

CROHN'S DISEASE PRESENTING AS A RECURRENT PERIANAL FISTULA: A CASE REPORT

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ABSTRACT

Crohn's disease (CD) is a multifactorial polygenic disease characterized by chronic inflammation of the gastrointestinal tract (GIT), often complicated by the development of intestinal strictures and/or formation of fistulas. Several diagnostic criteria have been proposed, usually relying on clinical, endoscopic, radiological or histological features.

We report a case of Crohn's disease of the entire colon with rectal sparing presenting with recurrent perianal fistula that had earlier on been misdiagnosed and treated for other things. The patient was treated successfully with corticosteroids and aminosalicylates and had since remained stable.

Key Words: Crohn's disease, perianal fistula

INTRODUCTION/REVIEW OF LITERATURE

Crohn's disease (CD) is a multifactorial polygenic disease characterised by chronic inflammation of the gastrointestinal tract (GIT)¹. It may involve any part of the GIT. The transmural inflammation characteristic of Crohn's disease predisposes patients to the formation of fistulas and up to 50% of patients with Crohn's disease are affected by fistulas^{2,3}. The extent of involvement is usually based on radiological, endoscopic, macroscopic, or routine histologic examination. These criteria alone probably underestimate the diffuse nature of the disease process².

The disease presents in various forms, depending on its location, its inclination to develop anatomical complications, or response to treatment. Attempts have been made to define clinical subgroups on the basis of disease location, extent (diffuse or localized), behaviour (primary inflammatory, fistulating, or fibrostenotic), and by surgical history. Recently, NOD2/CARD15 has been disclosed as the first gene associated with CD by two independent groups³ and rapidly confirmed by others. Studies in affected families have shown that affected siblings frequently present at a similar age and concordance rates of up to 80% have been reported for disease site, behaviour and presence of extra intestinal manifestations of disease⁴. In addition, case-control association studies have reported genetic associations with the presence of extra intestinal manifestations and perianal fistulating disease⁵. In approximately 10% of patients, perianal fistulization

is the initial manifestation of Crohn's disease. In fact, the formation of perianal fistulas might precede the onset of Crohn's disease by several years⁵.

The behaviour of CD is clinically relevant as it is associated with the development of complications and need for surgery. The majority of patients present with non-stricturing, non-penetrating disease at diagnosis while after 25 years the majority harbour either a stricturing or penetrating pattern. This changing behaviour may still be determined by both genetic and environmental factors that may influence its inclination and speed of evolution. The only environmental factor clearly associated with CD is active smoking. Smoking is significantly more frequent in CD than in healthy controls⁶. Smoking has also been associated with more aggressive disease but not with other clinical or biological characteristics, particularly CD behaviour. Besides smoking, the demographic and clinical characteristics of the disease, including treatment used, may influence its changing behaviour. Antisaccharomyces cerevisiae antibodies (ASCA) represent the main serological marker associated with CD.

The migratory potential of mucosa fibroblasts in patients with CD has been reported to be less than that of fibroblasts from control individuals which suggest that mucosal fibroblasts from patients with CD might have an impaired ability to respond to tissue injury. An even greater reduction in migratory ability has been reported in fibroblasts from fistula tissue of patients with CD, which suggests a potential cause for the impaired wound healing noted in these patients.

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CASE REPORT

A 23-year-old male Asian patient presented with a recurrent history of abdominal pain, flatulence, indigestion, fever, arthralgia and swelling of the feet of three months duration. Abdominal pain was said to be non-specific, dull and mainly involving the lower half of the abdomen. The pain was relieved by passing flatus. Fever was low grade with no chills or rigors. No associated headache or body aches.

Six years earlier, he had presented at another hospital with passing drops of blood after defecation, swelling in the perianal region for which he had incision and drainage operation with antibiotics coverage. Two months later, he had a recurrence of the perianal swelling and had another incision and drainage operation done. He had another recurrence 2 years later and presented at another hospital where he was diagnosed to have perianal fistula and had fistulectomy done. Biopsy of the fistula tract showed non-specific inflammatory changes.

