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RAPID COMMUNICATION

Endoscopic findings and pathologic characteristics of gastric eosinophilic granuloma: A report of 18 patients

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Abstract

AIM: To investigate the endoscopic findings and pathologic characteristics of gastric eosinophilic granuloma (GEG).

METHODS: A retrospective study of 18 cases of gastric eosinophilic granulomas was conducted. Gastroscopy was performed and all specimens of biopsies were stained by H&E and observed under light microscopy.

RESULTS: Ulcer was the most frequent endoscopic appearance. The others included deformed pylorus and/or duodenal bulb, esophagitis, mucous hyperemia and/or mucosal erosion. Eosinophilic cell infiltration and generous hyperplasia of arterioles, venules and lymph vessels were found in the lesions of the patients. Interstitium had massive eosinophilic infiltrates and was made up of collagen fibers and fibroblasts. Lymphoid follicles were revealed in some sections of biopsies.

CONCLUSION: GEG is lack of specific symptoms and physical signs. It can be misdiagnosed as gastric ulcer in most cases before biopsies. Endoscopy and endoscopic multiple deep biopsies in suspected areas are indispensable for correct diagnosis of GEG.

Key words: Gastric eosinophilic granuloma; Endoscopy; Pathology

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INTRODUCTION

Gastric eosinophilic granuloma (GEG) is characterized by pathological changes including eosinophil cells infiltrated into the submucous layer and muscular layer of the stomach. Its etiology is still unknown. The patients are prone to be misdiagnosed as having gastric carcinoma and gastric ulcer[1]. In order to investigate the endoscopic findings and pathologic characteristics so as to improve the diagnostic accuracy and therapeutic effect for GEG, 18 patients finally diagnosed by endoscopy and pathology are analyzed.

MATERIALS AND METHODS

Patients

From 2002 to 2006, a retrospective review of endoscopic mucosal biopsies and pathologic examinations was performed at the Digestive Endoscopic Center of Renmin Hospital of Wuhan University (Wuhan, China). In the routine gastroscopies performed during this period, 18 GEG patients (14 males, 4 females) were found among the 14 396 cases. Their mean age was 44.85 ± 11.70 years (range 22-65 years).

Endoscopic diagnoses were GEG (7 cases; including 5 definite cases and 2 suspected cases), gastric ulcer (5 cases), gastric ulcer accompanying esophagitis (1 case), gastric ulcer accompanying superficial gastritis (2 cases), superficial gastritis (1 case), and superficial gastritis accompanying duodenal ulcer (2 cases).

Design

Gastroscopy was performed in the 18 cases. All the patients underwent endoscopic mucosal biopsies and pathologic examinations. All specimens of biopsies were stained by H&E and observed under light microscopy. Diagnostic criteria were used in accordance with the literature[2].

Ethics

This is a retrospective study and data were collected by the common methods used in clinical practice.

RESULTS

Endoscopy

Ulcer is the most frequent endoscopic appearance. The endoscopic appearances include ulceration in 15 cases,

