ANNALS OF GASTROENTEROLOGY 2008, 21(1):59-62

Case report

Diagnosing a Patient With Severe and Protracted Diarrhea due to Celiac Disease: When And How Should Capsule Endoscopy Be Used?

K. Soufleris, G. Chatzimavroudis, I. Stergiou, C. Zavos, I. Vasiliadis, I. Kapitsinis, I. Triantafillidis, P. Tsolkas, P. Katsinelos

SUMMARY

We present the case of a 68 year-old man with renal failure and metabolic acidosis due to severe and chronic protracted diarrhea. Previous examinations, including IgA AGA and IgA tTG, endoscopy, and duodenal biopsies, were inconclusive. Wireless capsule endoscopy (WCE) of the small bowel showed flattened and scalloped folds and a characteristic mosaic pattern of the entire small intestine, consistent with the diagnosis of celiac disease (CD), which was also confirmed with a positive examination for antiendomysial antibodies. A gluten-free diet led to gradual clinical improvement. The case underscores the emerging role of WCE in the diagnosis of celiac disease in light of the recent evidence provided by relevant studies.

Key-words: Celiac disease, wireless capsule endoscopy, diagnosis, management

INTRODUCTION

Celiac disease (CD) is the most frequent enteropathy in the Western world.[1] Despite advances in serologic examinations and accurate classification in histological and endoscopic findings, its diagnosis remains challenging in the majority of cases.[2] The celiac iceberg is characterized by the fact that, for every patient diagnosed, three to seven patients remain undiagnosed.[3] It would be interesting to see whether wireless capsule endoscopy (WCE), as a new modality, with a mere six years of published history, can expand its spectrum of indications in the field of CD. The ability of WCE to depict detailed images of the whole small intestinal mucosa allows the gastroenterologist to detect both the nature and the extent of mucosal changes in CD that was previously not possible.[4] WCE is better tolerated than gastroscopy and researchers are trying to explore whether this newly embedded technology could overcome the caveats of traditional diagnostic tools in the field of CD. Our case demonstrates the potential value of WCE in diagnosing CD in a particular clinical setting.

Department of Endoscopy and Motility Unit, Central Hospital, Thessaloniki, Greece

Author for correspondence:

Dr. Panagiotis Katsinelos, Head, Department of Endoscopy and Motility Unit, Central Hospital, Ethnikis Aminis 41, Thessaloniki, Greece, Tel: 0030-2310-211221, Fax: 0030-2310-210401, E-mail: gchatzimav@yahoo.gr

CASE DESCRIPTION

A 68 year-old male patient was urgently admitted to our hospital due to severe watery diarrhea, weakness, significant weight loss and impaired level of consciousness. Physical examination revealed a cachectic man with apparent signs of dehydration and no palpable lymphadenopathy. Laboratory examinations revealed anemia, hypoalbuminaemia, metabolic acidosis and severe renal function impairment with creatinine levels up to 5.4 mg/dL. The impaired renal function was rapidly restored with crystalloid fluids and albumin infusions. He had had no abdominal surgery, had an unremarkable family history and had been receiving medication for arterial hypertension and mild diabetes. During the last four years, the symptoms of his present admission had led to a series of hospitalizations in different hospitals and numerous examinations but no established diagnosis. It should be emphasized that the continuously deteriorating severity of symptoms led to these repeated hospital admissions where resuscitation with fluids had led to temporary improvement. His extensive record included abdominal computed tomography

and magnetic resonance imaging (MRI), upper and lower endoscopy, duodenal biopsies, hormonal testing and a thorough search for infectious and autoimmune disorders, including immunoelectrophoresis, which were all inconclusive. In one of the several admissions to different hospitals an MRI exam of the thorax suggested the existence of a mediastinal thymoma. This incorrect diagnosis combined with inconclusive laboratory and histologic findings led to the consideration of the thymoma as the cause of chronic diarrhea. An operation was suggested, but he declined. After a successful resuscitation with fluids and electrolytes, a decision was made to proceed with wireless capsule endoscopy of the small intestine. The examination showed flattened (Fig.1) and scalloped (Fig.2) folds and a mosaic appearance of almost the entire intestinal mucosa (Fig.3), consistent with the diagnosis of celiac disease. Although previous serologic examinations of antigliadin (IgA AGA), and tissue transglutaminase (IgA tTG) antibodies were in the normal range, a repeated examination of antiendomysial (IgA EMA) antibodies was positive this time, thus confirming the diagnosis. The patient was discharged on a gluten-free diet and, as a result, he has remained asymptomatic ever since for at least three months of regular follow-up visits.

