Rare cause of severe hematemesis due to IgG4-related gastric ulcer

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Cite this article as: *He YQ, Fu X, Chen DF. Rare cause of severe hematemesis due to IgG4-related gastric ulcer. Turk J Gastroenterol 2019; 30(10): 925-7.*

Dear Editor,

Immunoglobulin G4-related disease (IgG4-RD) is a systemic fibroinflammatory condition with multiorgan involvement, which includes the exocrine and endocrine glands, kidneys, soft tissues, skin, lymph nodes, digestive system, cardiovascular system, and respiratory tract. Since IgG4-RD pancreatitis was first reported in 2001 and officially named in 2010, IgG4-RD has received increasing attention. Umehara et al. (1) proposed the 2011 comprehensive diagnostic criteria and recommended that the diagnosis should be pathologically confirmed. The established diagnostic criteria are as follows: the IgG4 plasma level >135 mg/dl; IgG4-positive plasma cells/IgG-positive plasma cells >40%, or plasmacytic infiltration with infiltrating IgG4-positive plasma cells >10/high-power field (HPF). A recent cohort study presented that the demography of IgG4-RD was an adult disease, 90% of these patients were >50 years old, and pancreatitis was the leading manifestation (2). In the present reports a rare case of IgG4-related gastric ulcer not combined with other organs, which is very rare in clinical setting. Furthermore, it is not common for 14-year-old adolescent patients. The importance of considering IgG4-related gastric ulcer as a possible cause was highlighted when the patient had prior unexplained gastrointestinal ulcer.

A 14-year-old boy was admitted to the Gastroenterology Department of our hospital due to melena and severe anemia that lasted for 2 days. During the past 4 years, the patient had suffered from recurrent hematemesis 4 times and was diagnosed with duodenal ulcer and bleeding each time. The patient had never used nonsteroidal anti-inflammatory drugs and has never suffered from other diseases or systemic inflammatory disorders. A computed tomography scan did not show the presence of other organs injured, and there was no history of a systemic clinical symptom disorder. Furthermore, the patient denied the existence of any hereditary disease in his family, and he had no psychosocial history and other medical treatment history. The 14C-urea breath test and serum Helicobacter pylori IgG antibody test were negative. Each time, the patient was regularly treated with esomeprazole. However, these treatments were almost ineffective.

In the present study, the physical examination of the patient revealed the following: body temperature, 36.8°C; blood pressure, 89/60 mmHg; respiratory rate, 20 bpm; and heartbeat rate, 95 bpm. Other pertinent findings included Borborygmi bowel sounds, as well as abdominal tenderness and rebound tenderness, especially in the upper quadrant. The laboratory examination revealed that hemoglobin was 50 g/L. The esophagogastroduodenoscopy (Olympus, Japan) revealed a large duodenal ulcer accompanied by a small blood-like fluid effusion, luminal stenosis, and multiple small ulcers in the gastric (Figure 1a, b). The patient was regularly treated with a proton-pump inhibitor (esomeprazole, 40 mg per day) and hydrotalcite tablets. However, the patient's ulcer failed to improve after 7 days of treatment (Figure 2). Therefore, the investigators realized that the condition was not due to excessive gastric acid. The review of the history and clinical data of the 14-year-old male patient revealed an unexplained recurrent severe hematemesis. In addition, case reports on IgG4-RD were researched. At the same time, the diagnosis experience of IgG4 was combined in the present clinical work. Finally, the Ig-G4 levels were investigated. The plasma examination revealed that the IgG4 level was 423 mg/dL. For further evaluation, pathological tissues from the large duodenal ulcer were drawn. The immunohistochemistry revealed prominent immunoglobulin (IgG4)-positive plasma cells within an

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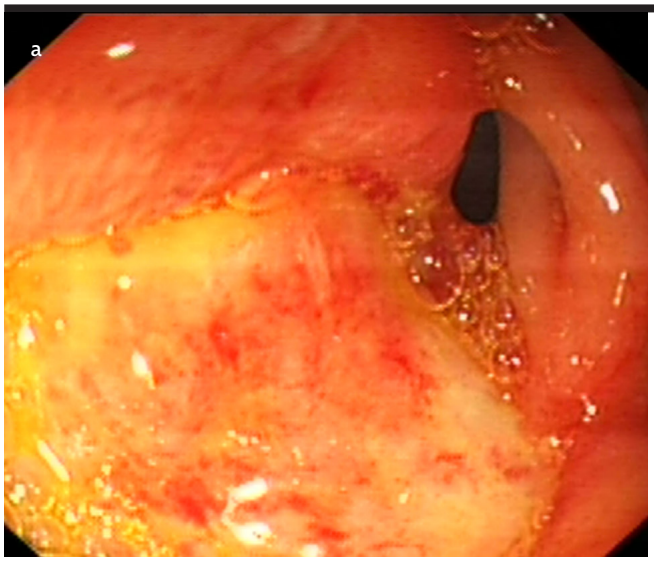
Received: ***July 11, 2018*** *Accepted:* ***December 4, 2018*** *Available online date:* ***August 28,2018***

