Tufting enteropathy

First described in 1994, tufting enteropathy is a clinicopathological entity in which infants present with watery diarrhea in the first month of life. The pattern of inheritance appears to be autosomal recessive. Jejunal biopsy shows partial or subtotal villous atrophy with normal or hyperplastic crypts. The lamina propria is not inflamed and intraepithelial lymphocytes are not increased. The most striking finding is of epithelial cell tufts, that is, closely packed enterocytes with rounded apical plasma membranes. While this appearance may be seen focally in other enteropathies, in tufting enteropathy between 80% and 90% of the surface exhibits the change. Treatment at present is with total parenteral nutrition.

Patients with autoimmune enteropathy present with diarrhea in the first year of life and may present in the neonatal period. A family history of autoimmune disease is often present. In some patients, the disorder may occur in the context of a primary immunodeficiency syndrome. Jejunal biopsies show mild, partial to subtotal villous atrophy with crypt hyperplasia. Surface enterocytes show numerous intraepithelial lymphocytes and numerous vacuolated and individually necrotic surface enterocytes as a marker of cytopathic damage. The lamina propria shows dense lymphocytic and plasma cell infiltration (although in agammaglobulinemia and hypogammaglobulinemia plasma cells are absent) and there may be crypt abscesses. Antigut antiepithelial or antigoblet cell antibodies are detected in the blood. Treatment is directed to the underlying immune defect in immunodeficient patients and immunosuppressive therapy in those who do not have a demonstrable immunodeficiency.

References


——

Gastric pathology in pediatric Crohn's disease

M. Peuchmair


Systematic endoscopic evaluation of the upper gastrointestinal (GI) tract of patients with Crohn's disease (CD) has revealed frequent endoscopic and histological abnormalities (1, 2). Recent studies have shown that there is gastric involvement in over three-fourths of patients with CD. However, in these studies, only a minority of these gastric lesions were specific cases of granulomatous gastritis. The most striking lesion was a focal acute inflammation of the stomach (3, 4). Other studies have shown that the majority of the gastritis that occurs in CD is not associated with Helicobacter pylori infection (5). The greatest challenge for understanding upper gastrointestinal involvement in CD is to define the value of this focal inflammation more precisely.

Focal inflammation may be defined as the presence of inflammatory cells surrounding at least a foveolar pit or a small group of foveolae or glands. The inflammatory cells are mononuclear cells (histiocytes and lymphocytes) and polymorphonuclear neutrophils. The neutrophils infiltrate the epithelium that shows alterations, such as discontinuities or cuboidal-shaped cells. The inflammation is often deep within the mucosa and is rarely associated with granulomas. This histological definition of focal inflammation rules out activity when the majority of crypts or glands are infiltrated by inflammatory cells or when adjacent normal mucosa cannot be found in a given biopsy specimen. Focal inflammation is characteristic of H. pylori-negative CD and is uncommon in non-CD cases. The value of focal enhanced gastritis is so great that some authors claim that this type of gastritis should encourage further investigations of patients not yet known to have CD, or that it could help to classify indeterminate colitis.

The concept that immunological changes play a key role in the pathogenesis of CD is now established (6). The cytokine production profiles in CD strongly suggest the prevalence of a Th1 response (7). In contrast, murine models of ulcerative colitis, such as the T-cell receptor alpha mutant, indicate the critical role of the Th2 cytokine in the pathogenesis of this colitis (8). The cytokine interleukin-12 (IL-12) is composed of two subunits, p40 and p35, encoded by two separate genes (9). IL-12 is produced mainly by monocytes and macrophages and plays a pivotal role in the differentiation of Th1 T-cells, as it induces naïve T-cells to produce interferon-γ (10,11). Murine models of experimental granulomatous colitis mimicking CD indicate that IL-12 plays a major role in the disorder (12). Recent studies have shown greater amounts of IL-12 in the intestinal tissues of CD patients than in the normal and inflamed tissues of controls (13).

