Gastric Calcifying Fibrous Tumor: A Case of Suspected Immunoglobulin G4-related Gastric Disease

Hejun Zhang, Zhu Jin, Shigang Ding

Department of Gastroenterology, Peking University Third Hospital, Beijing, China

Address for correspondence:
Dr. Shigang Ding,
No. 49 Road Huayuan North, Haidian District, Beijing - 100191, PR China.
E-mail: dingshigang222@163.com

ABSTRACT

Gastrointestinal lesions resulting from immunoglobulin G4-related disease are classified into two types: One is a gastrointestinal lesion showing marked thickening of the wall, and the other is an IgG4-related pseudotumor. We report the case of a woman with gastric calcifying fibrous tumor undergoing endoscopic resection that contained 62 IgG4+ plasma cells per high-power field and an IgG4-to-IgG ratio of 41% in lesional plasma cells, which shared clinical and histopathological features associated with gastric IgG4-related pseudotumor. So, we postulate that calcifying fibrous tumor as part of the spectrum of IgG4-related disease might be the unifying concept with IgG4-related pseudotumor. Meanwhile, the patient had coexistent autoimmune diseases, including autoimmune atrophic gastritis, Hashimoto’s thyroiditis, and possible primary biliary cirrhosis. The clinical follow-up evaluation was uneventful.

Key Words: Calcifying fibrous tumor, IgG4-related disease, IgG4-related pseudotumor, stomach

CASE REPORT

A 55-year-old woman presented with epigastric pain and flatulence. Physical examination was unremarkable. The laboratory tests revealed mild normocytic anemia (hemoglobin 106 g/L) and a mildly decreased free thyroxine (0.81 ng/dL, normal 0.89–1.80). Very high thyroglobulin antibodies (265.8 U/mL, normal <60) and thyroid peroxidase antibodies (>1300 U/mL, normal <60) were noticed. Other serum autoantibodies, including antinuclear antibody (1/80, normal <1/40), antiparietal cell antibody (APCA) (1/320, normal <1/40), antimitochondrial antibody M2 subtype (75R U/mL, normal <20R U/mL), were also positive. Other laboratory findings were all normal.

Gastroscopy revealed a submucosal tumor with intact overlying mucosa in the posterior wall of the upper corpus, and a Yamada type III polyp was found at its proximal side [Figure 1a]. Endoscopic ultrasonography visualized the tumor mainly within the third layers of the gastric wall, measuring 20 mm in its maximal diameter. These findings...
were interpreted as suggestive of a gastrointestinal stromal tumor, endoscopic submucosal dissection and endoscopic mucosal resection were performed to remove the submucosal tumor and the polyp, respectively.

Microscopic examination of whole-mount serial sections of tumor showed a well-circumscribed but nonencapsulated tumor in the submucosa associated with the multiple lymphoid follicles showing prominent germinal centers. Psammomatous calcifications were scattered throughout [Figure 1b]. Some psammomatous calcifications could be observed in the minute vascular lumina [Figure 1b insert]. The tumor consisted of paucicellular, densely hyalinized, collagenous matrix, which exhibited a predominant pattern of storiform arrangement. Uniform, spindle-shaped cells were dispersed among thick collagen bundles, and did not show any cellular atypia or mitotic activity. Lymphoplasmacytic infiltrates were present among the sclerotic stroma [Figure 1c]. Obliterative phlebitis was not observed. Immunohistochemically, the spindle-shaped cells showed Vimentin expression and no immunoreactivity for DOG-1, CD117, CD34, S-100, SMA, desmin, and Ki-67. Based on the above characteristic morphologic and immunohistochemical findings, a diagnosis of CFT was rendered. IgG4+ plasma cells were observed [Figure 1d]. Examining three high-power fields (HPFs, ×400) within the same hotspot produced a mean of 152/HPF IgG+ plasma cells and 62/HPF IgG4+ plasma cells. The IgG4-to-IgG ratio was 41%. The serum IgG4 level was within normal range (0.169 g/L).

The histology of overlying mucosa showed chronic atrophic gastritis, with pseudopyloric metaplasia and mild intestinal metaplasia [Figure 2a]. Parietal cell pseudohypertrophy [Figure 2b] and nodular enterochromaffin-like cell hyperplasia (immunostain for synaptophysin) [Figure 2c] were observed. The histology of the polyp revealed classic hyperplasic polyp [Figure 2d]. Combined with the serological findings (APCA, 1/320), a diagnosis of autoimmune atrophic gastritis was made. IgG4+ plasma cells were not observed in the mucosa. Additionally, taking into account the serological results above, the diagnoses of Hashimoto’s thyroiditis and possible primary biliary cirrhosis were also made. The patient refused to undergo biopsies from thyroid gland and liver. The patient was discharged with a good recovery and has been followed for 5 months without any signs of disease recurrence.

