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CASE BASED REVIEW

Pericarditis as a manifestation of IgG4-related disease

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Abstract

IgG4-related disease (IgG4-RD) is a systemic, immune-mediated fibro-inflammatory disease that can affect virtually every organ system. It is usually insidious in onset and often mimics malignant or other inflammatory disorders. Diagnosis frequently requires a combination of clinical, serological, radiographic, and histopathological features, including increased serum-IgG4 levels and tissue infiltration of IgG4-positive plasma cells with associated fibrosis. Unlike more frequently affected sites, including the hepatobiliary system, salivary glands and retroperitoneum, pericardial involvement of IgG4-RD has only rarely been described. We report the case of a 76-year-old woman presenting with refractory pericarditis and imminent cardiac tamponade, successfully treated with therapeutic pericardiectomy. A diagnosis of IgG4-RD was made based on elevated serum-IgG4 levels and the presence of typical pericardial histopathological findings, meeting all 3 of the 2011 comprehensive diagnostic criteria for IgG4-RD. Following pericardiectomy, the patient remained in remission without a need for glucocorticoids or additional immunosuppressive therapy. Adding to this case, we reviewed the literature for previously described cases of IgG4-RD presenting with pericarditis and described their characteristics and the available treatment options. Our case-based literature review provides a clear overview of the diagnostic process for IgG4-RD and the need to apply classification criteria with the necessary caution, particularly in the case of rare disease manifestations, including pericarditis.

Keywords IgG4 · IgG4-related disease · Pericarditis · Diagnosis · Diagnostic criteria · Classification

Introduction

IgG4-related disease (IgG4-RD) is an immune-mediated fibroinflammatory disorder with varying clinical manifestations that often mimic malignant, infectious, or other inflammatory disorders [1]. IgG4-RD has only recently been identified as a distinct condition and is associated with inflammatory and fibrosing lesions that can occur in a multitude of organ sites [2, 3], including the hepatobiliary system, the salivary and lacrimal glands, the kidneys, the lungs, the aorta, and the retroperitoneum [4–6]. While much of the etiopathogenesis of IgG4-RD remains unclear, it involves a complex interaction between genetic predisposition and environmental factors leading to a modified Th2-response and resulting in the production of IgG4-antibodies with unique glycosylation patterns and immunological properties [7].

IgG4-RD is typically challenging to diagnose and usually requires a combination of clinical, serological, radiological, and pathological features, after excluding numerous mimicking conditions [8]. Consequently, patients are often evaluated by multiple practitioners, including gastroenterologists, nephrologists, or other specialists, which can result in a delayed diagnosis [9]. To facilitate this diagnostic process, three comprehensive diagnostic criteria for IgG4-RD were first proposed in 2011: typical diffuse/localized swelling or masses in single or multiple organs, elevated serum-IgG4 concentrations ($\geq$ 135 mg/dL) and characteristic histopathologic findings [10]. These characteristic histopathologic features include a dense lymphoplasmacytic infiltrate, storiform fibrosis and obliterative phlebitis [11], in addition to an increased infiltration of IgG4-bearing plasma cells

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[12]. However, because obtaining a biopsy of an affected site is often challenging, the 2011 diagnostic criteria were later adapted to include several organ-specific criteria [13]. Most recently, the 2019 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria for IgG4-RD recommend a stepwise approach to diagnosis based on a set of entry, exclusion, and inclusion criteria [14].

However, while the introduction of different sets of diagnostic criteria have certainly contributed to a more accurate categorization of patients in both clinical practice and research, some manifestations of IgG4-RD do not meet these criteria. Furthermore, in some cases of IgG4-RD, the diagnosis is complicated by differences between the existing diagnostic and classification criteria. This is specifically the case with rare clinical manifestations of IgG4-RD, including pericarditis and pericardial effusion. We report a case of IgG4-RD presenting with massive pericarditis as the primary manifestation. The diagnostic process will be described in detail, with a focus on discrepancies with the recent classification criteria. Finally, we will discuss therapeutic options and conclude with a review of the literature dealing with pericarditis as a manifestation of IgG4-RD.

