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Case report

IgG4-related disease: A case of pancreatic and extrapancreatic involvement in an Afro-Colombian woman

Rita Sierra-Merlano,[1] Betty Morales-Arrieta,[2] Michel Rafael Pérez-Marrugo.[3*]

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[1] Physician, Specialist in Internal Medicine and Rheumatology. Doctor of Education Sciences. Professor of Medicine, Universidad de Cartagena. Cartagena, Colombia.
[2] Gastroenterologist, PhD in Hepatology, Universitat Autònoma de Barcelona. Professor of Medicine, Universidad de Cartagena. Cartagena, Colombia.
[3] General Practitioner, Internal Medicine Resident, Hospital Universitario del Caribe. Cartagena, Colombia.

***Correspondence**: Michel Rafael Pérez-Marrugo.
mperezm12@unicartagena.edu.co

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Abstract

Introduction: IgG4-related disease (IgG4-RD) is a recently described systemic fibroinflammatory disorder characterized by dense lymphoplasmacytic infiltrate, storiform fibrosis, obliterative phlebitis, and a favorable response to glucocorticoids. Its diagnosis remains challenging because it often mimics neoplastic or autoimmune processes. **Case presentation:** A 60-year-old Afro-Colombian woman with a history of obstructive jaundice, weight loss, and a pancreatic lesion initially suspected to be a neoplasm. She underwent cholecystectomy, with histopathological findings of lymphoplasmacytic sclerosing pancreatitis, showing an infiltrate rich in IgG4-positive cells and storiform fibrosis. Serology showed IgG4 levels >5 times the upper limit of normal. The patient also presented salivary gland hypertrophy and cervical lymphadenopathy, with a complete clinical response to glucocorticoid treatment. **Discussion:** The case corresponds to the multiorgan clinical phenotype described in the literature, meeting the 2019 ACR/EULAR classification criteria for IgG4-RD. The initial suspicion of pancreatic neoplasia led to an unnecessary surgical intervention, illustrating the diagnostic difficulty of this entity. This would be the first case reported in the Caribbean region of Colombia in an Afro-descendant patient, contributing evidence on phenotypic variability and the need for a multidisciplinary approach. **Conclusion:** IgG4-RD should be considered in the differential diagnosis of pancreatic and biliary masses. Early recognition prevents unnecessary invasive procedures and allows initiation of glucocorticoid treatment, which achieves clinical remission.

Keywords

Immunoglobulin G4-related disease, autoimmune pancreatitis, salivary glands.

INTRODUCTION

IgG4-related disease (IgG4-RD) is a systemic fibroinflammatory disorder first described 22 years ago[1], with its current nomenclature standardized in 2012[2]. Histopathologically, the disease is characterized by a dense lymphoplasmacytic infiltrate, IgG4-positive cells, storiform fibrosis, and obliterative phlebitis. IgG4-RD can simultaneously affect any organ and cause organ enlargement. It may mimic tumors, malignancies, infections, or autoimmune diseases, often without pain or fever, which makes diagnosis challenging[3,4].

The clinical spectrum of IgG4-RD is broad and varies according to the organs involved. The disease has an insidious presentation and is often accompanied by constitutional symptoms. Certain organs and anatomical sites are more frequently affected, including the pancreas, biliary tree, retroperitoneum, kidneys, salivary and lacrimal glands, and lymph nodes[5,6]. A definitive diagnosis of IgG4-RD requires histologic findings with immunohistochemistry,

clinicopathologic correlation, and supportive serologic findings. Elevated serum IgG4 levels or isolated tissue infiltration does not confirm the diagnosis[7,8].

The epidemiology of IgG4-RD has not been fully defined. In the United States, a retrospective cohort study of insurance claims among adults reported a mean age of 56.5 years. Women were more frequently affected (57.6%), as were individuals with white skin phototypes (66% of cases). The prevalence in 2019 was 5.3 per 100,000 population, with an incidence of 0.78 and 1.39 cases per 100,000 person-years in 2015 and 2019, respectively. The authors suggest that this increase may be related to improved recognition of the disease[9].

IgG4-RD has been extensively characterized in Japan[10] and the United States[9], but much less so in Latin America, including Colombia. Knowledge of IgG4-RD in Colombia is based primarily on case reports. The largest series of IgG4-RD cases identified in our search was published in 2018 and included 16 cases with histopathologic confirmation at a university hospital[11]. In that series, the organs most frequently affected histopathologically were the pancreas, breast, appendix, and retroperitoneum. The low frequency of clinically detectable involvement of organs such as lymph nodes and lacrimal and salivary glands is noteworthy.

