Celiac Disease Patients Often Left Undiagnosed

BY DOUG BRUNK
San Diego Bureau

SAN DIEGO — Celiac disease affects an estimated 1% of people in the United States, yet only about 3% of people with the disease are being diagnosed, Dr. Peter H.R. Green said at the annual meeting of the American Academy of Allergy, Asthma, and Immunology.

Reasons for the poor rate of diagnosis are multifactorial, said Dr. Green, who directs Columbia University's Celiac Disease Center in New York. They include:

► **A shift to the silent form of celiac disease.** "The patients and the doctors are on the wrong pages in the [medical] textbooks," he said. "The patients got it wrong in that they forgot to get diarrhea, and the doctors got it wrong in that they thought that all patients with celiac disease had to have diarrhea." In fact, he explained, only about half of celiac disease patients present with diarrhea.

So-called silent modes of presentation include bone disease, anemia including iron-deficiency anemia, weight loss, dermatitis herpetiformis, psoriasis, and chronic urticaria. "There are increased rates of atopy and there are oral manifestations [in the form of] dental enamel defects such as yellow spots, white spots, and brown spots," he added.

High-risk groups that Dr. Green screens include patients with a family history of celiac disease, patients with type 1 diabetes, and those with primary biliary sclerosis and Sjögren's syndrome.

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DR. GREEN

► **Physicians are failing to recognize celiac disease.** Physicians "are taught that it's a rare condition," he said, when in fact it is not and the clinical manifestations vary widely. "That's one of the reasons why there is such a low rate of diagnosis, because no one set of doctors [is] looking at all of those patients."

► **Lack of support from the pharmaceutical industry.** "We know that over 80% of medical research is financed by the pharmaceutical industry, and by far the bulk of postgraduate education is financed by the pharmaceutical industry," said Dr. Green, who is also a professor of medicine at Columbia.

The major sources of referrals to Columbia's Celiac Disease Center are neurologists. Other common sources of referral include gynecologists, endocrinologists, and rheumatologists.

In patients with suspected celiac disease, Dr. Green and his associates consider a panel of tests that include the tissue transglutaminase 2 (tTG)-IgA, the tTG-IgG, the IgA endomysial antibody (EMA), and total IgA level. "The best test is probably tTG-IgA, and throw in the tTG-IgG," he said. "The IgA endomysial antibody need not be done routinely, but it's of value in difficult cases."

The accepted standard for diagnosis is a biopsy of the descending duodenum. Most celiac disease patients (90%) will have a March III lesion on biopsy, which includes partial, subtotal, and total villous atrophy.

Patients with celiac disease face a 10-fold increased risk of having at least one other autoimmune disease. Various malignancies have also been linked to having celiac disease, including esophageal and head and neck squamous cell carcinoma, small intestinal carcinoma, and non-Hodgkin's lymphomas.

The management of celiac disease is a lifelong gluten-free diet, which Dr. Green said is difficult to follow in the United States. He recalled seeing gluten-free options on the menu at an ice cream store in Buenos Aires, Argentina. In that country, he said, "there's a lot of celiac disease, and people have very good services."

Dr. Green predicted that in the future, more people will be diagnosed with celiac disease as physicians begin to learn about the wide variability of clinical presentation and the availability of sensitive and specific tests.

"As more people become diagnosed there will be greater awareness, and then people with celiac disease will get a better deal in this country," he said. ■

Knifelike Vulvar Ulcers Could Be a Sign of Crohn's Disease

BY KATE JOHNSON
Montreal Bureau

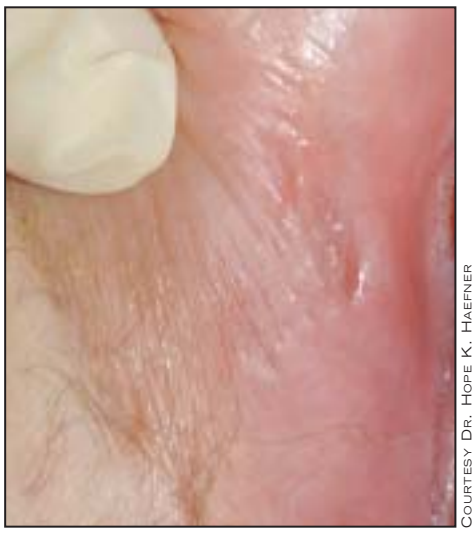
HOUSTON — Women with Crohn's disease can sometimes present with knifelike vulvar ulcers that are very specific to the disorder and may be its only manifestation, according to several experts who spoke at a conference on vulvovaginal diseases jointly sponsored by Baylor College of Medicine and the Methodist Hospital.