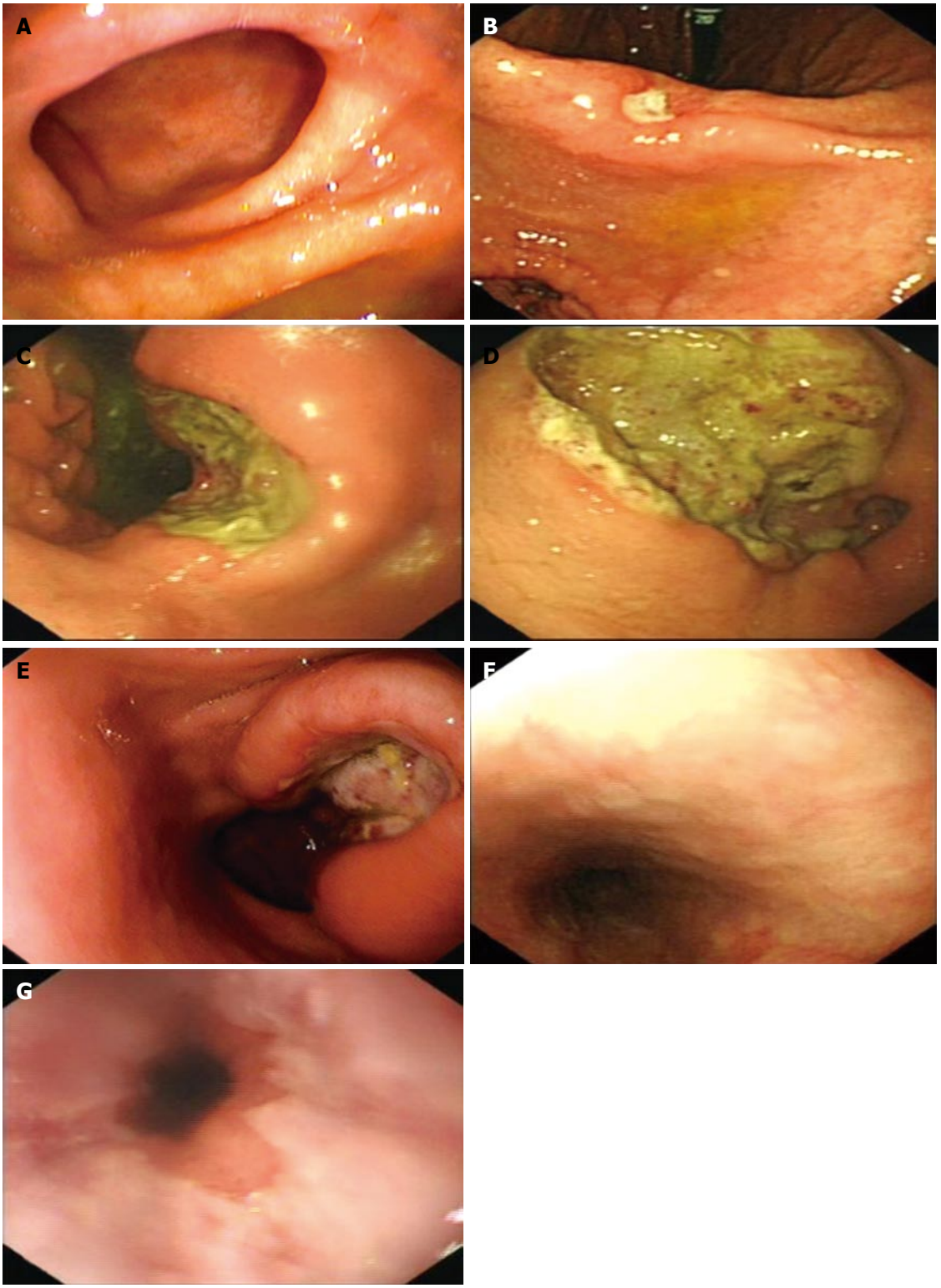

Figure 1 Endoscopic photographs of GEG. **A**: Retracted ulcer scar on greater curvature and incomplete closure of pylorus; **B**: A 0.3 cm × 0.4 cm ulcer on gastric notch had whitish base; **C**: A 3 cm × 4 cm ulcer on inferior wall of gastric body and lesser curvature side. Yellowish green base and tumid ulcer margin; **D**: A 4 cm × 5 cm giant ulcer on lesser curvature side of gastric antrum and gastric notch had thickened and irregular base. Anterior wall of duodenal bulb was involved; **E**: The deformed gastric antrum and a 2 cm × 3 cm giant ulcer on gastric antrum and posterior wall of pylorus. The ulcer had mignonette base and black spots. The ulcer margin presented indentation-shaped appearance. Ulcer tissue was rigid and prone to bleed; **F**: Rough esophageal mucous membrane, blurred vascular net, clear-cut esophageal Z line; **G**: Higher esophageal Z line.

retracted scar tissue in 1 case (Figure 1A), and erosive gastritis in 2 cases.

Sites of ulcers: Gastric notch (3 cases), gastric body (3 cases), gastric antrum (5 cases), complex ulcer (1 case of gastric notch H_1+duodenal bulb A_2, 2 cases of gastric antrum H_1+duodenal bulb A_1), multiple ulcers on cardia and gastric antrum (1 case) and duodenal ulcer (2 cases).

