Wireless capsule endoscopy in the investigation of intestinal Behçet’s syndrome

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Objective. Intestinal Behçet’s Syndrome (BS) is a difficult diagnosis to establish. We describe the use of wireless capsule endoscopy (WCE) in the investigation of 11 patients with suspected intestinal BS.

Methods. Out of 11 patients, 10 with suspected intestinal BS were found to have small intestinal ulcers on capsule endoscopy. Each case was retrospectively assessed for symptoms, signs, anaemia, other investigations, treatment and complications.

Results. All 11 patients had established diagnoses of BS as defined by the International Study Group criteria. Central abdominal pain and change in bowel habit were the predominant symptoms occurring in seven patients. Upper gastrointestinal (GI) endoscopy and colonoscopy identified duodenitis, ileitis, and colitis in three patients. Barium studies and CT were normal in all cases. WCE revealed small intestinal ulcers throughout the ileum in five patients and ulcers located either in the proximal and/or distal ileum in five other patients. One patient had significant symptoms, signs and ulcers leading to a change in treatment to infliximab, and this resulted in resolution of symptoms and ulcers. Ten age- and sex-matched controls investigated for unexplained GI symptoms had no intestinal lesions on capsule endoscopy.

Conclusion. WCE is useful in the investigation of GI symptoms in BS. It is particularly helpful in those patients in whom conventional investigations have been normal or fail to account for symptoms and signs. This technique may guide treatment and provide a better understanding of intestinal pathology in BS.

Key words: Behçet’s syndrome, Intestine, Wireless capsule endoscopy.

Introduction

Behçet’s syndrome (BS) is a multi-system condition of unknown aetiology, characterized by recurrent oral ulcers, genital ulcers, uveitis, skin lesions and pathergy [1]. Gastrointestinal (GI) disease outside the oral cavity is well recognized, and usually takes the form of small intestinal ulcers, with the most significant lesions occurring in the ileo-caecal region [2]. Patients often complain of nausea, vomiting, colicky abdominal pain and change in bowel habit. Diagnosing GI BS has previously been hindered by limitations in imaging the small bowel. Consequently, patients may present late with life-threatening complications requiring surgery [3–5]. Furthermore many patients have unexplained abdominal symptoms which may lead to psychological distress and dissatisfaction.

Wireless capsule endoscopy (WCE) is a relatively new technique, which for other disorders has a superior diagnostic rate for small bowel pathology than conventional techniques such as push enteroscopy, barium studies and CT enteroclysis [6–11]. The utility of WCE in the investigation of GI BS is unknown. We describe a series of 10 patients that were diagnosed with intestinal BS using this technique. Clinical features, laboratory findings, results of conventional GI investigations and treatment outcomes were analysed retrospectively.

Methods

We studied 11 patients who were known to have BS and who complained of GI symptoms. They were investigated for GI disease using upper/lower endoscopy, CT, abdominal ultrasound scans and barium studies. If these investigations were normal or positive findings failed to account for symptoms and signs, then patients were referred for WCE. If patients were suspected of having sub-acute obstruction, then a patency capsule was administered prior to WCE. The clinical course for each of these patients was known since the initial diagnosis of BS. Each case was retrospectively analysed for demographic factors, clinical features, haematological (full blood count) and inflammatory indices (ESR, CRP), and results of GI investigations (endoscopy, barium studies, CT and ultrasound). Treatment outcomes and complications over a 2-yr period following diagnosis were also assessed. Ten age- and sex-matched control patients investigated for GI symptoms were included in the study for comparison. Endoscopic studies were performed by experienced gastroenterologists and radiological findings were reported by experienced radiologists. A PillCam SB video capsule (Given Imaging Ltd., Duluth, USA) was used in all cases and video images were reviewed by an experienced investigator.

Results

WCE identified small intestinal ulcers in 10 of the 11 patients investigated for GI symptoms. Of those with small intestinal lesions, five patients were males and five females, with a median age of 52 yrs (range 23–61 yrs). All patients had established diagnoses of definite BS, as defined by the International Study Group criteria (Table 1) [1]. Disease duration ranged from 3 to 33 yrs (median duration of 4 yrs). ESR and CRP were normal in all cases. No patient was taking NSAIDs during the period of GI symptoms or investigations. Central abdominal pain and change in bowel habit were the predominant symptoms, with both occurring in seven patients (Table 2). Significant weight loss, anaemia and bleeding occurred infrequently. Physical examination was normal in all cases.

Upper GI endoscopy demonstrated duodenal erosions in one patient (Patient 4). Colonoscopy identified abnormalities in only two patients, showing terminal ileitis and sigmoid colitis in Patients 6 and 7, respectively. Abdominal ultrasonography and computerized tomograms were normal in all cases and five
patients had barium studies of the small intestine which were also normal. Capsule endoscopy revealed ulcers of varying size and location (Fig. 1). Small (<0.5 cm) superficial 'punched' ulcers were the main type of lesion and were located throughout the ileum in five patients (patients 3–5, 7 and 10). In contrast to a previous study, distal ulcers occurred less frequently [3]. Two patients had ulcers exclusively in the proximal ileum (Patients 2 and 9), and two other patients had ulcers in the proximal and distal ileum with sparing of the mid-ileum (Patients 1 and 6). One patient had ulcers in the proximal and mid-ileum with relative sparing of the distal ileum. In two cases (Patients 5 and 6), capsule endoscopy identified small gastric ulcers and duodenal erosions that were not diagnosed on upper GI endoscopy.

