CASE REPORT
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Immunoglobulin G4-related disease mimicking acute appendicitis: The first case report from Türkiye

Serra Bayrakçeken[1], Nilsu Güvencer[2], İsmail Ahmet Bilgin[1], Süha Göksel[3], Volkan Özben[1]

[1]Department of General Surgery, Acıbadem Mehmet Ali Aydınlar University Faculty of Medicine, İstanbul, Türkiye
[2]Department of Obstetrics and Gynecology, Acıbadem Mehmet Ali Aydınlar University Faculty of Medicine, İstanbul, Türkiye
[3]Pathology Laboratory, Acıbadem Maslak Hospital, İstanbul, Türkiye

ABSTRACT

Immunoglobulin G4–related disease (IgG4-RD) is a fibroinflammatory condition that can present as mass-like lesions mimicking tumors, infections or immune-mediated diseases. Although multiple organs may be involved, appendiceal involvement is extremely rare with only eight cases reported in the literature. Here, we report a case of a 38-year-old male patient who presented with clinical features of acute appendicitis and underwent laparoscopic appendectomy with cecal wedge resection. Intraoperatively, a mass-like lesion was observed. Histopathological examination revealed IgG4-positive plasma cells, non-necrotizing granulomas, submucosal and subserosal fibrosis consistent with IgG4-RD of the appendix. The patient was discharged on postoperative day one without complications and no clinical abnormalities were noted during a postoperative one-year follow-up period. This report describes the first case of appendiceal IgG4-RD reported from Türkiye. Despite its uniqueness, IgG4-RD should be considered in the differential diagnosis of appendiceal pathologies to ensure accurate diagnosis and patient management.

Keywords: IgG4-related disease, appendix, appendicitis, appendiceal neoplasm

INTRODUCTION

Immunoglobulin G4-related disease (IgG4-RD) is an autoimmune fibroinflammatory condition characterized by IgG4-positive plasma cell infiltration and inflammatory fibrosis which results in damage to the affected organs (1). The characteristics of IgG4-RD include tumor-like formation, lymphoplasmacytic infiltration with IgG4-positive plasma cells, storiform fibrosis, obliterative phlebitis, perineuritis, mild tissue eosinophilia and often elevated serum IgG4 concentrations. This condition involves a wide range of disorders that may affect a variety of organs including the pancreas, liver and bile ducts, skin, urinary tract, pleura, peritoneum, and meninges (2). However, appendiceal involvement is extremely rare, and to date, only eight cases have been reported in the literature (3-10). Because of its rarity and non-specific clinical symptoms, the diagnosis of IgG4-RD involving the appendix is challenging and patients are at increased risk for misdiagnosis.

Here, we report the first case of appendiceal IgG4-RD from Türkiye with special attention to its clinical, radiological and pathological findings.

CASE REPORT

A 38-year-old male presented to the emergency department of Acıbadem Maslak Hospital with a four-day history of right lower abdominal pain. He had no remarkable medical history except for a prior left inguinal hernia repair, tonsillectomy and right ulnar nerve repair due to traumatic injury. He had no chronic illnesses, regular medication use or significant family history.

On physical examination, rebound tenderness in the right lower quadrant was noted. Laboratory tests revealed leukocytosis (white blood cell: 14.52×10^3/μL, normal range: $4.06\text{-}10.60\times10^3$/μL) and elevated C-reactive protein (1.46 mg/dL, normal value: <0.50 mg/dL). Abdominal computed tomography (CT) scan demonstrated a dilated appendix that was 11.5 cm in length and 2.5 cm in diameter (Figure 1a). Periappendiceal fat stranding was evident. Multiple mesenteric lymph

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Corresponding Author
Serra Bayrakçeken

