CASE REPORT

Intestinal complications of Behçet's disease

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Dr David W Borowski,
DWBorowski@AOL.com**SUMMARY**

We report a case of a young female patient with long-standing oral and genital Behçet's disease (BD), who presented with progressive severe colonic inflammation and perforation, requiring multiple laparotomies. The case had ultimately a favourable outcome despite posing a number of diagnostic and therapeutic challenges. Intestinal complications, although rare, should be considered as important differential diagnoses in patients with BD presenting with abdominal pain, and is a difficult-to-prove differential diagnosis to Crohn's disease.

BACKGROUND

Behçet's disease (BD) is seen throughout the world, but is most prevalent in the Middle East, Far East and the Mediterranean basin.¹ In the UK, it affects around 1:100 000 people in the general population.² Owing to its pathogenesis causing small vessel vasculitis, it can have widespread visceral manifestations on the gastrointestinal (GI), pulmonary, musculoskeletal, cardiovascular and neurological systems.

The involvement of the GI tract is depending on the geographical region, and ranges between 3% and 26% in the Mediterranean to 15–60% in the Far East³; no data is available for the less prevalent zones. The treatment of intestinal BD in particular is problematic, and many immunosuppressants and immunomodulators have been used with varying degree of success. Surgery is reserved only for complications in a very small subgroup of patients, and very rarely encountered in the Western world. Thus, the present report is a reminder of an important clinical lesson for clinicians, many of whom do not have experience with such complications from BD, but may be confronted more

frequently in the future due to increasing migration throughout the world.

CASE PRESENTATION

A 19-year-old woman with known oral and genital BD presented with initially central, later localised pain in the right iliac fossa. With clinical suspicion of acute appendicitis, a diagnostic laparoscopy was carried out. During laparoscopy, a mildly inflamed appendix was found and removed; the large and small intestine appeared unremarkable. Postoperatively, preadmission steroids and antibiotics were continued, however, the patient's condition gradually worsened with signs of peritonitis on the seventh day. An abdominal CT scan demonstrated extensive free fluid and free intraperitoneal gas, and an immediate laparotomy was carried out. Extensive faecal peritonitis from multiple perforations in caecum, ascending and transverse colon (figure 1) resulted in a subtotal colectomy (figure 2) and ileostomy formation. Subsequent histological analysis of the colon revealed focal vasculitis with extensive fissuring ulcers with characteristic rolled out, everted and collar stud margins, associated with volcanic/eruptive inflammation and perforation (figure 3); the terminal ileum was, however, unremarkable. No granulomas were identified and, characteristically, no mesenchymal manifestations were identified as would be expected in Crohn's disease (CD) (figure 4).

Postoperatively, the patient was treated with broad-spectrum antibiotics, high-dose hydrocortisone and methylprednisolone. Inflammatory markers remained significantly raised, and a CT scan on the eighth postoperative day demonstrated residual collections in the pelvis and subhepatic space. Radiological drainage was deemed impossible; the patient nonetheless improved systemically on conservative management.

Figure 1 Intraoperative picture of the caecum and transverse colon with multiple perforations. Faecal peritonitis.

Figure 2 Subtotal colectomy: resected specimen. Forceps indicating some of the multiple perforations.

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Figure 3 Colonic ulcer: extensive fissuring ulcers with a characteristic rolled out, everted and collar stud margin.

However, at 2 weeks following laparotomy, further surgery was necessitated by the presence of small bowel content in the abdominal drain. At laparotomy further perforations within the distal ileum were noted, requiring resection of the affected segment and refashioning of the ileostomy. Subsequent histology was again consistent with perforated intestinal BD with neutrophilic vasculitis and focal foreign body giant cell but no granulomas, with normal small bowel at the proximal resection margin (figure 5).

Thus, increased immunosuppressive therapy with infliximab was initiated; there were no further symptoms and signs of continuing BD, and the patient was discharged after a total hospitalisation of 7 weeks, including two prolonged stays on the intensive care unit with temporary organ and nutritional support.

INVESTIGATIONS

Blood tests on admission showed a white cell count (WCC) of $19.1 \times 10^9/L$, neutrophilia of $16.7 \times 10^9/L$ and C reactive protein (CRP) of 430 mg/L. Following the appendicectomy, blood tests deteriorated (WCC $21.9 \times 10^9/L$, neutrophilia $20.0 \times 10^9/L$, CRP 494 mg/L), resulting in a CT scan that raised suspicion of intestinal perforation.

