Crohn's Disease Diagnosed by Wireless Capsule Endoscopy in Adolescents with Abdominal Pain, Protein-Losing Enteropathy, Anemia and Negative Endoscopic and Radiologic Findings

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Key words: Crohn's disease, wireless capsule endoscopy, diagnostic modalities, adolescents

Abstract

Background: Approximately one-fourth of new Crohn's disease diagnoses are made in individuals under the age of 20 years, in whom proximal Crohn's disease tends to be more common.

Objectives: To describe the role of wireless capsule endoscopy in diagnosing isolated small intestinal Crohn's disease in two adolescents.

Methods: Wireless capsule endoscopy was performed in two adolescents with severe protein-losing enteropathy and negative standard diagnostic workup.

Results: Wireless capsule endoscopy successfully diagnosed Crohn's disease with uncharacteristic presentations and negative radiographic and endoscopic findings in both patients.

Conclusions: The non-invasiveness and ease in performance of capsule endoscopy on an ambulatory basis make this diagnostic modality especially advantageous for children.

IMAJ 2005;7:216–218

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Crohn's disease is a chronic granulomatous disease that may involve any area along the gastrointestinal tract. The small bowel is involved in 80% of cases, with the terminal ileum being the most frequently affected segment [1]. Approximately 25% of new CD diagnoses are made in individuals under the age of 20 years, in whom proximal CD tends to be more common and often presents with abdominal pain and malaise [1,2].

The definitive diagnosis of CD has traditionally relied on barium radiography, endoscopy of reachable parts of the digestive tract, and histopathology. However, the diagnosis may be reached only after a long delay due to its insidious onset and the insufficient sensitivity of current diagnostic tools [3]. Several diagnostic methods were introduced over the past two decades, among them ^{99m}Tc leukocyte scintigraphy [4] and Doppler ultrasound [5]. These methods, however, provide indirect evidence of bowel inflammation and with various degrees of sensitivity or specificity.

The recently developed wireless capsule endoscopy allows for endoscopic imaging of the entire small bowel without procedure discomfort [6]. WCE appears to be superior to both small bowel radiography and push enteroscopy in diagnosing small bowel diseases [7–12]. We describe two adolescents with long-standing protein-losing enteropathy in whom a standard radiologic and endoscopic workup detected no abnormalities. WCE diagnosed small bowel CD in each patient.

Methods and Results

Patient 1

A 13 year old boy presented with abdominal pain of more than 2 years duration but without fever or diarrhea. Laboratory tests revealed iron and vitamin B12 deficiency anemia, prominent hypoproteinemia (serum albumin 1.9 g/dl) without proteinuria, and markedly elevated stool alpha-1-antitrypsin. Erythrocyte sedimentation rate, C-reactive protein and all other laboratory tests (electrolytes, liver function and kidney function profiles) were normal. Anti-endomysial and antigliadin antibodies were negative. Multiple gastroscopies revealed only *Helicobacter pylori*-positive gastritis, which was successfully treated. Colonoscopy, including ileoscopy with multiple biopsies, was normal. Push enteroscopy visualized approximately 100 cm of the jejunum and demonstrated normal mucosa. Biopsy results were inconclusive, showing only mild neutrophilic infiltration and lymphoid hyperplasia. Ultrasound and small bowel follow-through were normal. ^{99m}Tc leukocyte scintigraphy demonstrated mildly increased leukocyte uptake in the distal small bowel. After abdominal computed tomography revealed abdominal lymphadenopathy, the patient underwent laparoscopy, which demonstrated only reactive lymph nodes by histology.

Wireless capsule endoscopy demonstrated multiple aphthous and linear ulcers with surrounding edema and erythema, starting from the mid-jejunum and continuing along the entire small bowel [Figures 1 and 2], whose lumen appeared narrowed in several areas. This endoscopic picture was compatible with CD of the small bowel. Treatment with 5-aminosalycilic acid and

CD = Crohn's disease

WCE = wireless capsule endoscopy

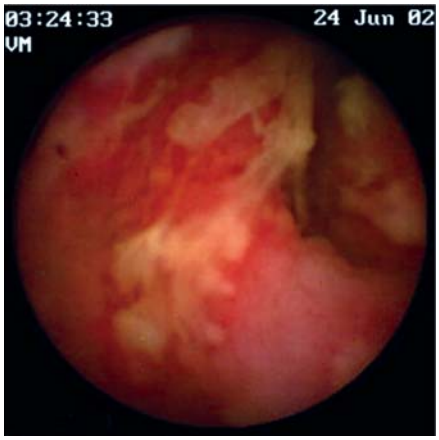

Figure 1. Patient 1: The capsule is seen entering a narrowed area with surrounding geographic ulceration.

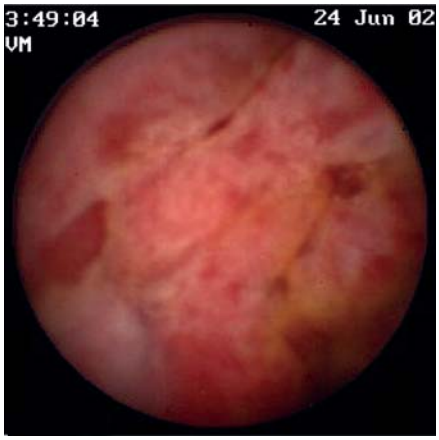

Figure 2. Patient 1: Evidence of extensive ulceration with small bowel stricture. The capsule passed easily.