E-mail: serra.bayrakceken@gmail.com
ORCID ID: orcid.org/0000-0002-3092-4955

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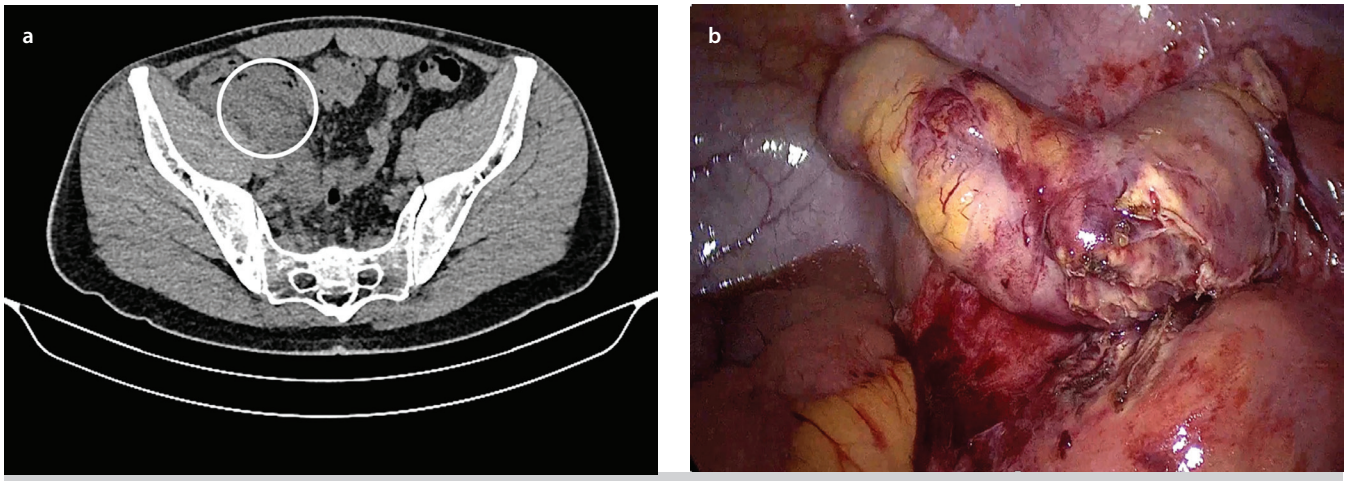

Figure 1. (a) Abdominal CT scan, axial plane, demonstrated a dilated appendiceal lumen (25 mm) and (b) coronal plane, periappendiceal fat stranding and multiple mesenteric lymph nodes were detected.

CT: Computed tomography.

nodes were detected, the largest measuring approximately 1 cm (Figure 1b). Based on these findings, the patient underwent laparoscopic appendectomy with a preoperative diagnosis of perforated acute appendicitis.

Intraoperatively, a mass-like lesion resembling a mucocele was observed and no additional pathological findings were detected during laparoscopic abdominal exploration (Figure 2). Laparoscopic appendectomy with cecal wedge resection using an endolinear stapler was performed since the radix of appendix was large and fibrotic. Following an uneventful recovery, the patient was discharged on the first postoperative day without any complications.

Histopathological examination revealed purulent material in the appendiceal lumen and the serosa exhibited fibrosis with areas of necrosis. Diffuse transmural inflammation was present in both the appendix and the resected cecal wall accompanied by variable eosinophilic infiltration. Multiple mucosal crypt abscesses and submucosal and subserosal lymphoid follicles resembling Crohn-like chronic inflammation were also noted. Submucosal and subserosal fibrosis with focal necrotic areas was identified along with obliterative lymphocytic phlebitis. A few histiocytic giant cells were observed in the appendiceal mucosa and a few non-necrotizing granulomas were detected near the tip of appendix (Figure 3). No evidence of malignancy was identified on histopathological examination of the appendix. Immunohistochemical evaluation demonstrated dense infiltration of IgG4-positive plasma cells in focal areas of the mucosa and submucosa of both the appendix and cecum. The density of IgG4-positive plasma cells was 75 cells per high-power field in the mucosa and 35 cells per high-power field in the appendiceal wall (Figure 4).

