Immunoglobulin G4-related gastric pseudotumor – An impostor: Case report

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A B S T R A C T

INTRODUCTION: Gastric pseudotumors are rare entities whose clinical presentation resembles typical gastric neoplasias, often making them unrecognized unless other causes are considered.

PRESENTATION OF CASE: We present a case report of a patient that debuts with dysphagia, with an abdominal computed axial tomography (CAT) scan revealing a mass at the gastro-esophageal junction suggestive of malignant origin, with studies revealing it to be Immunoglobulin G4-related (IgG4).

DISCUSSION: The diagnosis and identification of IgG4-related gastric pseudotumors is very complicated, often and most commonly an incidental diagnosis upon histologic analysis, as is the situation in this case.

CONCLUSION: Understanding its clinical course and early diagnosis can reduce unwarranted surgical intervention in some patients with IgG4-related disease.

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1. Introduction

Gastric pseudotumors are rare entities whose clinical presentation resembles typical gastric neoplasias, often making them unrecognized unless other causes are considered [1]. The subepithelial lesions have malignancy potential, thus making them a public health problem due to late diagnoses leading to high mortality rates [1]. It is not always evident, but pathologies resembling neoplasias should be thoroughly studied and differential diagnosis should be considered, such as IgG4-related inflammatory pseudotumors [2]. These are rare benign autoimmune diseases caused by IgG4-rich cells infiltrating different tissues and producing clinical features that resemble neoplasias, however their biopsies are often inconsistent with this [3,4]. We present a case report of a patient initially suspected of a malignant entity at the gastro-esophageal junction, with later studies revealing it to be IgG4-related, in accordance with the SCARE criteria [5].

2. Presentation of case

A 45-year-old female auxiliary nurse patient, from Bogota, consulted due to progressive dysphagia of six months, associated with weight loss and gastroesophageal reflux disease (GERD), until she could no longer tolerate solid food. Her previous clinical history included tobacco use and a daughter with systemic erythematous lupus. Upon initial examination, the patient was emaciated without any other particular findings. Previously, at another institution, an abdominal computed axial tomography (CAT) scan had been performed showing a mass at the gastro-esophageal junction with concentric stenosis. Endoscopic biopsies eventually ruled out malignancy and the patient was transferred to our institution for definitive management of a benign gastric-esophageal stenosis.

Upon arrival, patient was treated with pneumatic dilations on two occasions, using an 18 mm balloon, without symptomatic improvement. Five months later, in May of 2017, given the symptoms, a contrasted abdominal CAT scan was performed showing a nodular infiltrative wall thickening of the gastro-esophageal junction without adenopathy (Fig. 1A-B). Additionally, an esophageal motility test (cindeglution) confirmed a subcardial gastric stenosis (Fig. 2).

Based on these results, an upper gastrointestinal endoscopy was repeated confirming the gastric cardiac and subcardial lesion suggestive of an infiltrating neoplastic mass. Biopsies showed diffuse active stromal activity (chronic gastritis with erosion) and H. Pylori infection requiring treatment, without evidence of a neo-

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plastic lesion. However, given the persistency of symptoms as well as the inconclusive biopsy and images, an echoendoscopy was chosen as a useful study for sub-epithelial lesions [1]. This test showed a cardial hypoechoic concentric lesion affecting all layers approximately 12 mm thick, suggestive of a tumor of stromal origin. This was ruled out based on the biopsy that reported an active ulcer with stromal activity and chronic cardio-fundal erosion and gastritis, without neoplasia.

These results forced a medical board meeting to determine treatment considering the clinical course and lesions consistent with neoplasia, despite the biopsies reported. This led to a surgical approach determined and approved by the patient. A laparoscopic total gastrectomy with reconstruction in Y-de-Roux was the initial attempt. However, this was converted to a laparotomy due to several difficulties: the lesion had infiltrated the diaphragmatic walls, the arcuate ligament, the celiac trunk, and the dorsal pancreas; there was an ischemic spleen; and there were lymph nodes in the hepatic common duct. Ultimately, the mass was located at the gastro-esophageal junction, classifying it based on TNM as T4bN1M0 stage IIIC. The resulting gastrectomy, splenectomy and
partial segmentary pancreatectomy were completed without any complications.

In the post-operative state, the patient presented ileus that resolved with medical management, with hospital discharge seven days later. The patient reconsults and is readmitted multiple times due to nausea, anxiety, and depressive episodes requiring a multidisciplinary approach. During these admissions, an esophageal motility test confirmed adequate passage of medium contrast (Fig. 3A-B), without any filtration or stenosis, ruling out any surgical complications associated with the readmissions.

One month post-operatively, the patient reconsults due to abdominal pain. An abdominal CAT scan reveals a thrombosis of the inferior mesenteric and portal veins, requiring Dalteparin and ensuing coagulopathy studies without any significant findings. The intraoperative specimen reported a fibrosclerosing process rich in plasmatic cells, without any evidence of neoplastic lesions. Additionally, the lesion reported an inflammatory lymphoplasmocytic infiltrate from the lamina propria mucosa extending to the subserous tissue, accompanied by marked fibrosis and resulting severe thickening of the gastric wall. Immunohistochemical studies were IgG and IgG4 positive in plasmatic cells, with a IgG4/IgG ratio of 30% and up to 130 IgG4-positive plasmatic cells per high power field. Additionally, results showed ALK-negative cells and smooth muscle actin and cocktail cytokeratin markers (AE1/AE3) positive in normal muscle and epithelial tissue. With these findings, a histological diagnosis of gastric compromise due to IgG4-related disease is confirmed. A correlation with serum IgG4 levels is determined, with high serum levels of 1380 mg/dL (normal value of 1–135 mg/dL).