**DISCUSSION**

IgG4-related gastrointestinal diseases were classified into two types: One is a gastrointestinal lesion showing marked thickening of the wall, and the other is an IgG4-related pseudotumor.[2] A summary of reported cases of gastric IgG4-related pseudotumor (no. 1–6)[3-6] is described in Table 1. Histologically, there are obvious similarities between gastric IgG4-related pseudotumor and our case. Interestingly, obliterative phlebitis was not identified in all these cases,
and psammomatous calcifications could only be observed in case no. 5\(^{(5)}\) and our case. In the present case, some psammomatous calcifications, as described in the literature, could be observed in the minute vascular lumina, suggesting that psammomatous calcifications may be the calcified vascular channels and the result of obliteratorile phlebitis.\(^{(1,7)}\) In all cases, an elevated serum IgG4 was not found [Table 1].

Coexistent autoimmune disease in gastric IgG4-related pseudotumor had been described in case no. 2, while our case also had other autoimmune diseases. Increased numbers of IgG4+ plasma cells were found in the gastric mucosa of some autoimmune atrophic gastritis patients.\(^{(8)}\) However, in the present case, IgG4+ plasma cells were not observed in the mucosa. Hashimoto’s thyroiditis is the most frequently associated autoimmune condition in autoimmune atrophic gastritis patients. IgG4+ Hashimoto’s thyroiditis, characterized by thyroid inflammation rich in IgG4+ plasma cells and marked fibrosis, has been identified.\(^{(9)}\) Because the current patient refused to undergo a thyroid biopsy, it was uncertain whether there was a IgG4+ plasma cell infiltrate in the thyroid gland.

Whilst the histopathological differential diagnosis for sclerotic lesions within the gastroenterological tract is extremely wide and varied, the most important to be considered are “burnt-out” examples of GIST, smooth muscle neoplasm, nerve sheath tumor, inflammatory myofibroblastic tumor, solitary fibrous tumor. Immunohistochemistry is the obvious aid to reaching the correct diagnosis.

Gastric CFT described herein, with a significant IgG4-positive plasma cell infiltrate (62/HPF) and a high IgG4-to-IgG ratio (41%), supports the view that CFT may represent different stages of IgG4-related disease\(^{(1,7)}\) and fits with the unifying concept of IgG4-related pseudotumor.\(^{(10)}\) IgG4-related pseudotumor may respond to conservative treatment with steroids. Therefore, treatment with steroids should be attempted before surgical or endoscopic resection.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES
1. Agaimy A, Bihl MP, Tornillo L, Wünsch PH, Hartmann A, Michal M. Calcifying fibrous tumor of the stomach: Clinicopathologic and molecular study of seven cases with literature review and reappraisal of histogenesis. Am J Surg Pathol 2010;34:271-8.
2. Koizumi S, Kamisawa T, Kuruma S, Tabata T, Chiba K, Iwasaki S, et al. Immunoglobulin G4-related gastrointestinal diseases, are they immunoglobulin G4-related diseases? World J Gastroenterol 2013;19:5769-74.
3. Chetty R, Serra S, Gauchotte G, Märkl B, Agaimy A. Sclerosing nodular pseudotumor of the stomach (CFT) and its spectrum of disease; a molecular study of 5 cases. Histopathology 2008;52:837-44.
lesions of the gastrointestinal tract containing large numbers of IgG4 plasma cells. Pathology 2011;43:31-5.

4. Rollins KE, Mehta SP, O’Donovan M, Safranek PM. Gastric IgG4-related autoimmune fibrosclerosing pseudotumour: A novel location. ISRN Gastroenterol 2011;2011:873087.

5. Kim do H, Kim J, Park do H, Lee JH, Choi KD, Lee GH, et al. Immunoglobulin G4-related inflammatory pseudotumor of the stomach. Gastrointest Endosc 2012;76:451-2.

6. Na KY, Sung JY, Jang JY, Lim SJ, Kim GY, Kim YW, et al. Gastric nodular lesion caused by IgG4-related disease. Pathol Int 2012;62:716-8.

7. Jang KY, Park HS, Moon WS, Lee H, Kim CY. Calcifying fibrous tumor of the stomach: A case report. J Korean Surg Soc 2012;83:56-9.

8. Bedeir AS, Lash RH, Lash JG, Ray MB. Significant increase in IgG4+ plasma cells in gastric biopsy specimens from patients with pernicious anaemia. J Clin Pathol 2010;63:999-1001.

9. Luiz HV, Gonçalves D, Silva TN, Nascimento I, Ribeiro A, Mafra M, et al. IgG4-related Hashimoto’s thyroiditis - a new variant of a well known disease. Arq Bras Endocrinol Metabol 2014;58:862-8.

10. Lynnhtun K, Achan A, Lam V. IgG4 related pseudotumour (calcifying fibrous tumour) of adrenal gland. Pathology 2013;45:519-21.