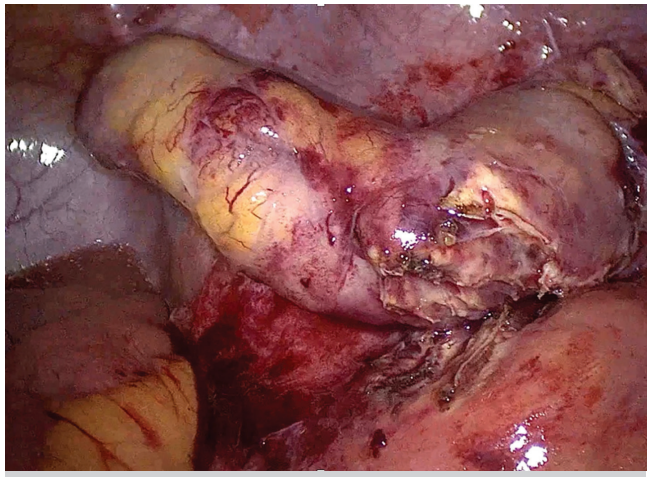

Figure 2. Intraoperative view, a mass-like lesion resembling an appendiceal mucocele was detected.

Regarding the follow-up period, we evaluated the patient within the postoperative first week, one month and one year. The patient had no symptoms and the clinical examination was unremarkable. The serum IgG4 level was 0.793 g/L (normal range; 0.03-2.01 g/L). Colonoscopic evaluation was recommended, however, the patient did not consent to undergo the procedure. At the one-year follow-up, the patient remained asymptomatic with a normal physical examination.

This case report describes routine clinical care and does not constitute human subjects research. According to our institutional policy, formal ethics committee approval is not required for single-patient case reports. The patient was informed about the publication of anonymized clinical data and images, and provided informed consent.

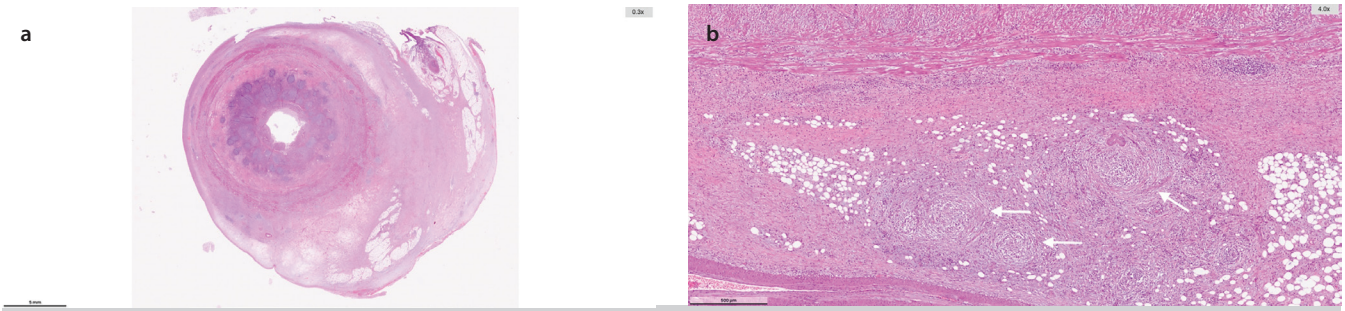

Figure 3. (a) Submucosa fibrosis associated with Crohn like lymphoid follicles and inflammation in the whole appendix wall, and mesoappendix (H&E, digital scan magnification x0.3) and (b) obliterative phlebitis (arrow), storiform fibrosis and inflammatory infiltration composed of plasma cells, lymphocytes and eosinophils (H&E, digital scan magnification x10).

H&E: Hematoxylin and eosin.