Case presentation

A 76-year-old woman was initially referred for cardiological examination because of bilateral pleural effusion and cardiomegaly on chest X-ray, performed because of a 2-month history of progressive dyspnea and non-productive cough. She had a history of diabetes mellitus, arterial hypertension, hyperlipidemia, and well-controlled chronic obstructive pulmonary disease and was on a steady regimen of oral antidiabetics, antihypertensive drugs, and a statin. Electrocardiogram showed sinus rhythm and an incomplete right bundle branch block. Transthoracic echocardiography was performed and revealed a large pericardial effusion, with a circumferential diameter of 3–4 cm. Left ventricular ejection fraction was within normal range. Because of the imminent cardiac tamponade, the patient was subsequently admitted for further evaluation and therapy. Laboratory tests performed on admission showed an elevated C-reactive protein (170 mg/L) and a borderline increased anti-nuclear antibody (ANA, 1:320) but were otherwise unremarkable. Urgent surgical pericardiocentesis was performed with the evacuation of 1400 mL of clear fluid, along with right-sided pleural drainage and a pericardial biopsy. Analysis of the pericardial fluid and biopsy showed no signs of inflammation, infection or malignancy. A thoracoabdominal contrast-enhanced computed tomography (CT) scan, performed 3 days after the procedure, showed no signs of ascites or tumoral masses. Remarkably though, a recurrence of the pericardial effusion was noted and confirmed by repeat transthoracic echocardiography. Additional cardiac magnetic resonance imaging (MRI) showed no pericardial thickening or intracardiac mass (Fig. 1).

A diagnosis of incessant pericarditis was made. The patient was empirically started on colchicine and non-steroidal anti-inflammatory drugs (NSAIDs) and subsequently discharged for regular cardiological follow-up. After 3 months of therapy, the pericardial effusion remained refractory on repeated echocardiographic evaluation, despite normalization of biochemical inflammatory markers.

The patient was subsequently referred for rheumatological examination to exclude autoimmune or autoinflammatory causes of persistent pericarditis. Additional blood tests showed increased serum IgG4-levels (179 mg/dL, 1.5 × ULN) and an elevated serum IgG4/IgG ratio (15.7%). Repeated ANA was now negative, as well as other autoantibodies, viral serology, and angiotensin-converting enzyme (ACE). After multidisciplinary discussion involving the treating rheumatologist, cardiologist, and cardiothoracic surgeon, therapeutic thoracoscopic pericardiectomy was performed along with a new pericardial biopsy for IgG4-staining. Histology of the pericardial tissue revealed a lymphoplasmacytic infiltrate (Fig. 2). On immunohistochemistry with staining by IgG4-antibodies, nearly all plasma cells were IgG4-positive (pericardial IgG4/IgG ratio > 80%, 10–50 IgG4 + plasma cells per high power field).

Based on these findings, a diagnosis of IgG4-related pericarditis could be made. Because of a history of dry mouth, a Schirmer-test and unstimulated whole saliva flow test were additionally performed which was strongly suggestive of xerophthalmia (2 mm/5 min) and xerostomia (0.06 mL/min). Consequently, a lip biopsy was taken and revealed a lymphoplasmacytic infiltrate and storiform fibrosis, consistent with IgG4-RD. However, immunohistochemistry of this biopsy showed no presence of IgG4-positive plasma cells. Additional screening, including positron-emission tomography (PET)– CT scan, showed no other sites of inflammation.

Echocardiography following pericardiectomy showed regression of the pericardial effusion. During 8 months of follow-up, the patient remained in remission without the need for glucocorticoids or additional immunosuppressive therapy.

Search strategy

We conducted a review of the literature by searching in MEDLINE and EMBASE from inception to December 2020, using the following search terms: “IgG4-related disease” AND “pericarditis”, “pericardial effusion” or “serositis”. Two authors (MD and SM) independently identified eligible articles, using a coordinated search strategy. Only case reports and case series in English language reporting on IgG4-RD with pericardial involvement and published in