DOI: ***10.5152/tjg.2019.18543***



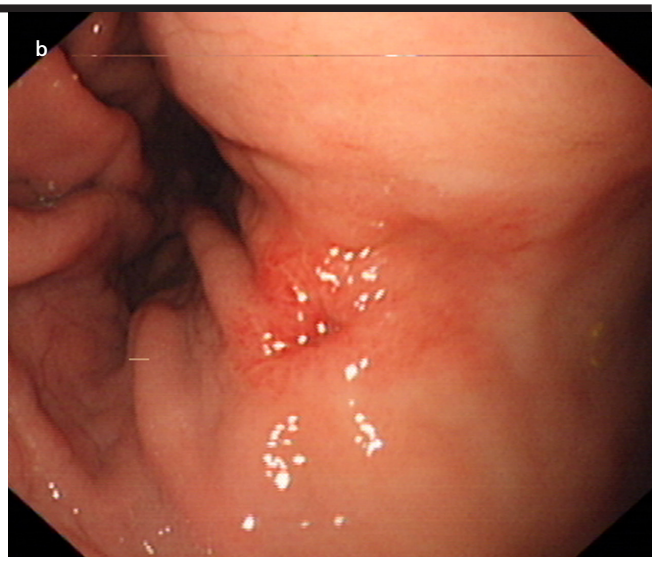


Figure 1 a, b. Endoscopic image. (a) A deep and large duodenal ulcer, 2 cm in diameter, presenting with edema, white fur, and stenosis. (b) Multiple small ulcers in the gastric.

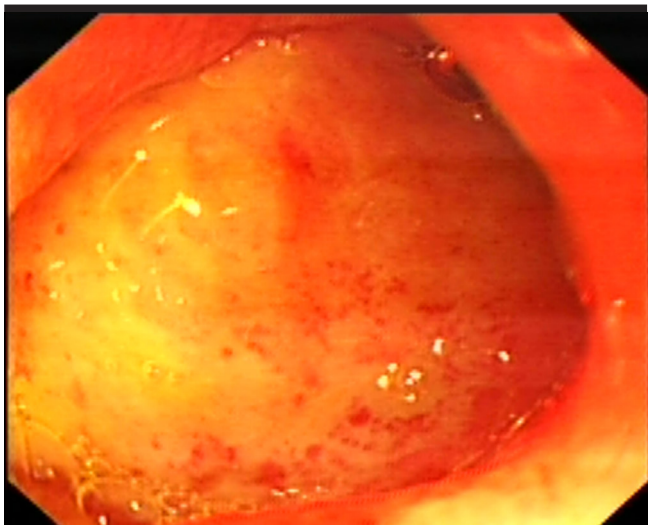


Figure 2. Endoscopic image. The gastroscopy revealed a deep and large duodenal ulcer after 7 days of treatment with esomeprazole at 40 mg per day.

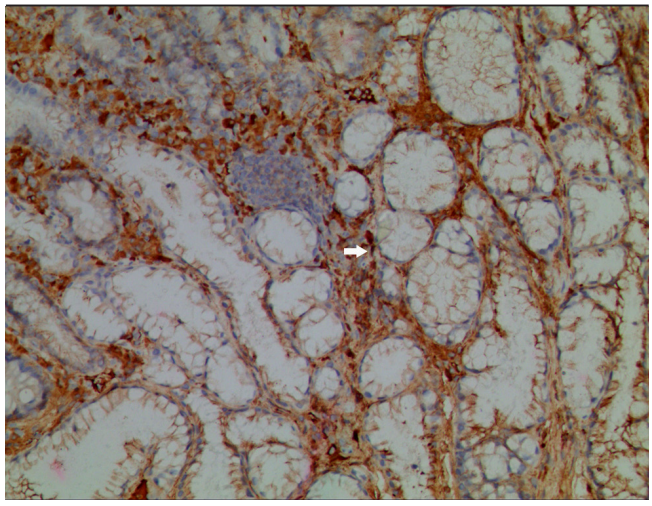


Figure 3. Histological examination of the IgG4 staining of the ulcer partial tissue specimens. Abundant IgG4-positive plasma cells were noted within the ulcer base (Immunohistochemical [IHC] staining, ×400).

inflammatory infiltrate of >210 cells per HPF. The ratio of IgG4-positive plasma cells to total IgG expressing plasma cells was 70% (Figure 3). The duodenal mucosa revealed storiform fibrosis. The patient was treated with methylprednisolone (40 mg per day), tapering the dose in the subsequent 3 weeks. After 4 weeks, most of the ulcers recovered, and the edema of the intestinal wall rapidly recovered. However, gastrointestinal fistulas were found between the duodenum and ileum, because of the long-standing fibrosis and persistent chronic inflammatory processes (Figure 4). No ulcer was detected at the last follow-up (14 months), and the patient's health significantly improved with weight gain.