He remained stable until March 2007, when he presented at MedIndia Hospital, India with the above complaints. He admitted to history of loss of weight, appetite and taste. No history of haematemesis or melaena. No change in bowel habits. He was neither diabetic nor hypertensive. He admitted to have smoked heavily (20 pack years) and ingested an average of four bottles of alcohol per day for the past fifteen years. These he claimed to have stopped six months into the present illness.

Examination revealed a chronically ill-looking slim built young man with low grade fever ($T=37.4^{\circ}\text{C}$). He was not pale and not jaundiced and had no peripheral lymphadenopathy.

Cardiovascular and respiratory examinations were essentially normal.

Abdomen was soft with mild tenderness in both iliac fossae; bowel sounds were heard and normal. No organomegaly. Rectal examination was also normal.

An impression of Abdominal Tuberculosis to rule out Inflammatory Bowel Disease (IBD) was made. He was admitted for further investigations and placed on intravenous fluids and antibiotics. The results of Full blood count, Liver function test, Electrolyte, urea & creatinine were essentially normal.

His Blood group was O^{+ve} while his Haemoglobin genotype was AA. Hepatitis B surface antigen and antibodies to hepatitis C were negative. Also HIV screening was non reactive while Mantoux test was negative. Abdominal ultrasound was equally normal. Colonoscopy carried out revealed features of Crohn's disease of the entire colon (thickened intestinal wall, narrow intestinal lumen and multiple serpentine linear ulcers) with rectal sparing and perianal fistula figures 1- 4. Biopsy specimens were taken from the caecum, ascending, transverse and descending colon. Biopsy report showed active, chronic crypt

destructive colitis involving the entire colon compatible with Crohn's disease.

A final diagnosis of Crohn's disease was made and patient was commenced on corticosteroids and aminosalicylates. He was discharged after three weeks on admission. His condition remained stable for the entire twelve months period of follow up.

Figure 1: Endoscopy Picture Showing Perianal Abscess.



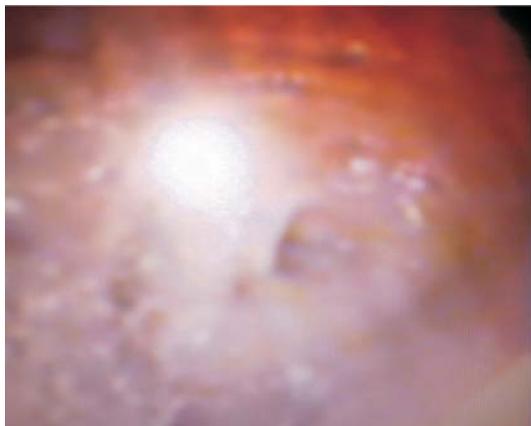
Figure 2: Descending colon showing the narrowed lumen with the granular appearances of the mucosa.



Figure 3: Transverse colon showing the narrowed lumen and the granular appearance of the mucosa wall.



Figure 4: Ascending colon with the typical narrowed lumen and mucosa ulcers.



DISCUSSION

CD is a multifactorial polygenic disease characterized by chronic inflammation of the GIT, often complicated by the development of intestinal strictures and/or the formation of fistulas². Several diagnostic criteria have been proposed, usually relying on clinical, endoscopic, radiological or histological criteria. So defined however, CD is still a heterogeneous entity. The disease can present in various forms for example depending on its location, its inclination to develop anatomical complications or response to treatment³. The association of anal lesions with Crohn's disease was not described by Crohn and colleagues in their original paper⁷, but was reported by Bissel shortly afterwards⁸. It was Morson and Lockhart-Mummery from St Mark's Hospital in London who, in 1959, described the sarcoid-like histological lesions⁹. More than one-third of patients develop fistulas during their lifetime with the majority suffering from perianal disease¹⁰. The patient under discussion developed recurrent perianal fistulas and perianal abscesses for which he had several drainages and fistulectomies. Perianal fistulization was the initial manifestation of Crohn's disease in this patient. Patients with colonic manifestations of Crohn's disease have the highest incidence of perianal fistulas; this is in keeping with the findings in this patient (total colonic involvement with rectal sparing). Despite the prevalence of fistulas in patients with Crohn's disease, fistula pathogenesis remains poorly understood. The first step in the formation of a fistula is generally assumed to be tissue destruction. The transmural inflammation that typifies Crohn's disease predisposes these patients to fistula formation; luminal bacteria might also have a role in the development and maintenance of fistulas⁵. Early development of stricturing or penetrating behaviour in CD is influenced by disease location, clinical entity of the disease, and smoking habit but