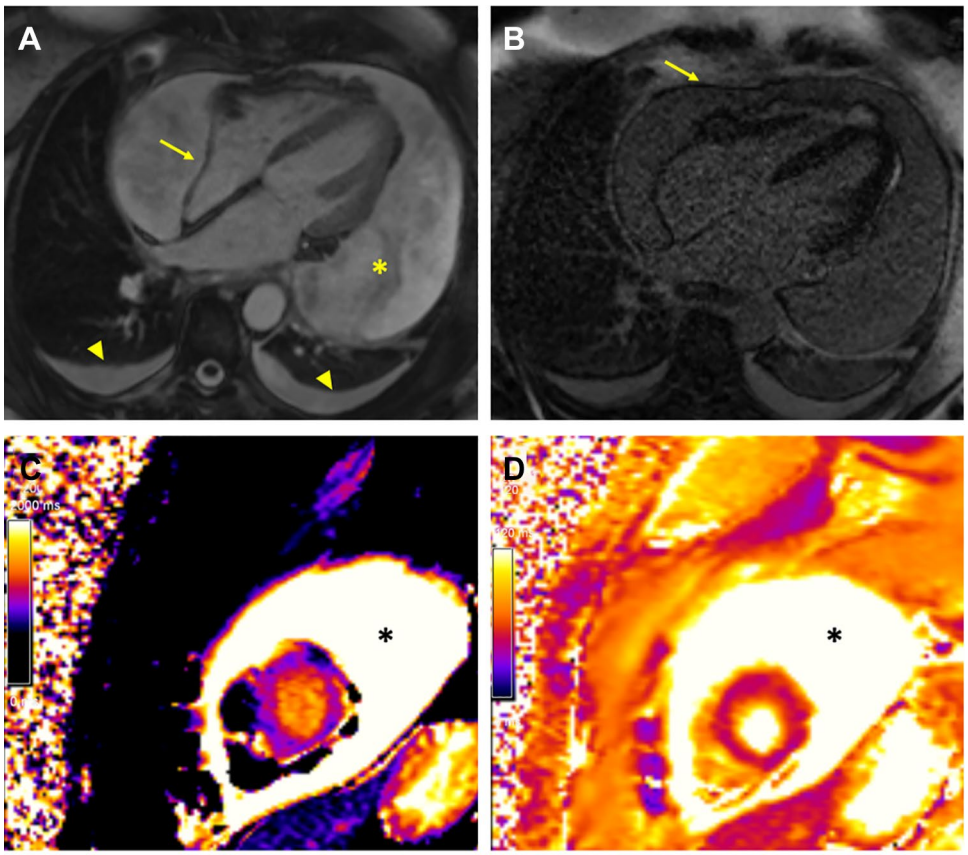

Fig. 1 Results of cardiac magnetic resonance imaging (MRI). **A** Cine horizontal long-axis (HLA) image shows extensive pericardial effusion (6.2 cm) (asterisk) with partial right atrial (RA) collapse (arrow) and small bilateral pleural effusion (arrowheads). **B** Late gadolinium enhancement (LGE) HLA image shows mild pericardial thickening (3 mm). **C**, **D** Native T1 (**C**) and T2 (**D**) map show high T1 and T2 values of 2826 ms and 204 ms, respectively (asterisk), consistent with pericardial exudate without evidence of hemopericardium

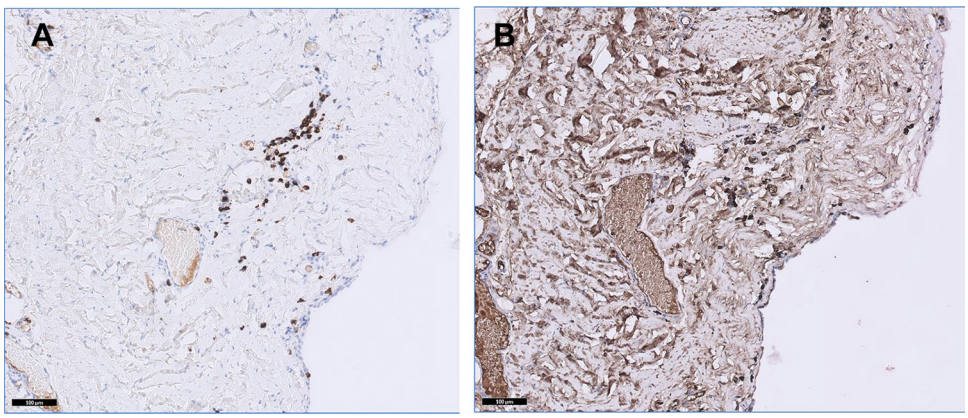

Fig. 2 Pathological findings of the pericardium following pericardiectomy. The pericardial tissue is characterized by a lymphoplasmacytic infiltrate with IgG4/IgG ratio > 80% and 10–50 IgG4 + plasma cells per high power field. **A** Immunostaining for IgG. **B** Immunostaining for IgG4

peer-reviewed journals were included. Additional reports were hand-picked via a snowballing approach guided by the references of included articles.

Retrieved abstracts were assessed for eligibility. Articles were excluded if they did not report on pericardial involvement of IgG4-RD or if they solely concerned other forms of serositis.

The following clinical and demographic data were extracted from both the cases retrieved through literature search and our case presented below: age, gender, pericardial involvement, pleural disease, other organ involvement, histopathologic features, serum IgG4-levels, initial and maintenance therapy, and evolution after treatment.

