# Capsule Endoscopy in Crohn's Disease

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For many decades the small intestine was at the "dark side" of the gastrointestinal tract. Unlike the stomach and the colon, which could be perfectly visualized, only a small portion of the proximal small intestine (up to 150 cm) could be visualized endoscopically. Small bowel follow-through and computerized tomographic enterography are considered the two main available modalities for the evaluation of the entire small bowel. Studies on the yield of SBFT in the diagnosis of Crohn's disease have reported a variety of results: some disappointing, and others reporting a sensitivity up to 90% [1–5]. CT enterography is now considered superior to SBFT in severe active disease, but its role in early CD remains to be determined. [6]. The novel technique of wireless capsule endoscopy is a great step forward in detecting small bowel pathologies. In 2003 the U.S. Food and Drug Administration indicated that capsule endoscopy may be considered the appropriate first-line test in the evaluation of small bowel diseases. It rapidly became the test of choice and has revolutionized the evaluation of obscure small bowel bleeding; however, its role in the diagnosis of CD is still not well established.

In this issue of *IMAJ*, Barkay et al. [7] report two cases of adolescents with severe protein-losing enteropathy as the clinical presentation of CD. The entire gamut of radiologic and endoscopic investigations showed normal anatomy, rendering the potential diagnosis of CD to be unlikely. Tc-99m labeled leukocyte scintigraphy demonstrated an increased uptake in the distal small intestine and the terminal ileum, although ileoscopy was negative in both cases. Based on the presence of multiple aphthous and linear ulcers with marked mucosal edema and erythema with areas of intervening normal mucosa, WCE confirmed the suspected diagnosis of CD in these two cases. The loss of mucosal integrity throughout the entire small bowel can potentially lead to protein-losing enteropathy [8,9]. The differential diagnosis is large and CD is considered one of the possible etiologies, especially in adolescents. Anemia attributed to deficiency of either iron or the combination of iron and vitamin B12 was reported in the two cases as well; therefore, protein-losing enteropathy was not the sole clinical manifestation in these two cases. These two deficiencies are considered a clear indication for WCE in cases with a negative thorough workup.

Several series have been published regarding the utility of capsule endoscopy in the diagnosis of CD. While some included patients with suspected CD, others found CD to be the causative etiology in patients who were evaluated primarily for obscure bleeding. Fireman et al. [10] reported a 71% yield in diagnosing small intestinal CD using WCE. Among 17 patients with clinical suspicion of the disease and negative conventional workup, 12 were found to harbor lesions consistent with CD. The majority of the lesions were detected in the distal small bowel. Notably, in 6 of the 12 patients with positive capsule findings, the terminal ileum had not been intubated at colonoscopy. Although these patients were treated for CD, details on long-term follow-up were not provided. Eliakim and colleagues [11] studied 20 patients in whom CD was suspected based on abdominal pain, diarrhea and weight loss. Lesions were found in 14 of 20 patients, and included ulcers and erosions (36%), erythema (22%), aphthae (17%), absent or blunted villi (14%), and nodular lymphoid hyperplasia (5.6%). Herrerias and team [12] studied 21 patients with diarrhea and abdominal pain, identifying findings "compatible" with CD in 9 of them. Tabibzadeh et al. [13] used WCE to evaluate the extent of small intestinal CD in patients previously diagnosed with ileitis only. More than 50% of those patients were found to have proximal lesions as well. The various ranges of WCE diagnostic yield reported in these studies could be explained by the use of different levels of clinical suspicion for CD. WCE was used for the study of patients with verified CD. Chong and associates [14] found positive lesions compatible with CD in 17 of 22 patients with CD. In another study, only 25 of 41 known CD patients had positive findings on WCE examination. [15]. On the other hand, WCE was found to be useful in the diagnosis of CD of the small bowel in patients known to have Crohn's colitis or indeterminate colitis [16].

The most important issue regarding the diagnostic yield of WCE in CD is the interpretation of the various findings. The landmarks for the diagnosis of CD are based on long-term experience with the available endoscopic procedures and/or radiologic criteria. Nevertheless, there are no universal accepted definitions of endoscopic diagnosis of CD. The diagnosis of CD by WCE in the aforementioned studies was based on the presence of lesions considered

SBFT = small bowel follow-through
CD = Crohn's disease
WCE = wireless capsule endoscopy

characteristic for the diagnosis. Are all mucosal breaks/aphthae or ulcers seen in the small bowel due to CD? Indeed, in normal volunteers not taking non-steroidal anti-inflammatory drugs, Goldstein and co-workers [17] reported the presence of "mucosal breaks" in 23% of subjects at baseline capsule endoscopy. Furthermore, in 7% of the subjects treated with placebo (as compared to NSAIDs) "new" lesions "developed" during follow-up. Using WCE for the evaluation of patients with arthritis, Graham et al. [18] found a prevalence rate of 17% of small bowel mucosal lesions in the group of patients not using NSAIDs. It is therefore apparent that the findings of small mucosal breaks or even other descriptive pathologies may be common in the small bowel and are unlikely to have any clinical significance. The diagnosis of CD based on the presence of small lesions should therefore be regarded with caution before labeling patients with this life-long disease. A standard terminology is indeed mandatory. Voderholzer et al. [15] suggested that a minimum of 10 aphthous lesions is strongly suggestive of CD, while those patients with one or two lesions are less likely to be diagnosed with CD. Other studies should confirm such definitions.

The diagnosis of CD remains a challenge. The presentation of the disease varies, and WCE appears to serve as a valuable tool in detecting intraluminal lesions, including early stages of CD. It may have a role in assessing the extent of the disease as well. In addition to the clear indications for WCE, protein-losing enteropathy may be yet another indication for the use of this diagnostic modality.

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