Red Flags Mark Progression to Crohn's Disease

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LOS ANGELES — A number of clinical, laboratory, and serologic "red flags" may distinguish patients with ulcerative colitis who will progress to a diagnosis of Crohn's disease, researchers reported at the annual Digestive Disease Week.

Dr. Gil Y. Melmed and his associates at the Inflammatory Bowel Disease Center at Cedars-Sinai Medical Center and the University of California, Los Angeles, designed a nested case-control study to compare 21 patients whose diagnosis evolved into Crohn's disease with two groups of age-matched controls: 52 patients with simple ulcerative colitis and 56 patients with Crohn's disease.

Patients whose disease progressed were more likely than other ulcerative colitis patients to have extensive colonic involvement at diagnosis and a positive C Bir1 serology. In addition, they had an increased likelihood of having two or more red flags at initial presentation, including:

- ► Weight loss of more than 10% of body weight.
- ► Nonbloody diarrhea.
- ► Family history of Crohn's disease in at least one first-degree relative.
- ► Oral ulceration.
- ► Active smoking.
- ► Upper GI symptoms.
- ► History of blood transfusion.
- ► Perianal disease.
- ► Non–*H. pylori* gastritis.
- ► Thrombocytosis.
- ► Elevated C-reactive protein level.
- ► Hypoalbuminemia.

Other red flags included Crohn's disease–associated serologies, including ASCA IgA, ASCA IgG, anti-0mp-C, and anti-12.

A multivariate logistic regression analysis found three red flags that independently raised the odds of an ulcerative colitis patient progressing to the more serious diagnosis of Crohn's disease. These were nonbloody diarrhea at presentation (odds ratio, 23.5), weight loss (odds ratio, 12.4), and a positive C Bir1 serology (odds ratio, 6).

Nearly half of the patients who went on to develop Crohn's disease had pancolitis at initial colonoscopy, and two had an inflammatory condition of the ileum, "backwash ileus."

None of the control patients with ulcerative colitis had total colonic involvement, and just 9 of 52 had pancolitis. The majority had left-sided involvement or proctitis.

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Although "red flags" were present in all patients who went on to develop Crohn's disease, the length of time to a change in diagnosis was variable, ranging from 6 months to 17 years, with a mean of 4 years, Dr. Melmed noted in his poster presentation.

In an interview after the meeting, he said members of his group were surprised by the strength of the associations they identified, despite the small sample size.

"Something about the initial disease presentation seems to be very indicative in our cohort of a change in diagnosis, and we are beginning to learn about the role serology has to play in these patients as well," he said.

He advocated a further work-up of patients with ulcerative colitis who have these features, particularly if they are not responding to conventional therapy, considering surgery, or being considered for enrollment in a clinical trial.

An appropriate work-up would include colonoscopy with ileoscopy (if not previously performed), a small bowel series with barium, or CT, MR enterography, capsule endoscopy, or upper endoscopy.

"Another issue that came up in our study was that many people with ulcerative colitis had been diagnosed on the basis of a flexible sigmoidoscopy rather than a complete colonoscopy, which could potentially identify Crohn's disease. We had to exclude these patients, who may have been misdiagnosed from the outset of their disease course," Dr. Melmed said.

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