Figure 4 Ulcer with volcanic/eruptive inflammation and perforation. No granulomas and no mesenchymal manifestations identified pleading for Crohn's disease.

Figure 5 Neutrophilic vasculitis and focal foreign body giant cell (arrow) without granulomas.

Following the diagnosis of intestinal BD, blood immunology tests were carried out for differential diagnostic purpose; indirect immunofluorescence assay of organ-specific autoantibodies and antineutrophil cytoplasmic antibodies (ANCA) were negative; complement and basement membrane antibody levels were within normal range. Raised IgM $\alpha 2$ globulin levels were in keeping with acute infection.

DIFFERENTIAL DIAGNOSIS

Intestinal manifestations of BD is a rare differential diagnosis to many more common abdominal conditions, including appendicitis, diverticulitis, infectious enterocolitis, inflammatory bowel disease (IBD), other causes of colitis and intestinal tuberculosis; particularly the latter condition being also prevalent in areas with higher incidence of BD.

Intestinal BD often mimics IBD, particularly CD. Both diseases occur in younger patients, can have non-specific GI symptoms, similar extraintestinal manifestations and complications and disease courses that wax and wane over time.⁴ Fistula formation, GI haemorrhage and intestinal perforation in BD tend to occur earlier than in CD,⁵ making differential diagnosis difficult, as it is well represented by the present case. Perianal disease is very rare in intestinal BD and supports the diagnosis of CD.

Transmural enteritis or colitis can occur in intestinal BD or CD, but the presence of granulomas on biopsy suggests CD, whereas the finding of vasculitis suggests intestinal BD⁶; nevertheless, the distinction may be extremely difficult to make.

Various autoantibodies have been described in IBD, specifically perinuclear ANCA (pANCA) in ulcerative colitis (UC) and anti-*Saccharomyces cerevisiae* antibody (ASCA) in CD. ASCA is directed against the oligomannosidic epitope of the yeast *S cerevisiae* and is positive in 40–70% of patients with CD, 10–15% of patients with UC and 0–5% of healthy control subjects.⁷ pANCA is positive in 60–80% of UC patients and 10–30% of CD patients. In a Turkish study involving 18 patients with known BD, none were pANCA-positive.⁷ The immunological evidence in the present case was in keeping with intestinal BD.

OUTCOME AND FOLLOW-UP

Following administration of infliximab, no further exacerbations of BD took place; the patient remains on long-term low-dose steroid prophylaxis, with regular surgical and rheumatological follow-up.

DISCUSSION

The diagnosis of BD, or silk road disease—a rare immune-mediated small-vessel systemic vasculitis—is based on the clinical triad of recurrent oral ulceration associated with two of the following: recurrent genital ulcerations, ocular lesions (anterior or posterior uveitis, or cells in the vitreous on slit lamp examination, or retinal vasculitis), typical skin lesions (erythema nodosum, pseudofolliculitis) and a positive pathergy test (skin hyperreactivity). There is no pathognomonic laboratory test which could ascertain BD; the diagnosis is one of exclusion.

While mouth ulcers are by definition present in BD, the commonest intestinal manifestation is located in the ileocaecal region (96% of surgery-naïve patients).⁸ Colitis from BD is less common, and involvement of the rectum (less than 1%),⁹ oesophagus (2–11%) or stomach is rare.¹⁰ The patients usually present with anorexia, nausea, abdominal pain, diarrhoea and GI bleeding. Ulcers seen on endoscopy are typically irregular, round or oval, punched-out, large (>1 cm), single (67% of patients) to few in number, deep, and with discrete margins in a focal distribution.¹¹ Diffuse colonic involvement is rare, but it occurs in approximately 15% of patients who have GI involvement.¹²

In the Far East, colonic ulcers have been described as volcano-type lesions because they are deeply penetrating and have nodular margins caused by fibrosis.¹³ In contrast, enteroclysis findings of Turkish patients with intestinal BD showed usually shallow intestinal ulcers, multiple and commonly localised to the terminal ileum.¹⁴ Thus, not only the frequency but also the type of bowel disease seems to differ between the two regions. The intestinal ulcers are less responsive to medical therapy and frequently require surgical resection due to complications from perforations, fistulae formation, and massive GI bleeding, which occur in up to 50% of patients.¹⁵

