertensive, was admitted with dysphagia for solids, throat pain since 5 days and low grade fever associated with easy fatiguability since 4 days. Patient had no major past medical history. On examination he was afebrile, pulse was 108/min, BP 100/70mmHg with severe pallor and koilonychia along with multiple oral ulcers. Rest of the examination was within normal limits.

Investigations showed hemoglobin 6.4 gm/dl, total leucocyte count 15,400/cmm with neutrophils 87%, lymphocytes 4%, MCV 56.8 fl, MCH 16.1 pg MCHC 28.3 gm/dL, platelets 3.13 lac/cmm with microcytic hypochromic smear. Renal function and serum electrolytes were within normal limits, ESR 55mm/hr, total protein 5.8 gm/dl, albumin 3.4 gm/dl, serum bilirubin total 1.1 mg/dl, SGOT/SGPT 26/41 U/L serum alkaline phosphatase level 149 U/L, serum ferritin 69ng/ml (normal), serum iron 26 μgm% (normal range 60-160 micgm%), TIBC 450 μgm% (normal range 200-400 μgm%), reticulocyte count 3%, HIV, HBsAg and ANA were negative.

He was started on antibiotics and needed multiple packed cell transfusions for anemia during his course. Gastroscopy showed pharyngitis and multiple discrete esophageal ulcers (Figure 1). On day 2 he had fresh bleeding per rectum and erythematous rash over extremities and back suggestive of erythema nodosum. On repeated questioning, patient gave history of genital ulcers (Figure 2). Ophthalmic examination was normal. Based on this clinical background, with a suspicion of Behcet’s disease, he was started IV Methyl prednisolone 1 gm daily. On the following day he was planned for colonoscopy for evaluation of lower gastrointestinal bleed but early morning he started complaining of severe abdominal pain and had generalized abdominal tenderness and guarding. X ray erect abdomen showed air under diaphragm. Patient was immediately taken up for exploratory laparotomy. An ileal perforation was seen and right hemicolecotomy was done. Post operatively course was uneventful until on post operative day 3, when he again developed severe abdominal pain, tachycardia, tachypnoea and repeat X ray abdomen showed air under diaphragm. Patient was taken up for re-exploration, which showed an anastomotic leak which was sutured but post operatively he had a rapid downhill course with septic shock and succumbed 2 days later. Histopathology report of colon showed chronic active ileitis with fissuring ulcers with lymphoplasmacytic inflammatory infiltrates with venulitis without granulomas or any other...
Fig. 3: Histopathology picture showing lymphoplasmacytic inflammatory infiltrates with venulitis

inclusions which was consistent with Behcet’s disease (Figure 3).

**Discussion**

Behcet’s Disease (BD) is a chronic inflammatory rheumatic disease, characterized by recurrent episodes of oro-genital ulceration and ocular inflammation due to an overreactive immune system. It was first reported in 1937 and defined by Hulusi Behcet, a Turkish dermatologist, as a triad of recurrent aphthous stomatitis, genital aphthae and relapsing uveitis. Young adults between the second and fourth decades of life are mainly affected. Pathologically, the disease is characterized by vasculitis targeting the vasa vasorum and other small blood vessels, which is usually lymphocytic and affects veins more than arteries, although occasionally there may be more necrotizing inflammation with leucocytoclasis. Fibrinoid necrosis may be present in involved veins and venules. Susceptible genes identified by Genome-wide association Studies (GWAS) strongly suggest that abnormal immunological responses may play a role in the pathogenesis of BD. However, the precise mechanisms underlying the pathogenesis of intestinal BD have not yet been identified. Abnormal innate immune responses have been reported to be associated with intestinal BD. Approximately 3–16 % of patients with BD have gastrointestinal tract involvement.

A typical gastrointestinal lesion consists of a giant oval-shaped deep punched-out ulcer in the ileocecal area. The most common gastrointestinal symptoms are abdominal pain, diarrhea and bleeding. Deep ulcers are responsible for most common intestinal complications i.e. severe bleeding and perforation. Therefore, intestinal lesions have been considered a factor associated with poor prognosis in BD patients, resulting in emergency abdominal surgery and bowel resection. Despite such dreaded complications, the diagnosis and management of intestinal BD lesions has not been standardized. The widely used International Study Group (ISG) for Behcet’s disease criteria include recurrent oral ulcers, plus at least two of the following four factors—recurrent genital ulcers, eye lesions, skin lesions, and positive pathergy test. Our patient had recurrent oral and genital ulcers with esophageal and ileal ulceration complicated by perforation and unfortunately had a poor outcome. It is essential to differentiate intestinal Behcet’s from Crohn’s disease (CD) and Intestinal tuberculosis. CD share many intestinal and extra-intestinal features with BD. Typical endoscopic and radiological findings in patients with CD include longitudinal ulcers and a cobblestone appearance and histopathology shows granulomas. All these are important diagnostic features of CD and differentiate it from BD. In this patient HLA B51 could not be done, which also has an association with BD. Treatment of BD aims at modifying the inflammatory response. Commonly used agents are corticosteroids (up to 1 mg/kg/day), azathioprine, or cyclosporine. Others include cyclophosphamide, colchicine, mycophenolate, thalidomide and TNF alpha inhibitors like infliximab.

So as a physician it is important to keep a high index of suspicion for intestinal Behcet’s which warrants early intervention to prevent a fatal outcome.

**References**