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Post-infectious Functional Dyspepsia - A Novel Disease Entity among Functional Gastrointestinal Disorders - Relation to *Helicobacter pylori* Infection?

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Summary

Kindt et al.[1] published a report entitled "Intestinal immune activation in presumed post-infectious functional syspepsia" in the August issue of Neurogastroenterology and Motility in 2009. By comparing the signs of inflammation and the degree of hyperplasia of the enterochromaffin cells (EC) in duodenal biopsies obtained from patients with presumed post-infectious functional dyspepsia (PI-FD) and unspecified-onset functional dyspepsia (U-FD), they showed that PI-FD is associated with persistence of focal T-cell aggregates, decrease in $CD4^+$ cells and increased macrophage counts surrounding the crypts, without any significant differences in the numbers of EC or chromogranin A (CA)-positive cells (mast cells). This finding may indicate impaired ability of the immune system in these cases to terminate the inflammatory response after an acute insult.

Comment

In irritable bowel syndrome (IBS), a post-infectious disease entity was reported in 1962 by Chaudhary and Truelove, who showed that 23% of IBS patients gave a history of an episode of bacillary or amoebic dysentery.[2] Ever since, an increasing number of studies have reported on the development of post-infectious IBS.

In relation to PI-FD, Mearin et al.[3] reported a significantly increased prevalence of FD up to 1 year after an outbreak of Salmonella gastroenteritis. In PI-FD patients, early satiety, weight loss, nausea, and vomiting are more frequently reported, while gastric sensorimotor function testing revealed a particularly high prevalence of impaired gastric accommodation.[4] In the study by Kindt et al.,[1] the focal aggregates of $CD8^+$ T cells, decrease in $CD4^+$ T cells and increased macrophage counts surrounding the duodenal crypts persisted for several months after the acute infectious episodes, suggesting delay or impairment of termination of the inflammatory response even after adequate re-

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moval of the infecting pathogen.

Why did Kindt et al. choose duodenal mucosa over gastric biopsies for the histopathological evaluation in the FD patients? As is well known, FD symptoms are mainly attributable to disturbed gastric function. However, the approach of studying inflammation in the duodenum has been used previously[5] and in fact, was reported to be more successful for detecting the changes in FD as compared to gastric biopsies.[6] According to the report by Lee et al.,[7] since duodenal acidification induces proximal gastric relaxation, increases the sensitivity to gastric distension, and inhibits gastric accommodation to a meal, duodenal mucosa is also an important sensory portion for the pathogenesis of FD. Furthermore, when histological inflammation is assessed by gastric biopsy, we have to bear in mind the possible co-existence of *Helicobacter pylori* (*H. pylori*) infection of the stomach. Even though the Rome III classification does not require ruling out of *H. pylori* infection for diagnosing FD,[8,9] the *H. pylori*-colonized gastric mucosa exhibits significant levels of inflammatory cell infiltration with $CD8^+$-, $CD4^+$-T cells and macrophages.[10-13] Even after the eradication of *H. pylori*, many mononuclear cells as T cells or macrophages persist in the mucosa. Such inflammatory changes present before and even after *H. pylori* eradication could play a significant role in the pathophysiology of this type of dyspepsia. Taken together, functional dyspepsia with a present or even past history of *H. pylori* infection should be considered as a different disease entity from FD, such as *H. pylori*-infectious FD or post-*H. pylori*-infectious FD.

In conclusion, the concept of PI-FD is potentially valid and the causal relationship between remnant inflammatory features and the gastroduodenal motor or sensory machinery should be further investigated. However, the major microorganism infecting the stomach, *H. pylori*, should not be overlooked when considering the pathophysiology of FD, especially in Asia.

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