Results

We identified 32 published cases of IgG4-RD presenting as or with pericardial involvement (Table 1). In addition to these 32 cases, pericardial involvement was also reported in 1/235 patients in a Japanese observational cohort study [4]. However, since clinical and demographic details of

Table 1 Clinical and demographic characteristics, treatment strategy and evolution of reported cases of IgG4-RD with pericarditis

Reference	Age	Gender	Pericardial involvement	Pleural disease	Other organ involvement	Histology	sIgG4 (mg/dL)	Initial therapy	Maintenance therapy	Evolution
Our case	77	F	Effusion	Yes	None	Pericardium	179	Pericardiectomy	None	No recurrence over 7 months
[18]	68	M	Thickening Constrictive pericarditis	Yes	None	Pericardium	206	Pericardiectomy	None	Regression, no follow-up data
[19]	63	F	Thickening Effusion	Yes	Pancreatitis	NA	420	Prednisone (dose unknown)	Unknown	No recurrence over 22 months
[20]	69	M	Effusion	Yes	Retroperitoneal	FNAC	408	Prednisone 50 mg	Unknown	Regression, no follow-up data
[21]	83	M	Thickening Effusion	Yes	Retroperitoneal Pancreatitis	Pericardium	812	Unknown	Unknown	Rapid progression, fatal outcome
[22]	76	M	Thickening Constrictive pericarditis	Yes	Peritoneal	Pericardium	NA	Pericardiectomy	None	No recurrence over 24 months
[23]	29	F	Thickening Effusion Constrictive pericarditis	Yes	None	Pleura	136	Prednisone 40 mg	None	No recurrence over 12 months
[24]	60	F	Thickening Effusion	No	Parotitis Dacryoadenitis	Pericardium	1800	Prednisone 30 mg	Prednisone 2.5 mg	No recurrence over 18 months
[25]	81	M	Thickening Constrictive pericarditis	Yes	None	Pericardium	196	Pericardiectomy + Prednisone 30 mg	Prednisone 10 mg	Regression, no follow-up data
[26]	50	F	Thickening	Yes	Lymphadenopathy	Lymph node	428	Prednisone 0.6 mg/kg	None	No recurrence over 28 months
[27]	65	M	Thickening	No	Pancreatitis	–	637	Prednisone 30 mg	Prednisone 2.5 mg	No recurrence over 24 months
[28]	58	M	Effusion	Yes	None	Pericardium	150	Pericardiectomy + Prednisone 40 mg	None	Regression, no follow-up data
[29]	73	M	Effusion	Yes	None	Pericardium	122	Pericardiectomy + Prednisone 0.6 mg/kg	Prednisone 2.5 mg	Regression, no follow-up data
[30]	75	M	Effusion Thickening	Yes	Periaortitis Lymphadenopathy	Lymph node	625	Prednisone 20 mg	None	Regression, no follow-up data
[31]	72	M	Thickening	Yes	None	Pericardium	177	Unknown	Unknown	Unknown
[32]	47	M	Thickening	Yes	None	Pericardium	668	Pericardiectomy	None	Regression, no follow-up data
[33]	53	M	Effusion	No	Retroperitoneal	Pericardium	163	Pericardiectomy	AZA + Prednisone (dose unknown)	No recurrence over 4 years

Table 1 (continued)

Reference	Age	Gender	Pericardial involvement	Pleural disease	Other organ involvement	Histology	sIgG4 (mg/dL)	Initial therapy	Maintenance therapy	Evolution
[34]	70	F	Subclinical pericarditis Coronary periarteritis	No	Dacryoadenitis Retroperitoneal Pancreatitis Periaortitis	Lacrimal gland	785	Prednisone 30 mg	None	Regression, no follow-up data
[35]	83	M	Effusion	No	Periaortitis	Pericardium	Normal[a]	None	None	No recurrence over 18 months
[36]	64	F	Effusion	No	Renal	NA	962	Prednisone 0.6 mg/kg	Prednisone 5 mg	No recurrence over 24 months
[37]	72	F	Effusion	No	Lymphadenopathy	Lymph node	3580	Prednisone 1 mg/kg	None	No recurrence over 12 months
[38]	36	M	Effusion Thickening	No	None	Pericardium	NA	Prednisone 60 mg	MTX	Recurrent episodes, initial success MTX
[39]	43	F	Effusion	Yes	Peritoneal	Pleura	Normal[a]	Prednisone 30 mg	Prednisone 10 mg	No recurrence over 4 months
[40]	70	M	Effusion	Yes	Periaortitis Renal	Pleura	437	Prednisone 1 mg/kg + Cyclophosphamide	Unknown	No recurrence over 10 months
[41]	60	M	Thickening	No	Pancreatitis Skin	Pericardium Liver, gall bladder Pancreas Lymph node	948	Pericardiectomy + Prednisone 40 mg	Prednisone 10 mg + 6-MP	Onset while on 30 mg Prednisone, regression after pericardiectomy and 6-MP, no follow-up data
[42]	75	M	Thickening Effusion Constrictive pericarditis	No	None	Pericardium	Normal[a]	Pericardiectomy	None	Regression, no follow-up data
[43]	53	F	Thickening Effusion	Yes	None	Pericardium	NA	Rituximab	None	Regression, no follow-up data
[44]	78	F	Thickening Effusion	No	Lymphadenopathy Pancreatitis Retroperitoneal	Pericardium Lymph node	921	Prednisone 30 mg	Unknown	Regression, no follow-up data
[45]	45	M	Effusion	No	Lymphadenopathy Retroperitoneal Intra-cardiac mass	Cardiac mass	703	Prednisone 40 mg, followed by cyclophosphamide and rituximab	Prednisone (dose unknown)	Progression of retroperitoneal fibrosis and constitutional symptoms, regression after RTX
[46]	55	M	Thickening Effusion	Yes	Subcutaneous and periorbital masses	Pericardium Lymph node Orbital mass	534	Prednisone 1 mg/kg + MMF	MMF	No recurrence over 18 months