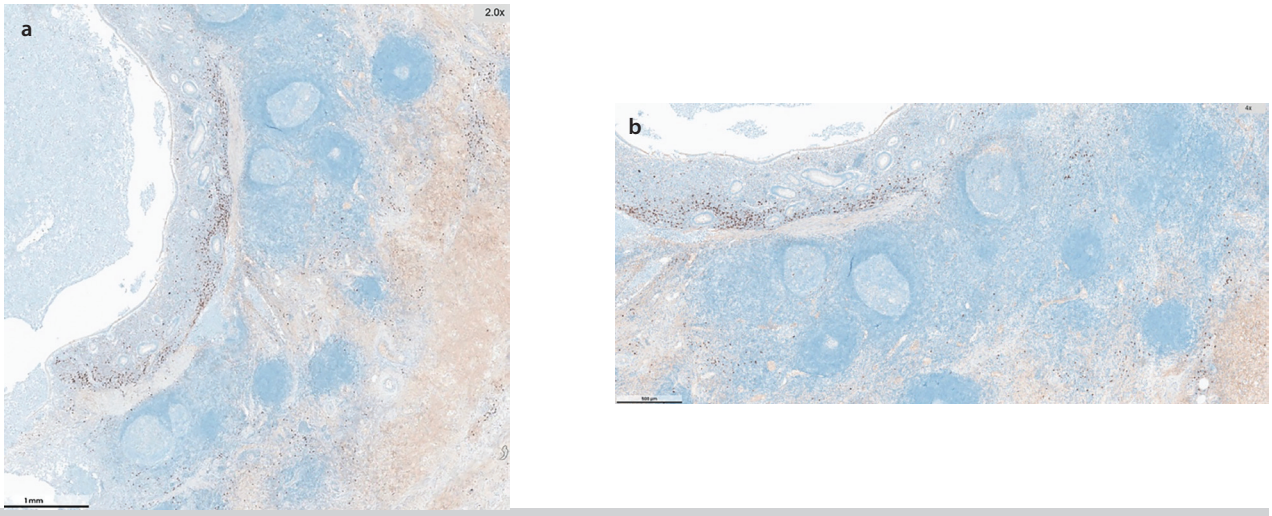

Figure 4. (a) Dense IgG4 positive plasma cell population in the mucosa and submucosa of the appendix (75/1 HPF in the mucosa (IgG4 immunostain, digital scan magnification x2) and (b) 35/1 HPF in the wall (IgG4 immunostain, digital scan magnification x4).

Ig: Immunoglobulin, HPF: High-power field.

DISCUSSION

In this report, we describe a very rare case of an IgG4-RD involving the appendix. IgG4-RD is a systemic and immune-mediated fibroinflammatory condition that can affect multiple organs. This condition was first described in a case series by Kamisawa et al. (11). Although the exact pathogenesis still remains unclear, previous studies suggest that type II T-helper cells and B-cell activating factors may contribute to the disease development (12). Commonly affected sites include the submandibular glands, lymph nodes, retroperitoneum, pancreas, orbital tissues, kidneys, and biliary ducts (13,14). Appendiceal involvement, however, is exceedingly rare and poses a significant diagnostic challenge due to non-specific clinical and radiologic features, often mimicking acute appendicitis or malignancy. As in our case, no specific diagnostic test exists and most cases are diagnosed postoperatively.

In 2020, the Japan IgG4-RD team published a revised comprehensive diagnostic (RCD) criteria, consisting of three components: (1) one or more organ involvement with diffuse or localized swelling, mass or nodularity; (2) serum IgG4 >135 mg/dL, and (3) at least two of three histopathologic findings; dense lymphoplasmacytic infiltration with fibrosis, IgG4+/IgG+ plasma cell ratio >40% with >10 IgG4-positive cells/HPF, and typical storiform fibrosis or obliterative phlebitis (15). These criteria allow classification into definite, probable, or possible IgG4-RD. If all three criteria presents, patients are diagnosed with definite IgG4-RD. In case of criteria 1 and 3 positivity, patients are diagnosed with probable IgG4-RD. Possible IgG4-RD is diagnosed when criteria 1 and 2 are fulfilled. Accordingly, the presented case meets the criteria 1 and 3 thus it can be considered in the "probable" category.

