Intraepithelial Lymphocytosis in Architecturally Normal Small Intestinal Mucosa: Association With Morbid Obesity

To the Editor.—We appreciate the publication in the July 2006 issue of the Archives of Pathology & Laboratory Medicine of the thorough and timely review by Brown et al of the differential diagnosis of intraepithelial lymphocytosis with normal villous architecture (IELNVA) in small intestinal biopsies. As noted in the article, the list of known etiologies for this phenomenon does not account for many cases encountered in practice. We would therefore like to call attention to morbid obesity (MO) as an additional etiology of IELNVA.

An unexplained excess of intraepithelial lymphocytes was noted in the otherwise normal jejunal mucosa of many patients undergoing bariatric surgery involving Roux-en-Y gastric and segmental jejunal resections. We therefore compared CD3+ intraepithelial lymphocyte scores in randomly selected intestinal resection specimens from 16 MO cases and 15 control patients undergoing Whipple resections for pancreatic neoplasia at our institution during a 2-year interval. Scoring was performed independently by 3 pathologists in blinded fashion and achieved excellent interobserver agreement. In the MO group, 69% of the patients had abnormally high counts of more than 25 lymphocytes per 100 epithelial cells, including 38% with counts of 25 to 40 and 25% with counts more than 60, compared with 27% in the control group, all of whom had counts of 25 to 40 ($P = .047, \chi^2$ test). The CD3+ cells in the MO group were distributed evenly throughout the villi, and the villous architecture and density and composition of mononuclear inflammatory cells in the lamina propria were normal as determined subjectively by hematoxylin-eosin staining. None of the cases showed evidence of Helicobacter pylori–associated chronic gastritis in their accompanying gastric tissues. A clinical survey of all the cases revealed one patient taking nonsteroidal anti-inflammatory drugs, another with loose bowel movements, and none with a known family history of celiac disease.

The basis of this apparent association between IELNVA and MO is obscure. Obesity is associated with multiple aberrations of immune function involving a variety of hormonal, genetic, biochemical, and microbiological mechanisms. In considering potential relationships between intramucosal lymphocytes and obesity, it is tempting to speculate on a possible role in the elevated leptin levels in this setting. In addition to its role in regulating appetite and energy expenditure, leptin is also a cytokine-like mediator of intestinal inflammation that stimulates intraepithelial and lamina propria T cells and causes profound alterations in gut immune responsiveness in mouse experimental models.

The potential clinical and basic science implications of an association between body mass and intraepithelial lymphocytosis in the small intestine warrant systematic study of patients in nonsurgical settings.

As suggested by Brown et al, the presence of IELNVA deserves mention in diagnostic pathology reports despite the current elusiveness of specific causes in some cases. We would add that the possible role of obesity should be borne in mind in formulating a differential diagnosis.

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The authors have no relevant financial interest in the products or companies described in this article.
Letters to the Editor

Medical Examiners, Coroners, and Public Health

To the Editor.—As a former chief medical examiner of the District of Columbia, I would like to add a brief historical footnote to Hanzlick’s comprehensive review of the relationship between medicolegal investigative agencies and the public health.1 In 1971, a data retrieval system that permitted ready sorting of demographic, circumstantial, and postmortem findings was installed at the District of Columbia medical examiner’s office. During the first 6 months of its use, we recognized what seemed to be epidemiological clustering of narcotic-related overdose deaths. At the same time, the primary drug recovered postmortem in these cases was changing from heroin to methadone. I brought these data to Philip Brachman, MD, head of epidemiology at the Center for Disease Control (now Centers for Disease Control and Prevention [CDC]), for consultation. He assigned an Epidemic Intelligence Service officer to work with our office and the Irritant’s office. 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In Reply.—I thank Dr Luke for his valuable footnote. There are probably other examples of important public health projects of decades past that have escaped appropriate attention, and those in the know are encouraged to report them.

Also, in addition to the 8 state medical examiner systems that are organized within health departments,1 Iowa needs to be added to the list because it was moved from the Department of Public Safety to the Department of Public Health in 1999.

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Access to medical examiners’ office case material brings the opportunity to learn from these accidents of nature by involving professionals from other specialties in problem issues that cross discipline lines. It was a privilege to work with the CDC in this capacity.

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Follicular Tumors of the Thyroid

To the Editor.—Dr Suster makes a surprising statement in his review of follicular tumors of the thyroid.1 On page 985 of the July issue of the Archives, he states: “I agree with Li-Volsi and Baloch that capsular invasion should only be diagnosed when there is through-and-through [my emphasis] infiltration of the capsule into the surrounding thyroid parenchyma. . . .” On page 281 of their article, Li-Volsi and Baloch2 state: “In our practice, unifocal or multifocal invasion into [my emphasis] or through the capsule without vascular invasion is sufficient to render a diagnosis of minimally invasive follicular carcinoma. . . .”

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In Reply, Correction.—I apologize for misquoting Drs Baloch and Li-Volsi in my recent article.1 My statement should have read: “I disagree with Baloch and Li-Volsi that invasion into the capsule (as opposed to complete invasion through the capsule) is sufficient to render a diagnosis of minimally invasive follicular carcinoma.”

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