Table 1 (continued)

Reference	Age	Gender	Pericardial involvement	Pleural disease	Other organ involvement	Histology	sIgG4 (mg/dL)	Initial therapy	Maintenance therapy	Evolution
[47]	78	M	Thickening Constrictive pericarditis	Yes	Sclerosing cholangitis	Pericardium Pleura	760	Prednisone (dose unknown), followed by pericardiectomy	None	Regression, no follow-up data
[48]	79	M	Thickening Effusion	Yes	Lymphadenopathy	Pericardium Pleura Lymph node	306	Prednisone 60 mg, followed by pericardiectomy	None	Regression, no follow-up data
(49)	71	F	Thickening Effusion	Yes	Periaortitis Lymphadenopathy	Pleura	684	Prednisone 40 mg	Unknown	Regression, no follow-up data

[a]Numerical values not specified in publication

IgG4-RD IgG4-related disease, *sIgG4* serum IgG4-concentration, *AZA* azathioprine, *MTX* methotrexate, *6-MP* 6-mercaptopurine, *MMF* mycophenolate mofetil, *RTX* rituximab, *NA* not applicable

this patient were not available, this case is not included in Table 1.

Among the 32 cases where clinical and demographic data were reported, the mean age was 64 years (SD 14) and 65.7% of patients (21/32) were male. Pericardial involvement was mostly reported as pericardial thickening (21/32, 66%) and/or effusion (22/32, 69%) and was the only disease manifestation in only 2 cases. IgG4-related pericarditis was most frequently associated with pleural involvement (20/32, 62%), while peritoneal disease was reported in only 2 cases. Other affected organs included the hepatobiliary system, the aorta and retroperitoneum, lymph nodes and salivary glands. In most cases (19/32, 59%), a pericardial biopsy was obtained to support the diagnosis of IgG4-RD. In one case, pericardial fluid was obtained through FNAC. In 28% of cases (9/32), the diagnosis of IgG4-RD was supported by a non-pericardial biopsy, while in 3 cases no histopathologic findings were reported. Serum-IgG4 levels were reported in the majority of cases (29/32, 90%), with a mean concentration of 676 mg/dL (SD 699), and were > 135 mg/dL in many of them (25/29, 86%), in accordance with the 2011 comprehensive diagnostic criteria [10].

Table 1 presents initial treatment and evolution of the reported cases. Most patients were initially treated with glucocorticoids (17/32, 53%), pericardiectomy (5/32, 16%) or a combination of both (5/32, 16%). In glucocorticoid-treated patients, prednisone doses ranged from 0.6 mg/kg/day to 1 mg/kg/day. In one case, initial therapy additionally included cyclophosphamide, while another patient was treated with rituximab in monotherapy. In 24% of patients initially treated with glucocorticoids alone (4/17), treatment escalation to pericardiectomy or additional immunosuppressive therapy was needed because of recurrence or insufficient treatment response. In all 5 reported cases where patients were initially treated with pericardiectomy alone, remission was achieved without a need for maintenance therapy.

Discussion

We reported a case of IgG4-RD presenting with refractory, effusive pericarditis and imminent cardiac tamponade as the main manifestation, successfully treated with therapeutic pericardiectomy.