This case describes an Afro-Colombian woman with IgG4-RD who presented with systemic, pancreatic, and biliary involvement, with suspected prior salivary gland involvement suggestive of Sjögren syndrome. The case emphasizes a comprehensive diagnostic approach, treatment, and correlation with recently proposed clinical phenotypes[12,13].

CASE PRESENTATION

A 60-year-old woman with skin phototype IV was referred to the Rheumatology Department from Hepatology with a working diagnosis of IgG4-RD for differential diagnosis from autoimmune rheumatic diseases. She had been receiving prednisone 40 mg/day for two months. At the time of consultation, she was asymptomatic, with complete resolution of the gastrointestinal and musculoskeletal manifestations and of the ocular and cervical enlargement documented in her medical record. She also denied any symptoms or signs of inflammatory autoimmune disease, as well as personal or family histories of toxic exposures, occupational exposures, or autoimmune disease.

One year earlier, she had presented with obstructive jaundice, asthenia, adynamia, dark urine, acholic stools, and weight loss. She was referred from the General Surgery outpatient clinic to the emergency department with a suspected diagnosis of acute cholecystitis. During hospitalization, an obstructive jaundice syndrome was identified. Magnetic resonance cholangiopancreatography was subsequently performed and revealed a lesion with a neoplastic appearance in the pancreatic head, loss of the cleavage plane between the lesion and the adjacent left hepatic lobe and gastric wall, a proximal common bile duct measuring 16 mm in diameter, a normal intrahepatic biliary tree, and a poorly distended gallbladder that could not be adequately evaluated. Because of suspected periampullary tumor, a pancreatic biopsy was performed by endoscopic ultrasonography. The biopsy showed a chronic inflammatory process associated with fibrosis, although interpretation was limited by the small sample size. Given the inconclusive findings, she underwent a surgical procedure consisting of cholecystectomy and intraoperative cholangiography.

Following the surgical procedure, the gallbladder specimen was reported as follows: the cystic duct showed extensive fibrosis and acute and chronic inflammation; the gallbladder exhibited altered histoarchitecture due to chronic transmural inflammation; and the pancreatic tissue showed storiform fibrosis and a lymphoplasmacytic infiltrate with eosinophils. The pancreatic parenchyma showed no evidence of malignancy. The lymph node had normal morphology. The findings were diagnosed as chronic cholecystitis, cystic duct fibrosis, and lymphoplasmacytic sclerosing pancreatitis (LPSP) (**Figures 1** and **2**). Before the histochemical evaluation, cervical lymphadenopathy had been documented during a General Surgery outpatient visit. Neck ultrasonography showed heterogeneous, enlarged submandibular glands with mixed intraglandular lesions and increased vascularity. The parotid glands and thyroid gland were normal.

Immunohistochemical analysis of the pancreatic specimen revealed fibrous connective tissue, stromal hyalinosis, marked chronic plasmacytic inflammation, and an IgG4/IgG ratio of 90%, consistent with IgG4-RD. Serologic testing showed serum IgG4 levels >5 times the upper limit of normal (ULN). The complete blood count showed no cytopenias or peripheral eosinophilia. Antibodies against double-stranded DNA (anti-dsDNA), Ro and La antigens (anti-Ro/La), and Smith antigen (anti-Sm) were negative. Antineutrophil cytoplasmic antibodies (ANCA) were also negative (**Table 1**).

Bilateral salivary gland enlargement, clinical and histopathologic pancreatic and biliary involvement, together with the immunohistochemical findings, elevated serum IgG4 levels, and favorable response to glucocorticoids established the diagnosis of IgG4-RD. **Table 2** presents the 2019 ACR/EULAR inclusion criteria for IgG4-RD; none of the exclusion criteria were met (**Table 2**).