Treatment is dictated by the type of organ involvement and its severity. Several effective anti-inflammatory and immunosuppressive regimens for BD currently exist, but none result in cure. Controlled studies have shown that colchicines,¹⁶ thalidomide,¹⁷ dapsone,¹⁸ azathioprine,¹⁹ interferon α^{20} and etanercept²¹ are effective to some degree. However, refractory, relapsing disease is still associated with marked physical and psychological morbidity in some patients.

Regarding intestinal BD, efficiency can be expected from corticosteroids combined with azathioprine. Infliximab is standard treatment for severe IBD, but its benefits have also been described in patients with severe BD, although data from randomised controlled clinical trials is not yet available and its use should be limited to patients with severe BD only.²²

Surgical intervention is reserved for the treatment of complications. Risk factors found to be associated with free bowel perforation are young age (<25 years) at the time of diagnosis, previous history of laparotomy, CRP levels greater than 44 mg/L and volcano-shaped ulcers seen on colonoscopy.²³

Opinions vary between authors, whether resection margins on the bowel should be wide or limited to the parts of the bowel macroscopically affected by the disease.²⁴ Intestinal anastomosis formation is usually discouraged, as anastomotic leaks, re-perforation and fistula formation are common. It is necessary to search for skip lesions, because multiple ulcers may be present. The incidence of postoperative complications and postoperative recurrence of ulcers is so high that supplementary management is often required. Long-term recurrences occur in 40–56%, usually at the site of the previous anastomosis.²⁵

According to present recommendations follow-up radiographic and endoscopic imaging should begin within 2 years

after surgery, with initiation of early medical treatment if disease activity is present. The overall prognosis in intestinal BD is more reserved than in CD. Remission rates with medical therapy are similar to those achieved in CD patients, but recurrence rates are higher and patients require surgical intervention more frequently in intestinal BD.²⁶

Prior to admission, this patient had been controlled with peridol corticosteroid treatment, having few mild exacerbations of BD without any prior visceral involvement. Her GI symptoms had an exponential manifestation with multiple severe complications. Intestinal complications, although rare, should be considered as important differential diagnoses in patients with BD presenting with abdominal pain, and is a difficult-to-prove differential diagnosis to Crohn's disease.

Learning points

- ▶ Intestinal complications from Behçet's disease (BD) in the Western world are rare, and its differential diagnoses include many more commonly seen diseases including appendicitis, diverticulitis, infectious enterocolitis, inflammatory bowel disease, other causes of colitis and intestinal tuberculosis.
- ▶ Antitumour necrosis factor α drugs (namely infliximab) has proven beneficial in the suppression of intestinal BD symptoms, but it should still be reserved for severely ill patients.
- ▶ Surgery should be limited to the management of the complications and resections be limited to the areas already affected by the disease, as progression could result in further surgical interventions and potentially lead to short-bowel syndrome.

Contributors DBK was involved in the management of patients, writing of the manuscript in literature research and in compiling images. DKR and DWB were involved in the management of patients and in reviewing the manuscript. KD was involved in histopathology analysis, in compiling images and in reviewing the manuscript

Competing interests None.