"There are three things in the vulvar or perianal area that might make you think of unrecognized Crohn's: knifelike ulcerations, vulvar edema that has no other cause, or fistula around the anus," said Dr. Libby Edwards, a dermatologist in private practice in Charlotte, N.C. "It has been said that vulvar Crohn's is rare, but it is not. It's uncommon but it's not rare. I see it several times a year, and most gynecologists will see it without necessarily recognizing what it is," she said in an interview.

While for some patients, vulvar signs may be the first presentation of Crohn's, this tends to be the exception, said Dr. Hope K. Haefner, professor of obstetrics and gynecology at the University of Michigan and director of the university's Center for Vulvar Diseases in Ann Arbor.

"There is the rare patient who doesn't have any gastrointestinal symptoms and might develop them later, but usually the majority already have a diagnosis of gastrointestinal Crohn's and are seeking gynecologic care for their vulvar symptoms," she said in an interview. In her opinion, perianal fistulae may be the most common of the three gynecologic manifestations of Crohn's. "I see them every couple of months, in children and in the elderly—there's a big age range," she said.

Vulvar and perianal Crohn's is a marker for severe disease that needs to be aggressively treated systemically, said Dr. Edwards, also of the department of dermatology at the University of North Carolina at Chapel Hill. "First of all, if [these patients] don't have an aggressive gastroenterologist, they really need one," she said, adding that aggressive systemic treatment for Crohn's might relieve some vulvar symptoms. But, she said, patients also need local vulvar care. "These patients get secondary infections, and when they do, they need oral antibiotics—maybe even on a long-term basis if they have open, draining sores." In addition, both oral antibiotics and immunosuppressive therapy for Crohn's can make patients susceptible to yeast infections, which may require weekly antifungal therapy, she said. ■



COURTESY DR. HOPE K. HAEFNER

For some patients, fistulous tracts on the vulva may be Crohn's first presentation.

Salicylates May Cause Diarrhea In Ulcerative Colitis Patients

BY MITCHEL L. ZOLER
Philadelphia Bureau

FORT LAUDERDALE, FLA. — About 10% of patients with ulcerative colitis who are taking 5-aminosalicylic acid medications develop worsening diarrhea that may be linked to these drugs.

"Continued treatment with a salicylate in a patient who isn't responding can be worse than useless, because 5-ASA [5-aminosalicylic acid] can trigger diarrhea in some patients," Dr. Raymond Sandler said in an interview at an international colorectal disease symposium sponsored by the Cleveland Clinic Florida.

Many patients with ulcerative colitis who are receiving ineffective treatment with a salicylate also take an antidiarrheal drug, as well as other motility-inhibiting drugs such as antiemetics or even narcotics. These additional drugs may well exacerbate the adverse effects of 5-ASA by prolonging its presence in the gut.

Instead, physicians should withdraw patients who are nonresponders to 5-ASA from the drug if the patients require "step-up" therapy with steroids or immunomodulator drugs, Dr. Sandler said.

Salicylates are for patients with mild to moderate disease. "Once a patient remains symptomatic despite treatment with a 5-ASA drug, such as mesalamine, [he or she] can no longer be considered to have mild disease," said Dr. Sandler, a gastroenterologist at the Cleveland Clinic Florida in Weston.

"The first thing I do is stop the salicylate" and see how the patient responds. "I've seen no refractory [ulcerative colitis] patient get worse when taken off a 5-ASA drug," he said.

Dr. Sandler recommended starting patients with mild ulcerative colitis on a low-dose salicylate regimen and monitoring them for 1-2 months. If a patient's condition worsens, he or she should be taken off the drug rather than increasing the dosage.

If the patient's condition remains the same or improves slightly, doubling the dose is reasonable. But the higher dosage should be continued only if the patient improves. If the patient fails to improve, the salicylate should be stopped and treatment with another drug should be started.

For immunomodulator treatment of ulcerative colitis, Dr. Sandler prefers either 6-mercaptopurine or azathioprine. But he cautioned that patients who start one of these drugs should be tested to see if they have an adequate level of thiopurine methyltransferase, an enzyme necessary for the safe metabolism of these drugs.

Patients with inadequate enzyme levels can develop leukopenia and life-threatening agranulocytosis. In addition, bridge therapy with steroids or other drugs is usually necessary because of the relatively long delay before 6-mercaptopurine and azathioprine start to work.

A promising alternate immunomodulating drug is tacrolimus, which appears safe and effective in retrospective studies. However, the safety and efficacy of systemic tacrolimus for ulcerative colitis still needs to be confirmed in prospective studies, Dr. Sandler said. ■