Table 1. Summary of previously reported cases of appendiceal IgG4-related disease

First author	Year	Country	Age/ gender	Symptoms	Imaging findings	Treatment	Surgical approach	IgG4/ IgG >40%	Obliterative phlebitis	Storiform fibrosis	Lymphoplasmocytic infiltration	Serum IgG4 levels (g/L)	Follow-up
Comtesse	2014	Switzerland	20/F	Abdominal pain	NA	Appendectomy	Laparoscopic (converted to open)	+	+	-	+	NA	6th month, colonoscopy and biopsy normal; 18th month no symptoms
Kim	2016	Korea	51/M	RLQ pain	Solid mass-like swelling at the appendiceal tip, perimesenteric fat haziness	Right hemicolectomy	Open	+	-	-	+	NA	NA
Veerankutty	2018	India	57/M	RLQ pain, weight loss	Dilated appendix with thickened walls	Right hemicolectomy	Laparoscopic	+	-	+	+	NA	3rd month, no symptoms, weight gain
Kwon	2019	USA	46/F	RLQ pain, nausea, vomiting	Mass forming lesion at the proximal appendix	Right hemicolectomy	Laparoscopic	+	+	+	+	NA	NA
Dias	2020	Brazil	42/F	RLQ pain	Enlargement and thickening of appendix	Right hemicolectomy	Open	+	+	+	+	1.80	Post-operative day 5 decrease in serum IgG4; 3rd year no symptoms and normal imaging findings
Hojo	2020	Japan	45/F	NA	Mass at the base of the appendix	Ileocecal resection	Laparoscopic	+	-	+	+	0.06*	NA
Cabrales-Escobar	2021	Mexico	17/M	RLQ pain, nausea, vomiting, fever	Thickened cecal appendix, pericecal fat inflammation	Right hemicolectomy, glucocorticoids	Open	-	+	+	-	5.24	Post-operative decrease in serum IgG4
Kim	2024	Korea	60/F	RLQ pain	Mass at the obliterated appendix, periappendiceal fat infiltration	Right hemicolectomy	Open	+	+	+	+	0.247	3rd year, no symptoms and normal imaging findings
Present case	2025	Türkiye	38/M	RLQ pain	Dilated appendix, periappendiceal fat stranding, multiple mesenteric lymph nodes	Appendectomy	Laparoscopic	+	+	+	+	0.793*	1st year, no symptoms

IgG4: Immunoglobulin G4, F: Female, M: Male, NA: Not available, RLQ: Right lower quadrant, USA: United States of America, *: Measured postoperatively.

A review of the literature identified only eight reported cases of appendiceal IgG4-RD to date (Table 1). Cases have been reported from various countries, including Korea, Brazil, India, the USA, Mexico, Switzerland, and Japan (3,10). Similar to our case, nearly all the patients presented with right lower quadrant pain leading to an initial diagnosis of acute appendicitis.

IgG4-related disease generally responds well to glucocorticoid therapy. However, gastrointestinal involvement, particularly appendiceal disease presenting as a mass-like lesion or acute appendicitis, may raise significant suspicion for malignancy. As a result, surgical intervention often becomes the primary approach in the cases. Consistent with this, most reported cases of appendiceal IgG4-related disease, including our case, have been managed surgically. Moreover, the role of glucocorticoid therapy in appendiceal involvement remains unclear, as only Cabrales-Escobar et al. (8) initiated corticosteroid therapy postoperatively due to the documented mesenteric lymphadenopathy and retroperitoneal involvement. This highlights the importance of considering IgG4-related disease in the differential diagnosis of appendiceal pathologies, as recognition of this entity may help avoid unnecessary extensive resections and guide appropriate postoperative management.