Although pericarditis remains a rare manifestation of IgG4-RD, a growing number of cases have been reported describing the pericardium as one of the affected sites. In reviewing the literature, we identified a total of 33 published cases of IgG4-RD with pericardial involvement, 32 of which included clinical and demographic data. However, pericardial involvement was the sole manifestation of IgG4-RD in only 2 of those cases. More frequently, pericarditis was associated with other forms of serositis, usually pleuritis, such

as in our case. In total, the disease was limited to serositis in 44% (14/32) of the reported cases of IgG4-RD with pericardial involvement. Therefore, in case of refractory idiopathic pericarditis, it seems particularly important to consider a diagnosis of IgG4-RD when pleuritis is also present.

The reported cases also demonstrate several tools that can aid in the diagnostic process. In our case, it was primarily the elevated serum-IgG4 levels that prompted consideration of IgG4-RD. Interestingly, in the majority (86%) of published cases where serum-IgG4 levels were available, IgG4 concentrations were ≥ 135 mg/dL, in accordance with the 2011 comprehensive diagnostic criteria. Therefore, although serum-IgG4 levels are normal in a substantial number of cases of IgG4-RD [15], serum-IgG4 does appear to be a useful diagnostic tool when IgG4-related pericarditis is suspected. Moreover, since most cases of IgG4-RD presenting with pericardial involvement also manifest with pleuritis, assessing serum-IgG4 levels is particularly warranted in those patients who present with multiple refractory or idiopathic forms of serositis.

However, even when serum-IgG4 levels are elevated, a definite diagnosis of IgG4-RD according to the 2011 diagnostic criteria also requires the biopsy of an affected site, with an IgG4/IgG ratio of > 40% and > 10 IgG4-positive cells/HPF. In this regard, a pericardial biopsy was obtained in 59% of reported cases of IgG4-RD with pericardial involvement. It should be noted that, when considering IgG4-related pericarditis as a diagnosis, it is imperative to request specific attention to the pathologic hallmarks of IgG4-RD and to retain a low threshold for IgG4-staining. However, in the case of pericardial involvement, obtaining a biopsy can be challenging and requires an invasive procedure. Moreover, our review of cases suggests a rather favorable prognosis for IgG4-related pericarditis, with most cases responding well to initial treatment with pericardiectomy and/or glucocorticoids. In addition, where follow-up information was available, most patients seemed to sustain remission without a need for intensive maintenance therapy, although additional immunosuppressive therapy (including rituximab, methotrexate, or mycophenolate mofetil) could be warranted in refractory cases. Therefore, the decision to perform a pericardial biopsy should be considered on a case-to-case basis. It could be argued that a pericardial biopsy should be restricted to cases where the benefits of a definite diagnosis outweigh the risks of the procedure, or to cases with a severe clinical presentation that requires surgical intervention. Conversely, in mild cases of pericarditis with a clearly elevated serum-IgG4, corresponding with a possible diagnosis of IgG4-RD according to the 2011 criteria, a trial of glucocorticoids could be considered as an alternative option.

Moreover, when other organ systems are also affected, a more accessible biopsy site can be chosen instead of the pericardium. In our case, a lip biopsy was additionally obtained because of both subjective and objective signs of xerostomia, which suggested salivary gland involvement, or IgG4-related sialadenitis (IgG4-RS). Although IgG4-RS often mimics other autoimmune conditions such as primary Sjögren's syndrome, there are several key epidemiological, clinical, serological, and histological differences between these entities [16, 17]. In our case, the presence of storiform fibrosis and elevated serum-IgG4 levels, and the absence of anti-Ro(SSA)/La(SSB)-antibodies were most consistent with IgG4-RS. However, since immunohistochemistry of the lip biopsy showed no IgG4-positive plasma cells, a definite diagnosis of IgG4-RD would likely not have been possible without pericardial tissue examination.

This way, our case also sheds new light on the ACR/EULAR classification criteria for IgG4-RD, proposed in 2019 [14]. These criteria are rather complex and require the involvement of a typical organ, such as the pancreas or salivary glands, as an entry criterion, in addition to the absence of exclusion criteria. Furthermore, 20 inclusion points need to be met to classify a patient. Our case meets all 3 of the 2011 comprehensive diagnostic criteria for IgG4-RD, which is compatible with a definite diagnosis [10]. Nevertheless, since pericarditis is not included in the 2019 ACR/EULAR entry criteria as a typical disease manifestation, pericarditis as a solitary presentation can never be classified as IgG4-RD according to these most recent criteria. It should be noted that, according to the authors, the ACR/EULAR criteria were not intended for use in clinical practice to establish the diagnosis of IgG4-RD, but were particularly developed for clinical trials, with high specificity in mind. However, our case does underline the pitfalls criteria can present and illustrates that a diagnosis of IgG4-RD usually requires a combination of clinical, radiological, serological, and histopathological features.