The important part played by IL-12 in CD prompted us to study its expression in the gastritis of pediatric patients with confirmed distal CD in an attempt to identify a link between cytokine production and nongranulomatous and granulomatous gastritis occurring in CD. We demonstrated in situ enhanced IL-12 production in the gastric mucosa of pediatric CD patients. The patterns of IL-12-positive cells in the small bowel and gastric mucosa were the same, with small to large foci of positive cells in the lamina propria. However, no IL-12-positive cells were found in the gastric mucosa of the patients with ileal CD and normal gastric mucosa, or in the controls and only few scattered positive cells were found in 50% of the gastric mucosa specimens from patients with H. pylori-positive chronic gastritis. Also, the amounts of IL-12 expression in the gastric biopsy specimens exhibiting granulomatous gastritis and non granulomatous gastritis were similarly enhanced. A recent study has shown that gastritis-associated CD is characterized by a focal periglandular accumulation of CD68+ histiocytes and CD3+ lymphocytes with a high content of TIA1+ cytotoxic T lymphocytes (3). As IL-12 is mainly produced by macrophages and enhances T-cell and natural killer cell cytotoxicity, with increased productions of granzyme B and perforin messenger RNA, IL-12 may play a major role in the pattern and accumulation of immune cells in gastritis-associated CD. The demonstration of focal enhanced IL-12 expression in both nongranulomatous gastritis and granulomatous gastritis, as well as in ileal specimens from CD patients, highlights the link between all these lesions in CD.

Finally, IL-12 expression is elevated at the time of CD diagnosis and remains increased for months or years during the course of CD, suggesting that IL-12 is important for both initiating and maintaining inflammation in this disease. In conclusion, IL-12 expression is focally enhanced in the gastric mucosa of pediatric patients
with CD, with or without granulomatous lesions, suggesting that both IL-12 and the lesions are indeed linked to CD (14,15). These data reinforce the idea that focal inflammation of the gastrointestinal tract is a hallmark of CD.

References
10. Wu CY, Demeure C, Kiniwa M et al. Enteroinvasive E. coli mainly affects children less than 3 months of age in developing countries. Enteroinvasive E. co/i rarely causes epidemics of diarrhea in developing countries and is acquired from contaminated food. Enterohemorrhagic E. coli occurs worldwide and causes a watery diarrhea that becomes bloody and is associated with neurologic manifestations. Some strains are associated with the hemolytic uremic syndrome. Enterovirulent E. co/i causes acute persistent diarrhea in infants in developing countries but infection is generally self-limiting. The Campylobacter group of organisms is now considered to be the dominant identifi- cable bacterial pathogen causing severe gastroenteritis in semi-urban or urban shack dwelling children (2) where informal butcheries and home slaughtering of chickens is common practice. During recent years there has been an accumulation of evidence to implicate C. jejuni in the occurrence of the acute motor axonal neuropathic form of Guillain-Barré syndrome (3). Salmonella and Shigella infections in the tropics are no different from those that occur in temperate areas except that they are more prevalent and there is a wider spectrum of virulence. In recent years there have been increased reports of hemolytic uremic syndrome complicating Shigellosis. Cholera is becoming more widespread throughout the whole of the tropics and manifests as an acute illness with a rapid loss of fluids and electrolytes from the intestines that leads to hypovolemic shock (4). Yersinia enterocolitica gastroenteritis is uncommon in the tropics.

Intestinal tuberculosis
In rural Africa milk is generally not pasteurized and children are increasingly becoming infected with bovine mycobacteria. Such infection usually results in a primary complex occurring in the ileum and mesenteric lymph nodes. However, most cases of intestinal tuberculosis occur as a secondary phenomenon when infected spum from primary pulmonary tuberculosis from human strains is swal- owed. The condition manifests as circumferential ulcers in the lower ileum, caseous mesenteric adenitis and peritonitis. Fibrosis many cause intestinal obstruction and in older children. Rectal infection may cause an schiorectal abscess or fistula.

Tropical sprue
This malabsorption syndrome responds to prolonged antibiotic ther- apy. It mainly occurs in the Middle East, India and the Caribbean. Patients have watery diarrhea, abdominal discomfort or pain with dis- tention, anorexia, weight loss, glossitis, stomatitis, alteration of skin pigmentation and edema. Persistence of symptoms leads to mega-loblastic anemia. Microscopy of intestinal mucosa shows atrophy with an inflammatory infiltrate that includes many eosinophils (5).