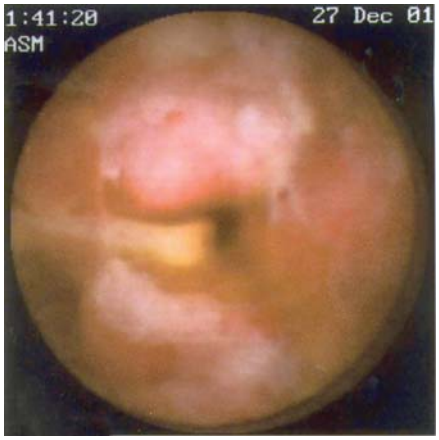

Figure 3. Patient 2: Visual documentation of inflammation, ulceration and near total obliteration of lumen.

prednisone was initiated, and the response was dramatic; the abdominal pain disappeared and blood albumin and hemoglobin levels normalized.

Patient 2

A 14 year old boy presented with unexplained abdominal pain of 1 year duration. Physical examination revealed facial and leg edema and a diffusely tender abdomen with no peritoneal signs. Laboratory tests showed iron deficiency anemia, hemoglobin 10.8, normal C-reactive protein and erythrocyte sedimentation rates and hypoproteinemia 2.3 g/dl without proteinuria. Anti-endomysial and antigliadin antibodies were negative. Multiple stool samples were negative for cultures and parasites. Stool alpha-1-antitrypsin was markedly elevated. The results of multiple gastroscopies, colonoscopies with ileoscopy and biopsies, and small bowel follow-through were normal. Two enteroscopies with visualization of ~100 cm of the jejunum were normal with normal biopsies. ^{99m}Tc leukocyte scintigraphy revealed increased uptake in the terminal ileum region. Small bowel CD was suspected, with partial response to treatment with 5ASA and budesonide. The albumin rose to 3.6 g/dl, but all symptoms reappeared with reduction of albumin after discontinuation of budesonide. WCE revealed multiple linear ulcers in the deep jejunum and ileum with areas of intervening normal mucosa [Figure 3], an endoscopic picture compatible with CD of the small bowel. Treatment with 6-mercaptopurine yielded a good clinical response, with normalization of blood albumin and hemoglobin levels.

Discussion

These two cases are unique for their clinical presentation of protein-losing enteropathy as the main manifestation of CD and for demonstrating the efficacy of capsule endoscopy in diagnosing adolescents in whom the clinical manifestation was atypical and the radiographic/endoscopic findings failed to provide definitive diagnosis.

PLE encompasses a wide range of gastrointestinal disorders associated with excessive losses of plasma protein into the gut lumen [13]. The two major pathogenic factors associated with PLE are lymphatic obstruction and mucosal erosion or ulceration. Both the increased permeability of the intestinal mucosa to plasma proteins and the loss of inflammatory protein-rich exudates into the intestinal lumen have been described in CD patients, as well as a clinical presentation dominated by severe nutritional disturbances, including PLE [13,14]. The differential diagnosis is complicated by the wide variety of other intestinal diseases that can produce inflammation and ulceration of the gastrointestinal mucosa.

CD is mainly diagnosed by endoscopic and radiologic studies of the bowel, but results may be negative in early stages. Recent clinical studies exhibited the superiority of WCE over barium X-rays, push enteroscopy and other imaging methods in diagnosing a range of diseases of the small intestine [7–10,15]. A comparison of the accuracy of WCE to barium follow-through examination and CT in 20 patients suspected of having CD showed that capsule endoscopy not only detected all the lesions diagnosed by CT and barium, but found 47% more lesions undetected by them and also ruled out 16% of lesions suspected by them [16]. Fireman et al. [17] found that WCE had a high efficacy for definitive diagnosis in 12 of 17 patients suspected of having Crohn's unconfirmed by standard modalities. Focal villous denudation, a condition sometimes seen in the small intestinal mucosa and a very early sign of CD, was detected by capsule endoscopy and not by any other diagnostic modalities. Sant'anna and colleagues [18] used WCE in nine children suspected of having small bowel disorders in whom standard radiologic examinations were not diagnostic. In all these reports, the capsule was highly effective in diagnosing obscure small intestinal disease, it was well tolerated and there were no complications. The yield of WCE versus ^{99m}Tc leukocyte scintigraphy in diagnosing small bowel Crohn's disease has never been studied. However, the latter exposes patients to radiation. Moreover, it demonstrates only non-specific inflammation and does not provide

5-ASA = 5-aminosalycilic acid

PLE = protein-losing enteropathy

small bowel mucosal details. Therefore, we believe that WCE may provide a more definitive diagnosis. One concern with this modality is that the capsule will be lodged in an intestinal stricture. This, however, may be circumvented by performing a small bowel series or enteroclysis prior to WCE to confirm normal lumen.

In conclusion, wire capsule endoscopy was demonstrated to be effective in establishing the diagnosis of Crohn's disease in two adolescents who presented with protein-losing enteropathy, abdominal pain, anemia and negative radiographic and endoscopic findings. WCE has significant advantages in children because it is a non-invasive procedure, the capsule is easy to swallow and the evaluation can be performed on an ambulatory basis. Therefore, it may be considered as the test of choice in young patients suspected of having Crohn's, particularly in those with negative radiographic and endoscopic findings.

Acknowledgment. We thank Esther Eshkol for editorial assistance.

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