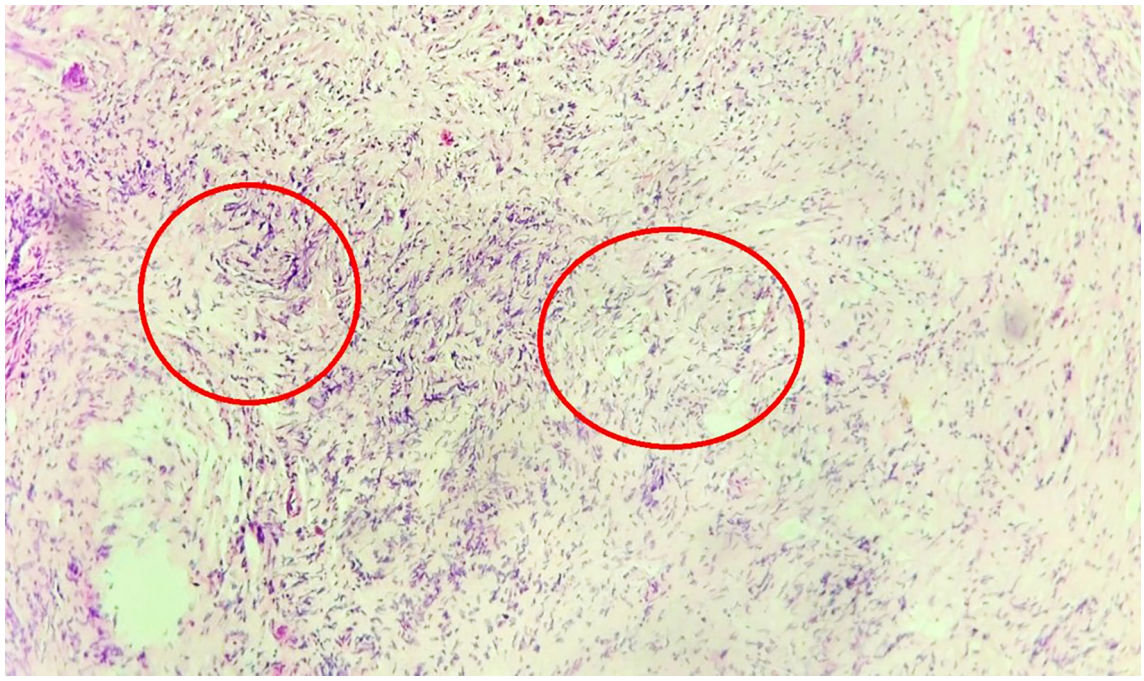


Figure 1. Labeled as pancreatic biopsy, 10× magnification. Tissue replaced by fibroinflammatory proliferation. Focal areas of storiform fibrosis (circles) and a chronic lymphoplasmacytic inflammatory infiltrate are present. Image courtesy of the authors.

DISCUSSION

IgG4-RD is a multisystem immune-mediated condition with a broad clinical spectrum, an insidious course, and low prevalence. Its prevalence is lower than that of other rare diseases, such as systemic lupus erythematosus and systemic sclerosis. Because it was described only recently, its clinical diagnosis remains challenging and carries a risk of irreversible organ damage when the disease is not diagnosed and treated promptly[5,7]. The case presented corresponds to clinical subtype 1 described by Lanzillotta et al., which is characterized by high serum IgG4 levels, multiorgan involvement, and a favorable response to glucocorticoids[12]. The patient met the 2019 ACR/EULAR criteria[8] and exhibited characteristic histopathologic findings, including a lymphoplasmacytic infiltrate with eosinophils, storiform fibrosis, and an IgG4+/total IgG ratio greater than 40%. These findings support the diagnosis of lymphoplasmacytic sclerosing pancreatitis (LPSP), the prototypical gastrointestinal manifestation of IgG4-RD[14].

One of the major diagnostic challenges of IgG4-RD is its presentation as tumor-like masses or organ enlargement that may mimic malignancy. In a Japanese cohort of 334 patients, more than 50% initially presented with imaging

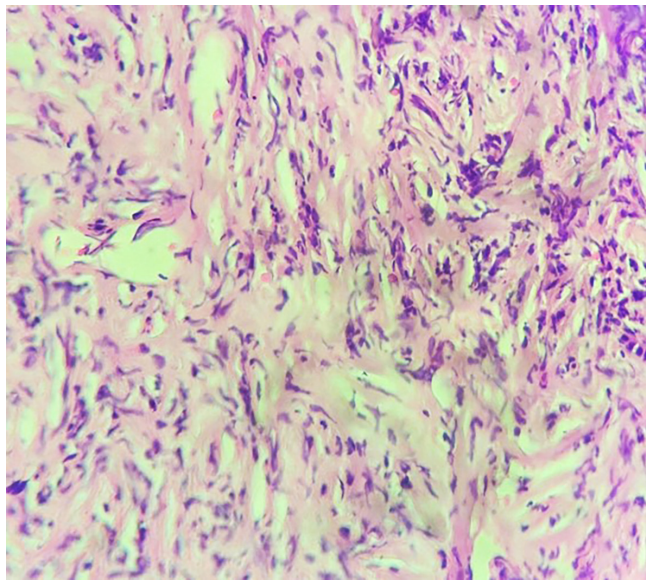


Figure 2. Labeled as pancreatic biopsy, 40× magnification. The specimen shows fragments of fibrous connective tissue with dense fibrosis organized in a storiform pattern, characterized by interwoven and whorled collagen bundles. A diffuse lymphoplasmacytic inflammatory infiltrate is also observed between the collagen bundles. Image courtesy of the authors.

