ADVANCES IN ENDOSCOPY

Current Developments in Diagnostic and Therapeutic Endoscopy

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The Use of Endoscopic Procedures in the Management of Celiac Disease

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G&H What are the prevalence and pathophysiology of celiac disease?

PG Celiac disease is a very common condition. Serologic screening studies have shown that celiac disease occurs in approximately 1% of the population worldwide, both adults and children.

Celiac disease occurs due to the interaction of genetic, immunologic, and environmental factors that affect the body's reaction to dietary gluten, the protein component of wheat, rye, and barley. Individuals susceptible to celiac disease have the human leukocyte antigen–DQ2 or -DQ8 genes, but although these genes are necessary, they account for less than 50% of the genetic influence. Other involved genes have yet to be confirmed.

Possible environmental factors include gastrointestinal infections in childhood, whether the patient was breast-fed, and the timing of gluten introduction in relationship to weening. These factors can converge in susceptible individuals during the development of an inflammatory, destructive lesion in the small intestine. The digestion of gluten is incomplete, leaving large toxic fragments that enter the lamina propria, probably during infections, and set off an immune reaction. This results in villous atrophy, intraepithelial lymphocytosis, and crypt hyperplasia, the pathologic manifestations of celiac disease.

G&H What are the presenting symptoms of celiac disease?

PG The clinical presentation is very diverse, and nongastrointestinal symptoms predominate. The classic presentation of diarrhea, malabsorption, and weight loss has been replaced by multiple other more common presentations, which include iron deficiency anemia, osteoporosis, and irritable bowel syndrome. There are also neurologic presentations such as peripheral neuropathy, migraine, and ataxia, as well as nonspecific gastrointestinal symptoms such as dyspepsia. The single greatest presentation is diarrhea, but it accounts for less than 50% of the presentations currently.

G&H What is the role of endoscopy in the screening and management of celiac disease?

PG Endoscopy plays an important role because the gold standard for diagnosis is duodenal biopsy. Patients undergo biopsy because they have abnormal serologic tests, because they have an abnormality of the duodenal mucosa noted at endoscopy, or simply because biopsy is often performed as a matter of course during endoscopy. Biopsy to detect celiac disease is taken from the ascending duodenum. The number of samples that should be taken has not been rigorously defined, but 4–6 are usually taken because celiac disease is patchy and might be missed if only 1 or 2 samples are taken. Endoscopy is also necessary to pathologically confirm a clinical response to gluten withdrawal.

There are no guidelines for follow-up biopsies in these patients, but they are frequently performed and should be conducted on a schedule that allows sufficient time for healing. Patients who are poorly responsive to gluten-free diet or who have refractory sprue or refractory celiac disease often receive many more endoscopies and biopsies. If someone is refractory to gluten-free diet, special studies have to be performed on the biopsies to determine the type of refractory celiac disease. These studies include flow cytometry, immunohistologic staining of the biopsies, and studies to determine whether there is clonal proliferation of the intraepithelial lymphocytes. The latter is the marker of Type II refractory celiac disease that is also regarded as a cryptic T-cell lymphoma.

G&H Who should undergo endoscopic screening for celiac disease?

PG It is often assumed that serologic tests are extremely accurate. They are a very powerful diagnostic tool, but are

not perfect. If there is a suspicion of celiac disease based on symptoms, even without confirmation via serologic blood tests, patients should undergo endoscopy and biopsy. Biopsy of the duodenum should be performed routinely if the indication for the procedure is weight loss, iron deficiency, or diarrhea, irrespective of the results of serologic testing.

G&H What new developments have arisen recently in the use of endoscopy in the screening and management of celiac disease?

PG The use of video capsule endoscopy is a new development in celiac disease. Capsule studies have a role in both the diagnosis and management of celiac disease. Because celiac disease is a very common condition, anyone undergoing capsule endoscopy for any indication could be examined for celiac disease. Endoscopists who perform capsule endoscopy should be aware of the varying visual manifestations of the disease because they may note them when they are performing capsule endoscopy on patients with anemia or internal bleeding. Capsule endoscopy allows visualization of the villi. Their presence or absence should be noted, as well as mucosal scalloping, mosaic appearance, and fissures, all evidence of villous atrophy. If present, these markers are a reliable indicator of atrophy. However, the lesser degrees of pathologic changes from celiac disease result in a normal capsule appearance. Thus, a normal video capsule study does not exclude celiac disease.

In addition, video capsule endoscopy can be used as a surrogate for standard endoscopy and biopsy in people who are either unwilling or unable to undergo standard endoscopy. This method relies on the accuracy of the visual determination of the abnormalities of the duodenum and the capsule's ability to predict abnormal biopsy. As mentioned above, a normal capsule study does not exclude the disease. Regression of the extent of the abnormalities has been noted after a period on gluten-free diet.

The other role of capsule endoscopy is in patients who have symptoms of complicated celiac disease such as evidence of refractory iron deficiency, anemia, bleeding, or abdominal pain, and in whom there is a possibility of ulcerative jejunitis or malignancy such as lymphoma or adenocarcinoma. Capsule endoscopy allows the exclusion of malignancy in these patients. This is often an issue in patients who have symptoms of celiac disease despite a gluten-free diet. A study conducted with my colleagues at Columbia University showed a high prevalence of small intestinal ulcers in these complicated patients.

The more video capsule endoscopy procedures performed, the more abnormalities in the jejunum and ileum that require visualization and biopsy that we have found. This has resulted in the greater use of double-balloon enteroscopy, which allows us to biopsy more distal lesions. Both video capsule endoscopy and double-balloon enteroscopy have an important role, especially in patients with complicated celiac disease or with alarm symptoms, in whom there is concern about ulcerative jejunitis, enteropathy-associated T-cell lymphoma, or adenocarcinoma.

G&H How does the accuracy of capsule endoscopy compare with other endoscopic techniques such as the immersion technique?

PG There are currently no published studies that compare the standard endoscopic appearance of the duodenum with its appearance on capsule endoscopy for the diagnosis of celiac disease. There are several techniques that improve visualization of villi with standard endoscopy including magnification endoscopy, water immersion techniques, and chromoendoscopy. These techniques are included in a standard endoscopic procedure.

G&H What aspects of the use of endoscopy in celiac disease require further investigation?

PG Certainly, the cost-effectiveness of video capsule endoscopy needs to be further investigated. Endoscopists also need to fine-tune the role of video capsule endoscopy in this field. Whether or not video capsule endoscopy can affect management strategies or be of use in screening for malignant complications also remains to be seen.

G&H Is there any other research currently ongoing in this field?

PG A major area of interest and active research is the development of nondietary therapies that may allow patients to avoid the rather rigorous gluten-free diet. Currently, the most attractive option is enzyme therapy, in which patients eat an enzyme along with gluten-containing foods. The recombinant enzymes digest the toxic components of gluten. The ultimate role of this therapy remains to be determined.

Suggested Reading

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