Early Cancer in Gastric Crohn's Disease

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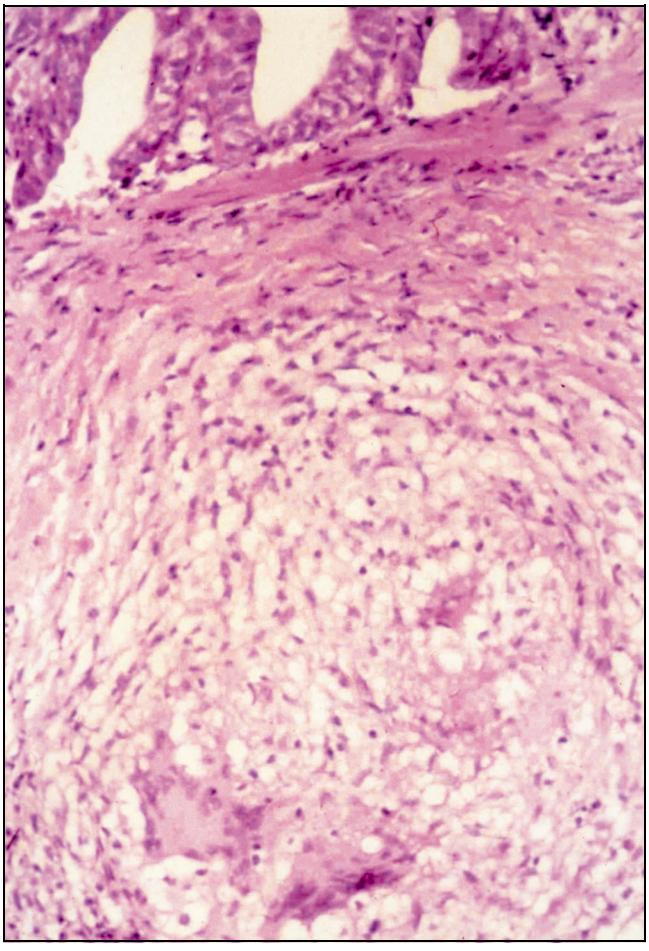
Several studies have reported an up to 20-fold increase in the risk of gastrointestinal cancers among patients with Crohn's disease. An increased risk for the development of small and large bowel adenocarcinoma has been reported in Crohn's patients, particularly those with long-standing and extensive disease. However, the association of gastric malignancy with Crohn's disease remains controversial. Our literature review identified only two cases of gastric adenocarcinoma reported to occur in Crohn's patients with long-standing involvement of the stomach [1,2].

We report the first case of severe dysplasia complicating a long-standing gastric Crohn's disease, subsequently developing into an early gastric cancer, and discuss the possible association of Crohn's disease and gastric malignancy.

Patient Description

A 58 year old woman with Crohn's disease of the right colon and stomach was followed during the past 13 years in the gastroenterology unit. She was under treatment with sulfasalazine and felt well. Her diagnosis was based on typical endoscopic features and supported by histological evidence obtained by biopsies. She had no history of gastrointestinal malignancies and was otherwise healthy. In December 1997 the patient was examined for recurrent epigastric pain. Blood tests revealed megaloblastic anemia, and esophagogastroduodenoscopy demonstrated an inflamed gastric mucosa with a polypoid lesion in the posterior wall of the antrum. Biopsies taken from this polypoid lesion showed severe dysplasia, intestinal metaplasia, and inflammation that was both acute and chronic. Surgery was proposed but the patient refused. Four months later, biopsies obtained during a follow-up EGD from the antral polyp revealed chronic inflammation with intestinal metaplasia and a small ulcerated area containing adenocarcinoma.

The patient agreed to surgery. Abdominal exploration showed a rigid, edematous and thickened ascending colon adherent to the cecum. The gastric wall was edematous, thickened and adherent to the pancreas and transverse mesocolon. A Billroth I hemigastrectomy combined with right hemicolectomy was performed. The pathological examination [Figure] revealed a moderately differentiated adenocarcinoma of the antrum, 0.5 cm



Early gastric cancer of the antrum with chronic inflammation and non-caseating, giant cells containing granulomas.

EGD = esophagogastroduodenoscopy

in diameter, which invaded merely the mucosa and submucosa. Twelve perigastric lymph nodes, including the omenta, were examined and found to be negative for metastases. The remaining stomach exhibited a chronically inflamed and atrophic mucosa with intestinal metaplasia and transmural fibrosis. Noncaseating giant cells containing granulomas, which were negative for acid-fast bacilli, were seen in the stomach, ascending colon and associated lymph nodes, corresponding with gastric and colonic Crohn's disease.

Comment

Crohn's disease of the stomach is rare, constituting less than 3% of all gastrointestinal Crohn's disease [3]. While several cases of gastric malignancy in patients with Crohn's disease have been reported in the literature, most of these patients did not have gastric involvement of Crohn's disease.

The literature reflects uncertainty regarding the association between Crohn's disease and gastric malignancy. Gyde and Glick [4,5] reported a few cases of gastric cancer in long-standing ileocolic Crohn's disease, but in none of these cases was there any evidence of gastric Crohn's disease. Only two cases of gastric adenocarcinoma complicating gastric Crohn's disease were described in the literature [1,2].

We report a patient with gastric Crohn's disease for more than 13 years who developed severe dysplasia within an area of chronic inflammation in the antrum, subsequently progressing to an early gastric cancer. In this case there are several factors suggestive of an association between Crohn's disease of the stomach and gastric cancer: the long-standing nature of Crohn's disease, the presence of Crohn's disease in the stomach, and the demonstration of a dysplasia to carcinoma sequence, i.e., the progression of a chronic gastric inflammation through intestinal metaplasia and severe dysplasia to an early gastric adenocarcinoma. Based on the literature review, disease activity does not appear to impact on cancer risk; however, the location in which the adenocarcinomas develop does appear related to activity of the disease, i.e., most of the neoplasms in Crohn's patients were found in areas of active disease. Nonetheless, it should be noted that the short time period between the first biopsy and the diagnosis of gastric cancer could be compatible with sample error of the first biopsy, rather than reflecting a progression from dysplasia to carcinoma. In the present case no family history of gastrointestinal malignancies was recorded that might suggest a possibility of familial gastric cancer, though a sporadic gastric cancer occuring in a Crohn's patient cannot be ruled out.

Nevertheless, the present case and those described by others suggest a possible association between gastric malignancy and long-standing gastric Crohn's disease. Indeed, we should have expected to see more cases of gastric cancer in patints with gastric Crohn's involvement if this association was not merely coincidental. Perhaps the difficulty that is encountered in reaching a definitive diagnosis of gastric malignancy in the setting of gastric Crohn's disease, together with the rare occurrence of these two conditions, can explain the paucity of similar reports in the literature. Thus, it might be reasonable to assume that when a long-standing inflammatory condition exists in the stomach, as in gastric Crohn's disease, it may with time cause a chronic atrophic gastritis that is known to predispose to gastric malignancy.

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Capsule

Antigen recognition

B cells appropriate help from T cells by expression of class II molecules, which display antigenic peptides to specific receptors expressed by the T cells. These receptors are wired up to complex intracellular signaling pathways that launch a program of activation and differentiation in the T cell upon the recognition of appropriate antigen. Lang et al. provide evidence that the interaction between the T cell receptor and class II molecule is not simply a one-way exchange of information. Signals could be delivered back to the B cell via the class II molecules. This process depended upon their association with the signaling chains of the B cell antigen receptor. This process may play a role in regulating T cell–B cell cooperation during immune responses to antigen.

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