Table 1. Clinical laboratory results

Test (unit)	Result	Reference range	Interpretation
Serum IgG4 (mg/dL)	**7880**	≥200	**>5 × ULN**
White blood cells (×10⁹/L)	8.01	4.5-10.9	Normal
Hemoglobin (g/dL)	**10.8**	12-15	Decreased
MCV (fL)	96.3	80-100	Normal
Platelets (×10⁹/L)	298	150-450	Normal
Absolute neutrophil count (×10⁹/L)	4.24	2.0-7.5	Normal
Absolute lymphocyte count (×10⁹/L)	2.21	1.0-4.8	Normal
Absolute eosinophil count (×10⁹/L)	0.20	0.04-0.50	Normal
C3 (mg/dL)	84	80-178	Normal
C4 (mg/dL)	25	15-45	Normal
Anti-dsDNA	Negative	Negative	Normal
Anti-Sm	Negative	Negative	Normal
Anti-SSA/Ro	Negative	Negative	Normal
Anti-SSB/La	Negative	Negative	Normal
ANCA	Negative	Negative	Normal

ANCA: antineutrophil cytoplasmic antibodies; anti-dsDNA: antibodies against double-stranded DNA; anti-Sm: antibodies against Smith antigen; anti-SSA/Ro: antibodies against Ro antigen (SSA); anti-SSB/La: antibodies against La antigen (SSB); C3: complement component 3; C4: complement component 4; Hb: hemoglobin; IgG4: immunoglobulin G subclass 4; ULN: upper limit of normal; MCV: mean corpuscular volume. Table prepared by the authors.

findings suggestive of cancer, which led to unnecessary surgical procedures[10]. In the present case, the surgical intervention was prompted by suspected pancreatic neoplasia, with no initial suspicion of IgG4-RD. Similarly, the presence of neck masses led to diagnoses of more common conditions familiar to the medical community, including lymphadenopathy and Sjögren syndrome. The latter was favored by the systemic polyarthralgias that preceded the onset of biliary tract manifestations.

Synchronous or sequential involvement of multiple organs in IgG4-RD has been documented in series from Colombia and other countries and is a very common pattern in other autoimmune diseases[6,11,15]. In this case, pancreatic, biliary, and salivary gland involvement raised suspicion of the diagnosis. To the best of our knowledge based on the literature reviewed, this would be the first reported case of IgG4-RD in the Colombian Caribbean region and the second case involving an individual with a high skin phototype among Afro-Colombians[16].

Response to glucocorticoids is an indicator of IgG4-RD diagnosis[8] and is related to the pathogenesis of the disease. The involvement of SLAMF7+ cytotoxic CD4+ T cells and B cells/plasmablasts in the process of fibrosis and tissue damage has been identified. In this case, treatment with prednisolone at the recommended doses resulted in a favorable response and complete remission. The literature reviewed recommends initiating treatment with prednisolone at a dose of 0.6 mg/kg/day for 2 to 4 weeks, followed by gradual tapering over 2 to 3 months. Dose reductions greater than 0.4 mg/day should be avoided, with a maintenance dose of 2.5 to 5 mg/day for 1 to 3 years[17]. Less information is available regarding relapse and its management. In refractory cases or relapses, reports have described the use of the CD20 inhibitor rituximab to maintain remission[18]. Less information is available on inebilizumab, which targets CD19 on B cells[19].

CONCLUSIONS

This clinical case demonstrates the multisystem, systemic, and insidious behavior of IgG4-RD. The clinical presentation began with biliary tract manifestations, a pancreatic mass, and obstructive jaundice. Advanced imaging studies and minimally invasive biopsy raised suspicion of a tumor with uncertain behavior. These findings, together with histologic evidence of a lymphoplasmacytic infiltrate and storiform fibrosis, led to suspicion and subsequent confirmation of IgG4-RD. This is a disease with very low prevalence in Colombia, with no previous case reports from the Colombian Caribbean region[20].

The case also demonstrates that greater awareness of IgG4-RD within the medical community, together with a multidisciplinary approach, facilitates diagnosis. It also enables integration of clinical manifestations with imaging, histopathologic, and serologic findings, given the limited diagnostic yield of isolated serologic markers such as serum IgG4 levels[3,8]. It is important to consider that glucocorticoid therapy contributes to the diagnostic assessment and represents the initial and central treatment recommendation for this disease. However, close monitoring and long-term treatment are required. This poses challenges that remain incompletely defined because IgG4-RD is a rare disease that has only recently been described in the medical literature[5].