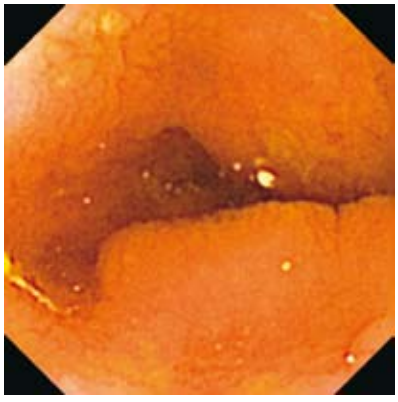

Figure 1. WCE showing flattened upper jejunal folds.

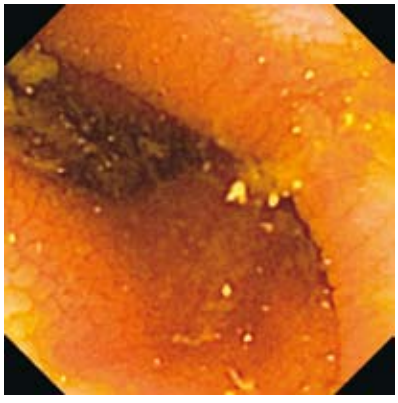

Figure 2. WCE view of scalloped jejunal folds.

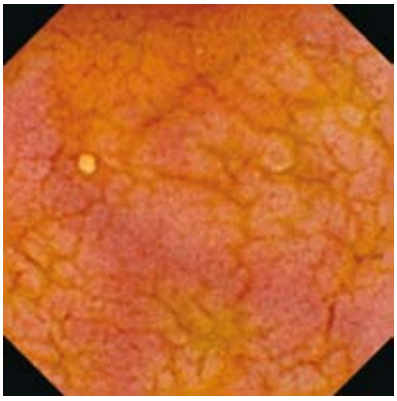

Figure 3. Diffuse mosaic appearance of intestinal mucosa.

DISCUSSION

CD is now considered a common disease with an estimated prevalence of 0.7-2.0% in studied western populations.[5] Interestingly, a recent population study in central Greece showed a much lower prevalence of 0,18%.[6] Recent concepts of the pathogenesis of CD assume that gluten intolerance in genetically predisposed individuals causes immune mediated damage to small bowel mucosa.[7] The histological changes characterizing the disease are an increased number of intraepithelial lymphocytes, crypt hyperplasia, and various degrees of villous atrophy.[8] Atypical presentations, such as iron deficiency anemia, osteoporosis, and neurologic disorders, begin to dominate over the classic presentation of severe diarrhea with malabsorbtion.[9] Moreover, it is increasingly being diagnosed incidentally during endoscopy performed for indications such as dyspepsia or gastroesophageal reflux. The endoscopic findings of CD are now established and have demonstrated a high sensitivity and specificity, possibly assisted by auxiliary techniques such as immersion and magnification endoscopy.[10] The presence of reduced duodenal folds, scalloping, fissures, mosaic pattern, and nodularity should be recognized by the endoscopist regardless of the indication. However, real life clinical practice shows a missed diagnosis in a surprisingly high number of cases.[11]

Serologic testing, usually being the first test ordered when CD is suspected, has a well-defined diagnostic role. Antigliadin and antireticulin antibodies tend to be abandoned because of their low accuracy compared to antiendomysial and tissue transglutaminase antibodies.[12] Indeed

IgA EMA and IgA tTG demonstrate specificity that almost equals 100% and sensitivity in the range of 95-96%. However, some limitations exist as these results were seen in high-probability populations, and they should be interpreted with caution when applied to the general population, especially in regions with a possibly lower prevalence such as Greece, or patients with lower degrees of atrophy, which have not been adequately studied thus far. In addition, technical expertise might also play a role as the tests are performed slightly differently depending on the substrate used (human/guinea pig) and there is little, but visible, variation among studies.[13]

Inevitably, positive serologic assays require histological confirmation.