Conclusion

In persistent idiopathic pericarditis, IgG4-RD should be considered as a possible cause, particularly in the presence of other forms of serositis. A serum-IgG4 measurement seems to be a useful first step. When considering a biopsy, specific attention to the pathological hallmarks of IgG4-RD and a low threshold for IgG4-staining are warranted.

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Author contributions SM collected the patient data. MD and SM independently conducted the literature review and compared their findings. MD and SM drafted the manuscript. RW and BV provided valuable feedback on the manuscript and revised the article critically for content. All authors gave final approval for the manuscript to be published.

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Declarations

Conflict of interest The authors declare no conflicts of interest.

Consent for participation and publication The patient provided informed consent for publication.

References

1. Kamisawa T, Zen Y, Pillai S, Stone JH (2015) IgG4-related disease. Lancet 385(9976):1460–1471
2. Kamisawa T, Funata N, Hayashi Y, Eishi Y, Koike M, Tsuruta K et al (2003) A new clinicopathological entity of IgG4-related autoimmune disease. J Gastroenterol 38(10):982–984
3. Stone JH, Khosroshahi A, Deshpande V, Chan JKC, Heathcote JG, Aalberse R et al (2012) Recommendations for the nomenclature of IgG4-related disease and its individual organ system manifestations. Arthritis Rheum 64(10):3061–3067
4. Inoue D, Yoshida K, Yoneda N, Ozaki K, Matsubara T, Nagai K et al (2015) IgG4-related disease: dataset of 235 consecutive patients. Medicine (United States) 94(15):1–8
5. Wallace ZS, Deshpande V, Mattoo H, Mahajan VS, Kulikova M, Pillai S et al (2015) IgG4-related disease: clinical and laboratory features in one hundred twenty-five patients. Arthritis Rheumatol 67(9):2466–2475
6. Wallace ZS, Zhang Y, Perugino CA, Naden R, Choi HK, Stone JH (2019) Clinical phenotypes of IgG4-related disease: an analysis of two international cross-sectional cohorts. Ann Rheum Dis 78(3):406–412
7. Hsieh SC, Shen CY, Liao HT, Chen MH, Wu CH, Li KJ et al (2020) The cellular and molecular bases of allergy, inflammation and tissue fibrosis in patients with IGG4-related disease. Int J Mol Sci 21(14):1–24
8. Brito-Zerón P, Bosch X, Ramos-Casals M, Stone JH (2016) IgG4-related disease: advances in the diagnosis and treatment. Best Pract Res Clin Rheumatol 30(2):261–278
9. Scott IA, Campbell DA (2018) The gaps in specialists' diagnoses. Med J Aust 208(5):196–198
10. Umehara H, Okazaki K, Masaki Y, Kawano M, Yamamoto M, Saeki T et al (2012) Comprehensive diagnostic criteria for IgG4-related disease (IgG4-RD), 2011. Mod Rheumatol 22(1):21–30
11. Deshpande V, Zen Y, Chan JKC, Yi EE, Sato Y, Yoshino T et al (2012) Consensus statement on the pathology of IgG4-related disease. Mod Pathol 25:1181–1192
12. Bledsoe JR, Della-Torre E, Rovati L, Deshpande V (2018) IgG4-related disease: review of the histopathologic features, differential diagnosis, and therapeutic approach. APMIS 126(6):459–476
13. Umehara H, Okazaki K, Nakamura T, Satoh-Nakamura T, Nakajima A, Kawano M et al (2017) Current approach to the diagnosis of IgG4-related disease—combination of comprehensive diagnostic and organ-specific criteria. Mod Rheumatol 27(3):381–391
14. Wallace ZS, Naden RP, Chari S, Choi HK, Della-Torre E, Dicaire JF et al (2020) The 2019 American College of Rheumatology/European League against Rheumatism classification criteria for IgG4-related disease. Ann Rheum Dis 79(1):77–87
15. Carruthers MN, Khosroshahi A, Augustin T, Deshpande V, Stone JH (2015) The diagnostic utility of serum IgG4 concentrations in IgG4-related disease. Ann Rheum Dis 74(1):14–18
16. Fragoulis GE, Zampeli E, Moutsopoulos HM (2017) IgG4-related sialadenitis and Sjögren's syndrome. Oral Dis 23(2):152–156