IgG4-RD is a newly recognized disease. It is a multiorgan immune-mediated condition that mimics many malignant, infectious, and inflammatory disorders. Multiple organs are involved in this disease, such as the pancreas, kidney, bile duct, lung, glands, aorta, and retroperitoneum (3,4). The epidemiology was characterized as a priority

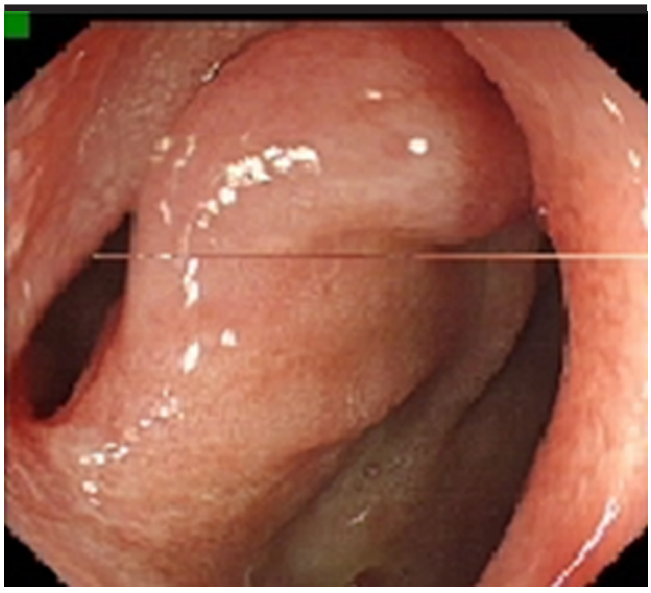


Figure 4. Endoscopic image. A gastrointestinal fistulas were found between the duodenum and ileum after 4 weeks of treatment with methylprednisolone.

for elderly males. The pathological features of IgG4-RD include diffuse lymphoplasmacytic infiltration, storiform fibrosis, obliterative phlebitis, and numerous IgG4-bearing plasma cells in affected tissues.

There have been some case reports of possible gastric involvement, and the manifestations include ulceration and pseudotumor formation in the gastrointestinal. The infiltration of IgG4-positive plasma cells was observed in the gastric mucosa in 33%-47% of patients with autoimmune pancreatitis (5). IgG4-RD can typically occur in middle-aged and elderly patients, and the age of these patients ranges between 54 and 78 years. However, merely IgG4-related gastric ulcers not combined with other organs are very rare in clinical practice. Frydman et al. (4) reported a case of IgG4-RD manifesting as an acute gastric-pericardial fistula, while Bateman et al. (5) revealed a 73-year-old female with an IgG4-related gastric ulcer. The present case had duodenal ulcer without the involvement of other organs. Unlike usual gastric ulcers, the present case suggests that these patients suffer from a long history of an IgG4-related ulcer. As the first feature, these patients are diagnosed with usual gastric ulcer and treated with proton-pump inhibitors at a regular dose several times without effect. The second feature is the esophagogastroduodenoscopy. The endoscopic feature of this disease is the thickening of the ulcer base. The long-standing fibrosis and persistent chronic inflammatory processes caused by lymphoplasmacytic infiltration, storiform fibrosis, and obliterative phlebitis may lead to ulcer formation. These factors explain why there was protruded stenosis and gastrointestinal fistulas. The clinical manifestation of IgG4-related gastric ulcer has no distinguishing characteristic feature from usual ulcer. Hence, IgG4-related gastric ulcer needs to be taken into account when the ulcer is not a simple case.

Gastric ulcer may be associated with IgG4-RD in some patients with a history and suffered from this for several years. Unfortunately, in the past, these patients were treated using regular treatment protocols (proton-pump inhibitor and hydrotalcite tablets), which had a poor response. The investigators would like to emphasize this condition. Due to the long-standing fibrosis and persistent chronic inflammatory processes, the ulcer had endoscopic findings of white fur overflow, the thickening of the ulcer base, and a clear sector. Corticosteroids may have an excellent effect in these patients.

Informed Consent: Written informed consent was obtained from the patient who participated in the present study.

Peer-review: Externally peer reviewed.

Author Contributions: Concept - D.F.C.; Design - D.F.C.; Supervision - D.F.C.; Resources - Y.Q.H., X. F.; Materials - Y.Q.H., X. F.; Data Collection and/or Processing - Y.Q.H., X. F.; Literature Search - Y.Q.H.; Writing Manuscript - Y.Q.H.; Critical Review - D.F.C., Y.Q.H.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: This work was supported by grants from the Natural Science Foundation of China (no. 81700466/H0307).

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