A properly performed duodenal biopsy remains the gold standard for the diagnosis mandating endoscopy with biopsies in virtually all suspected cases. Nevertheless, the assumed cornerstone of the diagnosis of CD also suffers from certain disadvantages. Endoscopy is invasive, although minimally, and, therefore, feared by some patients. The patchy nature of the disease could create confusion as seen from cases where lesions are present in the jejunum but not in the duodenum.[14] In addition, duodenal biopsy can be demanding in terms of orientation and adequate sampling.[15]

Recent implementation of the technology of WCE in small bowel diseases has raised the question of its utility in CD. A recent ICCE consensus has proposed that, at the moment, WCE represents a reliable alternative in people unwilling or unable to undergo routine endoscopy.[16] This statement was the result of several preliminary studies verifying its accuracy and demonstrating impressive rates of interobserver agreement.[17,18] Not surprisingly, the first cases to be studied were those of refractory sprue in which WCE displayed its efficacy in defining complications such as lymphoma or adenocarcinoma of the small intestine.[19] WCE of the patient described was also helpful in this sense, as no endoscopic signs indicative of enteropathy associated T-cell lymphoma (EATL) were found. The undisputed advantages of capsule endoscopy offering higher magnification, paucity of insufflation, and examination of the whole length of the intestinal mucosa along with its noninvasive nature have driven researchers of this field to evaluate its role in discovering new cases. The study by Hopper et al. shows very promising results with the positive and negative predictive value being 100% and 88.9%, respectively.[20] The larger multicenter study by Rondonotti et al. corroborates these results and also implies a correlation between length of damaged mucosa and severity of symptoms, although not statistically significant.[21]

The case reported herein highlights the limitations and difficulties of the traditional diagnostic tools in celiac disease in everyday situations. The serology was not performed perfectly, which is rare but not impossible. Histology was equivocal in the case of our patient allowing various interpretations. In fact review of the histological findings by an experienced pathologist showed findings compatible with celiac disease but insufficient per se to establish the diagnosis in this case. Nevertheless, we were prepared to submit the patient to yet another endoscopy with biopsies, in view of the high clinical suspicion. His reluctance to proceed with the procedure, probably as a result of previous inconclusive endoscopies along with his frail clinical condition, led us to the option of WCE, which ultimately had a critical effect on the clinical course of this patient.

One should not conclude that WCE represents a panacea for the diagnosis of CD. Duodenal biopsy is still regarded as the sine qua non of the diagnosis and serologic assays are extremely sensitive and useful, especially EMA. But in the appropriate clinical context, WCE serves as an invaluable tool contributing significantly to the management of suitable patients.[22] One important limitation that remains to be addressed is a cost effectiveness analysis which should be included in future studies. Another issue to be determined is the correlation between WCE findings with histology, especially in mild and moderate degrees. The significance of the variable length of involvement of the intestine is still unclear. It is somewhat intuitive that the larger the amount of the intestine involved, the sicker the patient may be, as in our case, but this awaits scientific confirmation.

Conclusively further studies are necessary - and are indeed under way - to delineate the exact role of WCE in the diagnosis and management of patients with CD.[23] Until then, the clinical scenario, case by case, will determine which set of diagnostic tools will be appropriate; nevertheless, the findings suggest that WCE is an attractive option for patients and physicians.