not by NOD2/CARD15 genotype¹¹. The smoking habit of the patient under discussion might have contributed immensely to the aggressive nature of this disease in him. The two main independent associations with change in disease behaviour within 5 years after diagnosis were ileal location of the disease and number of flares per year¹¹. Ileal location was essentially associated with the development of stricturing disease and was not a discriminant factor between penetrating disease and non-stricturing non-penetrating disease when only these two phenotypes were compared. However, when penetrating disease was divided into intra abdominal and perianal disease, ileal location was significantly more frequent in intra-abdominal than perianal penetrating disease and is reached in the first subgroups, a frequency similar to that observed in structuring disease. This association between stricturing disease or intra-abdominal penetrating disease and ileal location has been described in studies of disease behaviour based on surgical series, irrespective of the duration of the disease¹². One explanation for the association with stricturing disease may be the smaller diameter of the gut lumen in the ileum than in the colon making functionally significant strictures more likely to occur. Another explanation could be the nature of the immunoinflammatory reaction in the ileum. Compared with a matched control population, more patients with CD have been found to smoke tobacco¹³. Smoking has been recognized as a risk factor for surgery and recurrence of CD after surgery particularly in women and heavy smokers¹³. Other recognized factors for the development of CD are the type of diet consumed, increased intestinal permeability, and defects in colonic mucus². Contrary to expectations, CD does not seem to be more severe among black patients, who had an earlier age of diagnosis.

The traditional treatment paradigm in Crohn's disease is based on a "step-up" approach in which therapies with the least toxicity are used early, and subsequent therapies are added due to lack of response or toxicity. Unfortunately, under this treatment paradigm, agents with low efficacy such as aminosalicylates are used for prolonged periods of time while uncontrolled inflammation results in tissue damage. Patients who fail to respond to aminosalicylates are then treated with corticosteroids in the form of prednisolone, or alternatively with budesonide when disease is limited to the ileum or right colon. Immunosuppressant therapy is reserved for those patients with steroid-refractory or steroid dependent disease. This approach is endorsed by the American College of Gastroenterology¹⁴. Unfortunately, under this current treatment paradigm, rates of surgical intervention remain high, with as many as one third of patients requiring surgery within a year of beginning oral

steroids and with no significant decrease in the need for surgery over the last several decades despite the earlier and increasing use of immunomodulators¹⁵.

The "top-down" approach is currently being advocated using biologic therapy particularly anti-tumor necrosis factor (TNF)-alpha. The current goal of top-down therapy is to avoid steroids and their potential complications, achieve mucosal healing, and alter the natural history of the disease. Although steroids have significant anti-inflammatory activity, which presumably is responsible for their beneficial effect on Crohn's disease symptoms, there is evidence that glucocorticoids contribute to loss of immune tolerance¹⁶.

Perianal fistulas in Crohn's disease rarely heal without treatment, which comprises surgical and medical therapies. Although some patients only have mild symptoms or are asymptomatic without a need for intervention, perianal Crohn's disease may cause severe morbidity, resulting in disabling and impaired quality of life. Surgery is usually limited to simple fistula tracts and drainage of abscesses due to the risk of incontinence caused by more aggressive interventions¹⁷. Medical therapy represents the mainstay in the management of perianal fistulas¹⁷. Medical management of perianal fistulas includes the use of systemic antibiotics, immunosuppressive agents and infliximab¹⁸. Rapid reduction of fistula drainage by antibiotics improves the patient's general clinical condition and may provide a bridging strategy to azathioprine treatment¹⁸.

In this case report, the patient was placed on the step-up approach using corticosteroids (prednisolone) 10mg three times daily to a maximum of 20mg three times daily and tailing it down to 5mg daily over the period of 6 months and aminosalicylates 300mg twice daily in addition to antibiotics (Metronidazole and ciprofloxacin). He was placed on maintenance prednisolone 5mg daily and aminosalicylates 300mg daily for another 3 months. He was followed up for a total period of 12 months and had since remained stable with no recurrence of perianal fistulas and abscesses.

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