Morphologic characteristics of ulcers: Besides 3 cases of giant peptic ulcers, the diameter of ulcers in most cases was less than 1 cm. Most ulcers were in active stage (7 cas-

es of A_1 stage and 3 cases of A_2 stage) and had whitish or greyish bases (Figure 1B). Merely 2 ulcers had mignonette bases (Figure 1C). Black spots were seen in the ulcer base in 1 case (Figure 1D). In addition, minute protuberances were frequently seen and caused by hyperplasia of granulation tissues. An irregular base was only found at a giant ulcer on the gastric antrum (Figure 1D). But malignant gastric ulcers, regardless of hemorrhage or not, showed dun or mignonette base, and no minute protuberances occurred. The margin of most ulcers was smooth and regular, and congestion and swelling of the surrounding mucosa were frequently seen, and symmetrically thickened (inflammatory) folds typically radiated to the ulcer base (Figures 1C and D). The surrounding mucosa of one giant ulcer presented with an indentation-shaped appearance (Figure 1E), one (posterior wall ulcer of central gastric body) presented with a crater-like appearance, and one (irregular ulcer of the gastric body) had an obscure boundary and nodular base. These cases should be differentiated from malignant ulcer. In contrast, malignant ulcers characteristically have irregular edges, and the surrounding, asymmetrical folds do not radiate to the ulcer base. Such folds may appear nodular or clubbed. An obvious mass often surrounds the malignant ulcer.

Texture of ulcers: Biopsied tissue was relatively rigid but had certain tenacity, ulcer tissues were not fragile, and the sites of biopsies bled less. Nevertheless, ulcer tissues of a giant ulcer on the gastric antrum was rigid and the sites of biopsies were prone to bleed during biopsies (Figure 1E). This case should be differentiated from malignant ulcer. Malignant ulcer is stiff and ulcer tissues are fragile. The sites of biopsies are prone to bleed. Multiple biopsies from the ulcer margin are apt to find malignant cells.

All patients had mucous hyperemia in the gastric fundus and gastric body, and mucosa-mottled congestion in the gastric antrum. Most patients had no gastroduodenal mucosal erosion, except one patient (endoscopic appearance indicative of a complex ulcer) who had mucosal erosion in the gastric notch.

Esophagus was not involved in most patients. Only in 5 cases, esophageal mucosa presented esophagitis-like appearance (Figure 1F). The mucous membrane of esophagus in 4 cases was gray, with blurred vascular net and scattered whitish granulations; 1 case had higher esophageal Z line (Figure 1G), but the mucous membrane of esophagus was normal.

These lesions included 2 cases of deformed pylorus (Figure 1E), 2 cases of incomplete closure of pylorus (Figure 1A) and mucous hyperemia, 1 case of swollen and deformed duodenal bulb, and 1 case of deformed pylorus and duodenal bulb. Anterior wall of duodenal bulb was involved and deformed by a giant ulcer from lesser curvature of gastric antrum to gastric notch in 1 case. Pylorus and duodenal bulb was normal in the rest of the cases.

Pathology

Submucous layer of stomach presented significant inflammatory edema. Massive eosinophil cells and lymphocytes infiltrated into the stomach at full thickness, especially in submucous and muscular layers (Figure 2A-D). In granulated tissues, fibrous tissue proliferation around blood vessels, and fabric scars and hyalinization were found (Figure 2E). Arteriole, veinlets and lymph vessels abundantly proliferated (Figure 2F and G). The muscular layer was crushed and separated by eosinophilic cells, even the serous coat was involved. Lymphoid follicles formed and proliferated in the mucosal base. Intestinal metaplasia emerged in the epithelium of the gastric gland (Figures 2F and G). Chronic inflammation appeared in the peripheral lymph nodes. Ulcers emerged because of gastric mucosa necrosis around the lesions.

Fibroblasts and collagen fibers constituted interstitial substance of the lesions (Figure 2E). Massive eosinophilic cells and lymphocytes infiltrated into the interstitial substance. Occasionally, lymphoid follicles formed in the interstitial substance (Figure 2F and G). Arteriole, veinlets and lymph vessels also existed in the matrix.

DISCUSSION

Kaijser[3] first described GEG in 1937. In 1950, Polayars formally denominated this syndrome as gastric eosinophilic granuloma. In 1961, Ureles, *et al*[2] systematically synthesized and categorized 47 cases of eosinophil cell infiltration in gastrointestinal tract and described the clinical characteristics of GEG extensively.

The cause of GEG is still unknown, and the pathogenesis is poorly understood. The etiological hypothesis of GEG mainly includes familial inheritance, allergic response, inflammation, foreign body reaction, *H pylori* infection, fungous infection, *etc*.[1,4-6].