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REFERENCES

- 1 Zouboulis CC. Epidemiology of Adamantiades-Behçet's disease. *Ann Med Interne* 1999;150:488–98.
- 2 <http://www.nhsinform.co.uk/health-library/articles/b/behcet-s-disease/introduction> (accessed 31 May 2013).
- 3 Yurdakul S, Tüzüner N, Yurdakul I, et al. Gastrointestinal involvement in Behçet's syndrome: a controlled study. *Ann Rheum Dis* 1996;55:208–10.
- 4 Cheon JH, Celik AF, Kim WH. Behçet's disease: gastrointestinal involvement. In: Yazici Y, Yazici H, ed. *Behçet's syndrome*. 1st edn. New York, NY: Springer, 2010:165–88.
- 5 Bayraktar Y, Ozaslan E, Van Thiel DH. Gastrointestinal manifestations of Behçet's disease. *J Clin Gastroenterol* 2000;30:144–54.
- 6 Sayek I, Aran O, Uzunalimoglu B, et al. Intestinal Behçet's disease: surgical experience in seven cases. *Hepatogastroenterology* 1991;38:81–3.
- 7 Choi CH, Kim TI, Kim BC, et al. Anti-Saccharomyces cerevisiae antibody in intestinal Behçet's disease patients: relation to clinical course. *Dis Colon Rectum* 2006;49:1849–59.
- 8 Lee CR, Kim WH, Cho YS, et al. Colonoscopic findings in intestinal Behçet's disease. *Inflamm Bowel Dis* 2001;7:243–9.
- 9 Hamza M. Proctitis in Behçet disease. Study of 6 cases [in French]. *Rev Rhum Ed Fr* 1993;60:925–7.
- 10 Bayraktar Y, Ozaslan E, Van Thiel DH. Gastrointestinal manifestations of Behçet's disease. *J Clin Gastroenterol* 2000;30:144–54.

- 11 Lee CR, Kim WH, Cho YS, *et al.* Colonoscopic findings in intestinal Behçet's disease. *Inflamm Bowel Dis* 2001;7:243–9.
- 12 Masugi J, Matsui T, Fujimori T, *et al.* A case of Behçet's disease with multiple longitudinal ulcers all over the colon. *Am J Gastroenterol* 1994;89:778–80.
- 13 Kim JS, Lim SH, Choi IJ, *et al.* Prediction of the clinical course of Behçet's colitis according to macroscopic classification by colonoscopy. *Endoscopy* 2000;32:635–40.
- 14 Korman U, Cantasdemir M, Kurugoglu S, *et al.* Enteroclysis findings of intestinal Behçet disease: a comparative study with Crohn disease. *Abdom Imaging* 2003;28:308–12.
- 15 Moon CM, Cheon JH, Shin JK, *et al.* Prediction of free bowel perforation in patients with intestinal Behçet's disease using clinical and colonoscopic findings. *Dig Dis Sci* 2010;55:2904–11.
- 16 Yardacul S, Mat C, Tuzun Y, *et al.* A double-blind trial of colchicine in Behçet's syndrome. *Arthritis Rheum* 2001;44:2686–92.
- 17 Hamaryudan V, Mat C, Saip S, *et al.* Thalidomide in the treatment of the mucocutaneous lesions of the Behçet's syndrome. A randomized, double blind, placebo controlled trial. *Ann Intern Med* 1998;128:443–50.
- 18 Sharquie KE, Najim RA, Abu-Raghif AR. Dapsone in Behçet's disease: a double-blind, placebo-controlled, cross-over study. *J Dermatol* 2002;29:267–79.
- 19 Yazici H, Pazarli H, Barnes CG, *et al.* A controlled trial of azathioprine in Behçet's syndrome. *N Engl J Med* 1990;322:281–5.
- 20 Alpsoy E, Durusoy C, Yilmaz E, *et al.* Interferon alfa-2a in the treatment of Behçet's disease: a randomized placebo-controlled and double-blind study. *Arch Dermatol* 2002;138:467–71.
- 21 Melikoglu M, Fresko I, Mat C, *et al.* Short-term trial of etanercept in Behçet's disease: a double blind, placebo controlled study. *J Rheumatol* 2005;32:98–105.
- 22 Sfrikakis P, Markomichelakis N, Alpsoy E, *et al.* Anti-TNF therapy in the management of Behçet's disease—review and basis for recommendations. *Rheumatology* 2007;46:736–41.
- 23 Moon CM, Cheon JH, Shin JK, *et al.* Prediction of free bowel perforation in patients with intestinal Behçet's disease using clinical and colonoscopic findings. *Dig Dis Sci* 2010;55:2904–11.
- 24 Ebert EC. Gastrointestinal manifestations of Behçet's disease. *Dig Dis Sci* 2009;54:201–7.
- 25 Kasahara Y, Tanaka S, Nishino M, *et al.* Intestinal involvement in Behçet's disease: review of 136 surgical cases in the Japanese literature. *Dis Colon Rectum* 1981;24:103–6.
- 26 Grigg EL, Kane S, Katz S. Mimicry and deception in inflammatory bowel disease and intestinal behçet disease. *Gastroenterol Hepatol (NY)* 2012;8:103–12.

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