REFERENCES

1. Corazza GR, Andreani ML, Biagi F, et al. The smaller size of the “coeliac iceberg” in adults. Scand J Gastroenterol 1997;32:917–9.
2. Lee SK, Green P. Endoscopy In Celiac Disease. Curr Opin Gastroenterol 2005:21;589-594.
3. Rewers M. Epidemiology of celiac disease: What are the prevalence, incidence, and progression of celiac disease? Gastroenterology 2005;128:S47–51.
4. Murray JA, Brogan D, Van Dyke C et al. Mapping the extent of untreated celiac disease with capsule enteroscopy, Gas-

trointest Endosc 2004:59;AB101
5. Fasano A, Berti I, Gerarduzzi T et al. Prevalence of celiac disease in at-risk and not-at-risk groups in the United States: a large multicenter study. Arch Intern Med 2003;163:286-292.
6. Roka V, Potamianos SP, Kapsoritakis AN, et al. Prevalence of coeliac disease in the adult population of central Greece. Eur J Gastroenterol Hepatol 2007; 19: 982-7.
7. Kagnoff MF. Overview and pathogenesis of celiac disease. Gastroenterology 2005;128:S10–8.
8. Oberhuber G, Granditsch G, Vogelsang H. The histopathology of celiac disease: Time for a standardized report scheme for pathologists. Eur J Gastroenterol Hepatol 1999;11:1185–94.
9. Green PHR. The many faces of celiac disease: Clinical presentation of celiac disease in the adult population. Gastroenterology 2005;128:S74–8.
10. Gasbarrini A, Ojetti V, Cuoco L et al. Lack of endoscopic visualization of intestinal villi with the "immersion" technique in overt atrophic celiac disease. Gastrointest Endosc 2003; 57:348-351.
11. Harewood CG, Holub JL, Liebermann DA. Variation in small bowel biopsy performance among diverse endoscopy settings: results from a national endoscopic database. Am J Gastroenterol 2004; 99:1790-1794.
12. American Gastroenterological Association (AGA) technical review on the Diagnosis and Management of Celiac Disease. Gastroenterology 2006; 131: 1981-2002.
13. Rostom A, Dub`e C, Cranney A, et al. The diagnostic accuracy of serologic tests for celiac disease: A systematic review. Gastroenterology 2005;128:S38–46.
14. Thijs WJ, van Baarlen J, Kleibeuker JH et al. Duodenal versus jejunal biopsies in suspected celiac disease. Endoscopy 2004;36:993-996.
15. Rondonotti E, de Franchis R. Diagnosing coeliac disease: is the videocapsule the suitable tool? Dig Liver Dis 2007; 39: 145-147.
16. Cellier C, Green PH, Collin P, et al. ICCE Consensus for celiac disease. Endoscopy 2005;37:1055–9.
17. Petroniene R, Dubcenco E, Baker JP, et al. Given capsule endoscopy in celiac disease: Evaluation of diagnostic accuracy and interobserver agreement.AmJ Gastroenterol 2005;100: 685–94.
18. Biagi F, Rondonotti E, Campanello J et al. Videocapsule endoscopy and histology for small bowel mucosa evaluation: a comparison performed by blinded observers. Clin Gastoenterol Hepatol 2006;4:998-1003.
19. Culliford A, Daly J, Diamond B, et al. The value of wireless capsule endoscopy in patients with complicated celiac disease. Gastrointest Endosc 2005;62:55–61.
20. Hopper AD, Sidhu R, Hurlstone DP, et al. Capsule endoscopy: An alternative to duodenal biopsy for the recognition of villous atrophy in Coeliac Disease? Dig Liver Dis 2007;39:140–4.
21. Rondonotti E, Spada C, Cave D et al. Videocapsule enteroscopy in the diagnosis of celiac disease: a multicenter study. Am J Gastroenterol 2007; 102:1 8.
22. Sidhu R, Sanders DS, Kapur K et al. Capsule endoscopy changes patient management in routine clinical practice. Dig Dis Sci 2007; 52:1382-6.
23. Green PH, Rubin M. Capsule endoscopy in celiac disease: diagnosis and management. Gastrointest Endosc Clin N Am 2006;16:307-16.