One patient (Patient 2, Fig. 2) had sufficiently severe symptoms, signs and coexisting large, proximal ileal ulcers to warrant a change in treatment to infliximab (3 mg/kg). This resulted in complete improvement in abdominal symptoms by 3 months and a change in treatment to infliximab (3 mg/kg). This resulted in complete improvement in abdominal symptoms by 3 months and a change in treatment to infliximab (3 mg/kg).

In the remaining patients with small intestinal ulcers, symptoms were not sufficiently major to warrant a change or ‘step up’ in immunosuppression. No patient required hospital admission for symptoms nor were there any life-threatening complications over a 2-yr period following diagnosis of intestinal BS. There were no ulcers on capsule endoscopy in the age-matched control group that comprised 10 patients investigated for unexplained GI symptoms. These control patients were subsequently diagnosed as having functional bowel disease [five males and five females, median age 45 yrs (range 27–58 yrs)].

**Discussion**

We have described a series of 10 patients with BS in whom GI symptoms remained unexplained by conventional barium and endoscopic studies. However, further investigation with WCE identified the presence of small intestinal ulcers leading to a diagnosis of intestinal BS. To our knowledge this is the first series of patients diagnosed with intestinal BS using WCE. At present we have not screened asymptomatic BS patients with WCE, and therefore the frequency of ‘silent’ or subclinical ulcers in BS is unknown.

Intestinal BS can be a difficult diagnosis to establish, and may only be made upon the development of complications such as...
FIG. 1. Capsule endoscopy revealing ulcers of varying size and location.

Patient 3: Multiple, small punched-out ulcers (left), ulcer with surrounding erythema (right).

Patient 5: Punched-out ulcers with surrounding erythema.

Patient 7: Multiple, small 'punched' ulcers.

FIG. 2. Large ulcers with surrounding erythema (Patient 2).
perforation or fistulae [4, 5]. The severity and frequency of intestinal BS varies amongst different populations, with the highest occurrence reported in those of Japanese origin [12]. Macroscopically, the mucosal surface has a punched, ovoid appearance with surrounding areas of erythema, ‘skip’ areas and oedema. Microscopically lesions often demonstrate non-specific inflammatory changes with venulitis, with an appearance that differs from intestinal Crohn’s disease, the main differential diagnosis for intestinal BD [2].

Well-established imaging techniques of the small intestine, such as barium studies, push enteroscopy and CT enteroclysis have limited sensitivity and specificity in identifying small intestinal pathology, particularly superficial mucosal lesions. In addition, barium studies are poorly tolerated and may be difficult to interpret. WCE is proving to be superior to previous imaging techniques in diagnosing small bowel pathology, including intestinal Crohn’s disease and unexplained GI bleeding [6–11]. It has an overall false-negative rate of 11% (0.5% for ulcerative lesions and 18% for neoplastic lesions), which is a marked improvement over other techniques, and this can be attributed to many factors including small bowel preparation and cleanliness prior to WCE [13]. Furthermore, follow-up studies have shown that findings by WCE are reproducible [14–16]. Capsule retention and impaction are the main complication with an overall risk of 1%. Therefore, patients suspected of having small bowel strictures are advised to have a ‘patency capsule’ which is a sham, radiopaque capsule equal in size to the diagnostic capsule and which dissolves following impaction [17].

In our series of patients, GI investigations such as endoscopy and barium studies had failed to identify a cause for symptoms whereas WCE revealed intestinal ulcers. Previous studies of intestinal BS have described a predominance of ulcers in the distal ileum [3–5]. However, the findings in these studies have to be interpreted with caution as older conventional endoscopic techniques were employed and post-operative surgical specimens were utilized. Hence these studies were more likely to miss lesions in the proximal and mid-ileal regions and more likely to over-represent the more severe lesions in surgical specimens. In contrast, our findings from capsule endoscopy suggest a predominance of lesions throughout the ileum, including those in the proximal as well as the distal regions.

Intestinal BS is often resistant to conventional medical therapy and consequently difficult to treat [12]. Lesions often recur following intestinal resection for surgical complications, despite immunosuppression [5]. Recently, anti-TNF agents and autologous stem-cell transplantation have been shown to be promising approaches for the treatment of GI BS [18, 19]. In our series, knowledge of intestinal ulcers in one patient with significant symptoms resulted in a switch in treatment to infliximab, which led to complete resolution of symptoms and ulcers, as determined by follow-up capsule endoscopy at 12 months. Hence, WCE may also be useful in guiding treatment and monitoring intestinal disease activity as well as diagnosing intestinal BS. The remaining patients with intestinal BS had mild symptoms, signs and lesions which did not warrant further treatment. Symptoms and signs in these patients had spontaneously improved at follow-up at 2 yrs.

In summary, this small study has demonstrated that capsule endoscopy is useful in the investigation and diagnosis of intestinal BS and in some cases may aid therapeutic decisions. It should be considered in those patients with intense GI symptoms and/or anaemia, which remain unaccounted for by conventional bi-directional endoscopy and radiological investigations.

In addition to enabling early diagnosis before life-threatening complications develop, capsule endoscopy may assist the patient psychologically and improve satisfaction, by accounting for symptoms that would normally be unexplained. Further prospective studies are warranted to determine the full utility of this technique and to provide a better understanding of intestinal BS.

Rheumatology key messages

- WCE is useful in the investigation of unexplained GI symptoms in BS.
- Capsule endoscopy may provide a better understanding of intestinal pathology in BS.

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References