The publication of IgG4-RD cases in Colombia contributes to greater understanding of the disease, particularly the importance of early clinical suspicion in primary care. It also underscores the need to detect and investigate

Table 2. 2019 ACR/EULAR criteria for IgG4-RD

Domain	Criterion	Criterion present? Yes/No	Score	Case score
Histopathology A	Dense lymphoplasmacytic infiltrate		4	0
Histopathology B	Dense lymphoplasmacytic infiltrate + obliterative phlebitis		6	0
Histopathology C	Dense lymphoplasmacytic infiltrate and storiform fibrosis ± obliterative phlebitis		13	13
Immunostaining	IgG4+: IgG+ ratio of 0%–40% and 0–9 cells/hpf		0	0
Immunostaining	IgG4+: IgG+ ratio ≥41% with few cells or ≥10 cells but <41%		7	0
Immunostaining	IgG4+/IgG+ ratio of 41%–70% and ≥10 cells, or ≥71% with 10–50 cells/hpf		14	0
Immunostaining	IgG4+/IgG+ ratio ≥71% and ≥51 cells/hpf		16	16
Serum IgG4	Normal or not checked		0	0
Serum IgG4	>ULN but <2× ULN		4	0
Serum IgG4	Between 2× and 5× ULN		6	0
Serum IgG4	>5× ULN		11	11
Glands: bilateral lacrimal, parotid, sublingual, and submandibular gland involvement, which may be clinical or radiographic	No gland involvement		0	0
Glands	1 set of glands involved		4	4
Glands	≥2 sets of glands involved		14	0
Chest	Not assessed or none of the items present		0	0
Chest	Peribronchovascular and septal thickening		4	0
Chest	Paravertebral band-like soft tissue in the chest		10	0
Pancreas and biliary tree	Not assessed or none of the items present		0	0
Pancreas and biliary tree	Diffuse pancreatic enlargement (loss of lobulations)		8	0
Pancreas and biliary tree	Diffuse pancreatic enlargement and a capsule-like rim with decreased enhancement		11	0
Pancreas and biliary tree	Either of the above plus biliary tree involvement		19	19
Kidney	Not assessed or none of the items present		0	0
Kidney	Hypocomplementemia		6	0
Kidney	Renal pelvic/soft-tissue thickening		8	0
Kidney	Bilateral areas of low attenuation in the renal cortex		10	0
Retroperitoneo	Not assessed or none of the items present		0	0
Retroperitoneo	Diffuse thickening of the abdominal aortic wall		4	0
Retroperitoneo	Circumferential or anterolateral soft tissue around the infrarenal aorta or iliac arteries		8	0
	Total (≥20 suggests IgG4-RD): 63.			

hpf: high-power field; IgG: immunoglobulin G; IgG4: immunoglobulin G subclass 4; IgG4-RD: IgG4-related disease; ULN: upper limit of normal. Table prepared by the authors.

tumoral and pseudotumoral masses using diagnostic algorithms that allow their timely characterization. This is particularly relevant for findings that can be detected on clinical examination, such as salivary gland enlargement and lymphadenopathy.

Finally, publication of this case involving an Afro-Colombian woman from Colombia's Caribbean region contributes to strengthening the clinical evidence on IgG4-RD in Colombia and Latin America. This region remains underrepresented in the literature. Greater recognition may facilitate earlier active case finding and help prevent irreversible organ damage.

Ethical considerations

This case report was prepared in accordance with the ethical principles of the Declaration of Helsinki and the provisions of Resolution 8430 of 1993 of the Colombian Ministry of Health. The diagnostic and therapeutic procedures described were part of the patient's clinical care. No additional interventions were performed for research purposes.

Informed consent

The authors declare that they obtained the patient's express, voluntary, and informed consent for publication of the case described, while preserving the confidentiality of her clinical information.

Conflicts of interest

The authors declare no conflicts of interest.

Use of artificial intelligence

The tool was not used to generate data, analyze results, or develop conclusions, nor did it replace the authors' academic and scientific judgment.

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Author contributions

- Study design and conception: Betty Morales-Arrieta, Michel Pérez-Marrugo, Rita Sierra-Merlano.
- Data acquisition: Michel Pérez-Marrugo, Rita Sierra-Merlano.
- Manuscript drafting: Rita Sierra-Merlano, Michel Pérez-Marrugo.
- Critical revision: Betty Morales-Arrieta, Rita Sierra-Merlano.

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