Surgical approaches varied among the reported cases. In fact, right hemicolectomy was the most commonly utilized procedure which was performed in the six cases due to the suspected diagnosis of malignancy. Among these six cases, two patients underwent laparoscopy (3,9) while the remaining four underwent open surgery (4,6-8). Regarding the other two cases, one laparoscopic procedure was converted to an open appendectomy due to intraoperative findings of conglomerated swelling of both the cecum and appendix (5). In the remaining case, a laparoscopic ileocecal resection was performed (10). As seen, all the reported patients underwent surgical intervention, mostly extended resections.

To our knowledge, this is the first case report of IgG4-RD of the appendix in Türkiye. In line with the existing literature, we present a patient with similar histopathological findings consistent with IgG4-RD. Distinctively, we preferred to perform a limited resection (appendectomy with cecal wedge resection) rather than an extensive procedure in the absence of a confirmed malignancy.

Most reported cases demonstrate the classical histopathologic features of IgG4-RD, including dense lymphoplasmacytic infiltration, storiform fibrosis, obliterative phlebitis and an IgG4/IgG plasma cell ratio >40%. Exceptions include the cases reported by Comtesse et al. (5) and Kim et al. (7) who did not observe storiform fibrosis or obliterative phlebitis. Kwon et al. (3) additionally reported proliferation of S100-positive eosinophilic cells. In our case, all the histopathological features defined in the 2020 RCD criteria for IgG4-related disease were identified, further supporting the diagnosis. Serum IgG4 levels were measured in only four cases (4,6,8,10) with two showing elevated values (6,8). In the presented case, the serum IgG4 level was normal.

Follow-up period was variably reported; five reports describe follow-up ranging from three months to three years. Kim et al. (4) reported a 3 year follow-up with no complaints and normal imaging findings. Comtesse et al. (5) performed colonoscopy 6 weeks after surgery. Colonoscopic findings were normal and biopsies from the terminal ileum and colon showed no pathological abnormalities. At the 18-month postoperative follow-up, the patient was asymptomatic. Dias et al. (6) measured serum IgG4 level on postoperative day 5 and found that it had decreased to normal values. The patient was followed for 3 years with no clinical complaints and no abnormal imaging findings. Cabrales-Escobar et al. (8) performed a CT scan 2 months later, which demonstrated regression of adenomegaly. The patient had no clinical abnormality and reported weight gain. Serum IgG4 level was also measured and showed a decrease (preoperative value: 524 mg/dL; postoperative value: 170 mg/dL). Veerankutty et al. (9) planned a follow up examination after 3 months. The patient remained asymptomatic and weight gain was observed. In our case, the patient has been followed up for one year after surgery. The patient remained asymptomatic and no clinical abnormalities were detected.

CONCLUSION

Although appendiceal involvement of IgG4-RD is extremely rare, this condition should be considered in patients with appendiceal pathologies. The integration of radiologic, surgical, histologic and laboratory findings and recognition of atypical but classical features are essential for accurate diagnosis and patient management. In our case, recognition of characteristic histopathological features postoperatively allowed precise diagnosis without extensive surgical intervention. In the absence of clear evidence of malignancy, a limited surgical approach may be sufficient, as the diagnosis is often established postoperatively. These considerations may help avoid unnecessary extensive resections and support more optimized management strategies.

Ethics

Informed Consent: The patient was informed about the publication of anonymized clinical data and images, and provided informed consent.

Footnotes

This case report was previously presented as a poster at the 20th National and 3rd International Turkish Colon and Rectal Surgery Congress on May 18, 2025.

Author Contributions

Concept - S.B., N.G., İ.A.B., S.G., V.Ö.; Design - S.B., N.G., İ.A.B., S.G., V.Ö.; Data Collection or Processing - S.B., S.G., V.Ö.; Analysis or Interpretation - S.B., İ.A.B., S.G., V.Ö.; Literature Search - S.B., N.G., V.Ö.; Writing - S.B., N.G., İ.A.B., S.G., V.Ö.

Conflict of Interest: No conflict of interest was declared by the authors.

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