There are more male patients than females, and middle-aged patients (11 cases) are frequently seen in this group. Clinical manifestations are lack of specificity and usually include stomachache, belching, abdominal distention, sour regurgitation and pyloric obstruction[7]. Compared with peptic ulcers, epigastric pain usually is irregular and is independent of eating. Abdominal pain is often severe and complicated with bleeding and chronic perforation, and antacids are ineffective. Many patients had anemia of different severities. Eosinophilic cells can increase in the peripheral blood of some patients[1].

Gastric mucosa, thickened mucosal folds, and superficial erosion were seen prominently. Because the lesions were involved in the pylorus in some patients, pyloric deformity and obstruction occurred. A few patients still presented incomplete closure of the pylorus. Most patients have ulcers. The edge of most ulcers is usually smooth and regular, and the ulcers have sharp margins, congestion and hydropsia in the surrounding mucosa, which are frequently seen, and symmetrically thickened (inflammatory) folds typically radiated to the ulcer base. The areas of ulcerations in a few patients are comparatively large; the edges of ulcers are irregular or crater-like in appearance; ulcer tissue is relatively rigid but not fragile, and the sites of biopsies are not prone to bleed[8,9]. But bleeding occurred in the sites of biopsies in 1 patient, which should be differentiated from malignant ulcers. Besides the above-mentioned appearances, GEG still has congestion and swelling of the gastric body and gastric fundus; and a few patients involv-