Given the findings of an IgG4-related inflammatory gastric wall neoplasia, inactive moderate non-atrophic chronic gastritis, focal intestinal metaplasia without dysplasia (Figs. 4–6), and normal spleen, the consideration of an IgG4-related disease had to be considered. This led to IgG4-serum correlation with high levels, confirming the diagnosis and initiating the ensuing systemic corticoid treatment.

3. Discussion

Gastric neoplasias are a public health problem, given their late diagnosis and treatment difficulties, increasing its mortality rate [6]. Although in developed countries mortality has decreased, it remains a problem in developing countries causing a third of all cancer-related deaths [6]. This obligates a thorough study, with diagnosis and treatment of all malignant-suggestive lesions.
IgG4-related diseases are systemic diseases characterized by plasmatic cell infiltration staining positively for IgG4. These IgG4-rich plasmatic cells can be found in the gastric, colonic and duodenal mucosa layers, with macroscopic changes evident depending on the tissue [7,11]. The most common age group affected is adults between 45–47 years old, without any preference in either gender [2]. Despite this, more female patients have been reported, but given the scarce number of total cases a tendency for gender majority cannot be established [10].

Clinical features of IgG4-related diseases include: edema, diffuse mass in one or more organs, elevated IgG4 serum levels, or abundance of IgG4-rich plasmatic and lymphocytic cells infiltrating and causing fibrosis [11,12]. In medium-caliber venous vessels, fibrosis can be observed in late stages due to increased lympho-plasmatic infiltration [12]. IgG4 serum levels can be used as a diagnostic aid, however they are not always elevated, nor specific to IgG4-related diseases. Serum levels can also be elevated in lymphomas [2], ulcerative colitis and other inflammatory and infectious diseases [11]. Thirty percent of patients with clinical findings suggestive of IgG4-related autoimmune disease do not have elevated serum levels [7]. The established diagnostic criteria include [13]:

- Storiform fibrosis and obliterator phlebitis, multiple IgG4-rich cells, and elevated IgG4/IgG proportions [10,13,14].
- Elevated IgG4 serum levels (>135 mg/dL) [10].
- Thickening of organ walls, edema, or nodules in one or more organs [10].
- Effective response to corticoid therapy.

Gastric compromise in IgG4-related disease is unusual but can present itself in two forms: 1) diffuse wall thickening or presence of a mass or polyp, or 2) ulcerative compromise [2,3,12,15]. Although rarer, the latter can be single or multiple ulcers and often affects the pancreas [16]. In these cases, H. Pylori treatment can aggravate ulcers and the resulting clinical outcome of the patient [3,15]. Several other case reports have shown that gastric compromise is often accompanied by other affected organs [12]. This emphasizes the diagnostic challenge of IgG4-related diseases given its similarities with stromal and neuroendocrine tumors. Hence why many cases are diagnosed after surgical or endoscopic tumor resection and pathological specimen is completed [2,12,13].

There is also a histologic challenge that stems from the biopsy specimens often having ample fibrosis and sclerosis associated, hindering an accurate diagnosis [4,7]. The inflammatory component in the specimens is often seen on muscle, followed by subserous tissue [13], the latter often indicative of a neoplasia disease [7], thus favoring an early surgical resection in unclear diagnostic cases. Complementary imaging studies are also often confused with neoplastic entities [3]. Because of this, often a wide margin surgical resection is often employed, despite knowing that in accurate IgG4-related disease diagnosis the pharmacological treatment is often enough [4,10]. In terms of imaging, the abdominal CAT scan often reveals a gastric wall thickening with or without adenopathy associated [13], confusing a malignant diagnosis.

Inflammatory pseudotumors should be suspected when biopsies report storiform fibrosis and obliterator phlebitis [13,14], however clinical manifestations can be varied especially in cases of unclear clinical physiopathology [11]. Pharmacologic treatment after diagnosis is often sufficient with corticoid therapy [2–4], with titrated doses based on clinical response [16]. Corticoid treatment failure is associated with an additional stenotic compromise, the latter benefiting greatly from surgical resection or dilations [4]. Clinical response has to be monitored with corticoid treatment given the high risk of an erroneous diagnosis and risk of hiding a neoplasia [4].
4. Conclusion

All patients with presumptive tumoral gastric lesions should be thoroughly studied, especially when histologic results are inconclusive. At this point, IgG4-related pseudotumors should be considered as a differential diagnosis and the resulting studies should be performed to ensure diagnostic accuracy. In cases where treatment is warranted, close clinical response should be monitored taking into account the diagnostic marginal error. Additionally, surgical options should be considered in stenotic cases that fail to improve despite pharmacological treatment. Specific treatment has to be chosen on a case-by-case basis and always considering the possibility of a malignant disease.

IgG4-related lesions are a diagnostic challenge, surgeons must have awareness of this disease to ensure an opportunistic diagnosis and adequate treatment. Considering this entity as a differential diagnosis will help in the definitive management and diagnosis. Lastly, this case report supplements the existing literature ensuring a better understanding of IgG4-related gastric pseudotumors, given its limited clinical presentation.

Declaration of Competing Interest

The authors report no declarations of interest.

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Ethical approval

The Ethical and Research Committee of Fundación Cardioinfantil – IC and the General Surgery Research Group at Fundación Cardioinfantil – IC.

Consent

Written consent was obtained from the patient for publication of this report. Any details identifying the individuals to the clinical history and images associated were eliminated as to remain anonymous.

Author’s contribution

Suárez Gómez A, Moreno-Medina K, González-Orozco A, and Perez Rivera CJ designed the report, analyzed the data, and wrote the paper. Mosquera MS and Suárez Gómez A collected patient’s data and were the perioperative attending physicians. Herrera H collected and analyzed pathologic specimen.

Registration of research studies

N/A.

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