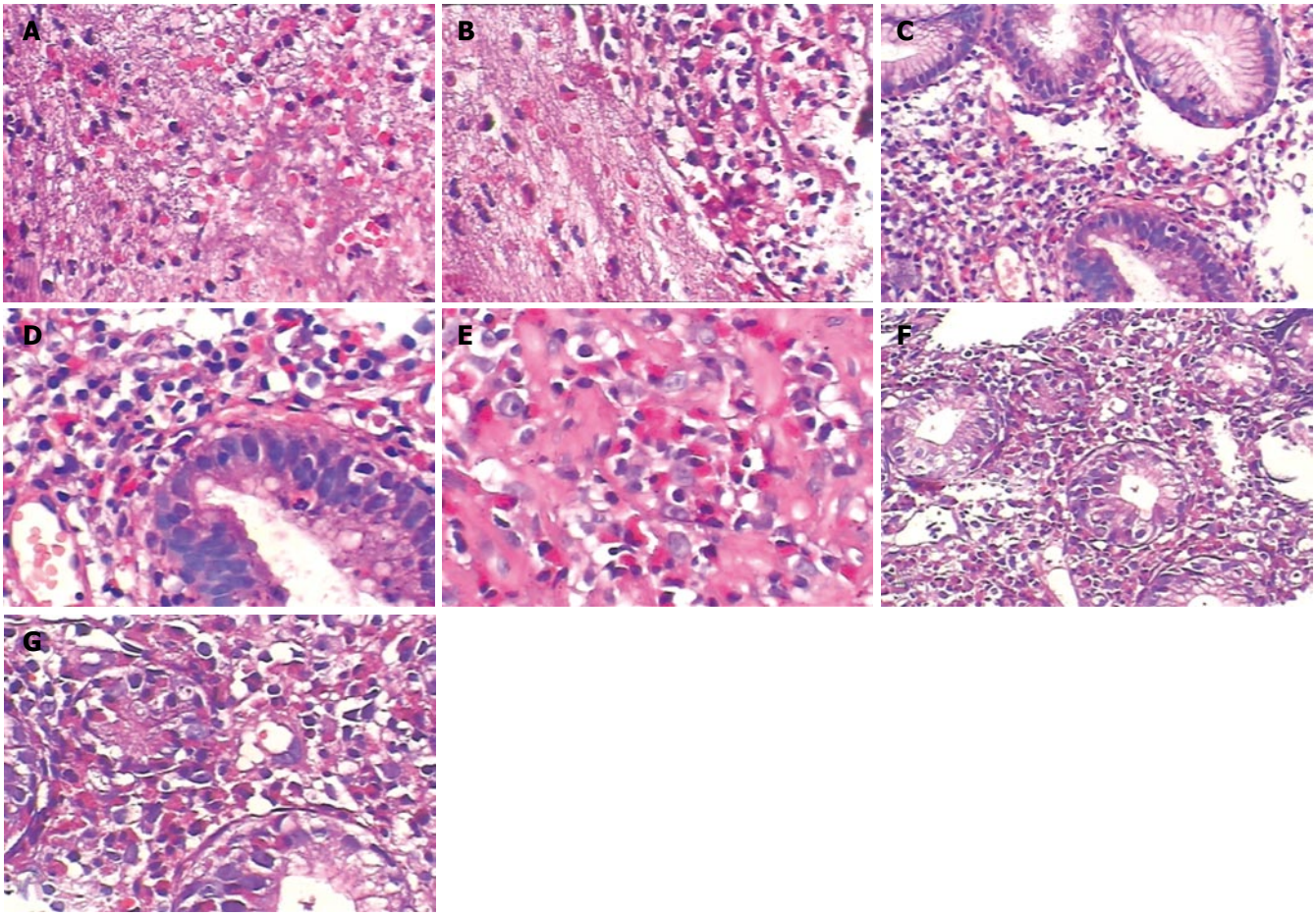

Figure 2 Histologic photographs of GEG (H&E staining). **A**: Massive eosinophil cells and lymphocytes infiltrated (original magnification x 200); **B**: Same view as A, at different magnification (original magnification x 200); **C**: Massive eosinophil cells and lymphocytes infiltrated, especially surrounding the vessels. Intestinal metaplasia (original magnification x 100); **D**: Same view as C, at different magnification (original magnification x 200); **E**: Massive eosinophil cells and lymphocytes. Fibrous tissue proliferation, fabric scar, intestinal metaplasia and hyalinization (original magnification x 400); **F**: Massive eosinophil cells and lymphocytes. Arteriole, veinlets and lymph vessels abundantly proliferated. Lymphoid follicles (original magnification x 100); **G**: Same view as F, at different magnifications (original magnification x 400).

ing the esophagus present an esophagitis-like appearance.

In this group, all patients had lesions in the gastric antrum, and about 45% ulcers were located in the gastric antrum. The causes of GEG ulceration are suggested in four aspects: (1) Thickened stomach wall or localized masses can induce pylorus dysfunction and ulceration[10]. (2) Food deposition caused by gastric emptying disorder results in persistent food contacting with gastric antrum mucosa, which intensively stimulates gastrin and gastric acid secretion. Gastric mucosa is thus damaged and an ulcer forms. (3) Fibrous tissue proliferation surrounding blood vessels, fabric scars and hyalinization in granulation tissue cause insufficient blood supply to the gastric wall, myxasthenia and H-ion counter-diffusion, thus impairing the gastric mucosa. (4) As mucosa of the gastric antrum and lesser curvature is comparatively friable, mucosal defense to causative agents is weak, which increases the incidence rate of ulceration.

In order to increase the diagnostic accuracy of GEG, endoscopic multiple deep biopsies should be performed in suspected areas because of the eosinophilic cells which mainly infiltrate into the submucosal layer. Accordingly, most patients are firmly diagnosed by this method. With regard to the lesions of widespread infiltrating type, gastric carcinoma must be excluded. Endoscopic biopsies should be performed again when biopsies in suspected areas are negative, but these patients normally have chronic digestive system symptoms and simultaneously combine with increasing eosinophilic cells in peripheral blood, or had histories of hypersensitiveness or anaphylactic disease before. Recently, eosinophilic gastroenteritis is diagnosed by percutaneous puncture biopsies under ultrasound guidance[11].

Vanek[12] suggests the criteria for pathologic diagnosis of GEG as follows: (1) Interstitial substance is composed of fibroblasts and collagen fibers; (2) Eosinophilic cells and lymphocytes infiltrate into interstitium. Lymphoid follicles form occasionally; (3) Arteriole, veinlets and lymph vessels exist in interstitium; (4) Ulcers emerge around the pathologic lesions. While malignant lesions must be carefully precluded, GEG should be differentiated from plasma cell granuloma of the stomach when more plasma cells and Russell bodies are found in pathological lesions of some GEG patients. Exceptional granulomatous lesions such as mycetes, parasite, etc. should also be excluded. The pathological lesions of the 18 cases are consistent with the diagnostic criteria.

Therefore, in order to decrease the misdiagnosis rate, it is extremely important to have an intimate knowledge of endoscopic findings and pathologic characteristics of

GEG. Meanwhile, endoscopic examinations and endoscopic multiple deep biopsies in suspected areas are indispensable for accurate diagnosis. In addition, because endoscopic findings of some GEG patients are similar to that of gastric carcinoma, gastric lymphoma, gastric fibroma, gastric ulcer complicated with fungus infection, *etc*., these diseases must be attentively discriminated.

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