17. Mavragani CP, Fragoulis GE, Rontogianni D, Kanariou M, Moutsopoulos HM (2014) Elevated IgG4 serum levels among primary Sjögren's syndrome patients: do they unmask underlying IgG4-related disease? Arthritis Care Res 66(5):773–777
18. Sugimoto T, Morita Y, Isshiki K, Yamamoto T, Uzu T, Kashiwagi A et al (2008) Constrictive pericarditis as an emerging manifestation of hyper-IgG4 disease. Int J Cardiol 130(3):e100-101
19. Rossi G, Marchioni A, Guicciardi N, Cadioli A, Cavazza A (2009) Recurrent pleural and pericardium effusions in a white woman with IgG4-related syndrome. Am J Surg Pathol 33(5):802–803
20. Kabara M, Nakagawa N, Chinda J, Hirai T, Nimura A, Ota H et al (2011) Diagnosis of IgG4-related systemic disease by cytology of large pericardial effusion with fine needle aspiration. Int J Cardiol 148(3):392–393
21. Sakamoto A, Nagai R, Saito K, Imai Y, Takahashi M, Hosoya Y et al (2011) Idiopathic retroperitoneal fibrosis, inflammatory aortic aneurysm, and inflammatory pericarditis-retrospective analysis of 11 case histories. J Cardiol 59(2):139–146
22. Sekiguchi H, Horie R, Suri RM, Yi ES, Ryu JH (2012) Constrictive pericarditis caused by immunoglobulin G4-related disease. Circ Heart Failure 5(2):e30-31
23. Sekiguchi H, Horie R, Utz JP, Ryu JH (2012) IgG4-related systemic disease presenting with lung entrapment and constrictive pericarditis. Chest 142(3):781–783
24. Morita T, Izawa A, Hamano H, Asano N, Kozuka A, Moteki H et al (2014) Significant pericardial involvement of immunoglobulin g4-related disease. Ann Thorac Surg 98(2):e47–e49
25. Yanagi H, Yamazaki I, Shimizu S, Himeno H, Suzuki SI, Masuda M (2014) Constrictive pericarditis caused by immunoglobulin G4-related disease. Ann Thorac Surg 97(3):e71–e74
26. Matsumiya R, Hosono O, Yoshikawa N, Uehara M, Kobayashi H, Oda A et al (2015) Elevated serum IgG4 complicated by pericardial involvement with a patchy 18F-FDG uptake in PET/CT: a typical presentation of IgG4-related disease. Intern Med 54(18):2337–2341
27. Mori K, Yamada K, Konno T, Inoue D, Uno Y, Watanabe M et al (2015) Pericardial involvement in IgG4-related disease. Intern Med 54(10):1231–1235
28. Seo J, Song IJ, Lee S, Jeong HJ, Kim HM, Koh BS et al (2015) A case of constrictive pericarditis due to immunoglobulin G4-related disease. Korean Circ J 45(2):161–164
29. Horie K, Tada N, Yamaguchi K, Inazawa K, Endo M, Inoue N (2016) Immunoglobulin G4-related constrictive pericarditis identified by cytological examination of pericardial effusion: a case report. J Med Case Rep 10(1):1–5
30. Hourai R, Miyamura M, Tasaki R, Iwata A, Takeda Y, Morita H et al (2016) A case of IgG4-related lymphadenopathy, pericarditis, coronary artery periarteritis and luminal stenosis. Heart Vessels 31(10):1709–1713
31. Ibe T, Nakamura T, Taniguchi Y, Momomura SI (2016) IgG4-related effusive constrictive pericarditis. Eur Heart J Cardiovasc Imaging 17(6):707
32. Luo WQ, Fang F, Zhen WJ, Ouyang XK, Wang HB, Wang Z et al (2016) A case of immunoglobulin G4-related constrictive pericarditis. Ann Transl Med 4(3):57
33. Terzic B, Spasic M, Djuric P, Vasiljevic V, Radjen S, Mijuskovic M (2017) Retroperitoneal fibrosis and constrictive pericarditis-IgG4 related diseases: a case report. Exp Ther Med 13(6):3603–3606
34. Matsuda J, Takano H, Shimizu W (2018) IgG4-related periarteritis in the coronary artery and subclinical pericarditis assessed

the presence and monitoring of therapy response by PET and CT scan. BMJ Case Rep bcr-2018-225172
35. Weiss MA, Aubry MC, Pflederer BR (2018) A case of IgG4-related aortitis and pericarditis: diagnostic challenges and natural history. Am J Case Rep 19:1232–1236
36. Arao K, Mase T, Iwanami K, Nakai M, Sekiguchi H, Abe Y et al (2019) IgG4-related pericarditis in which oral corticosteroid therapy was effective. Intern Med 58(8):1119–1122
37. Tomoda Y, Kometani T, Kato S, Tanaka K (2019) Immunoglobulin G4-related pericarditis. Eur Heart J 40(46):3803
38. Yassi U, Iqbal F, Stevenson HL (2019) IgG4-related sclerosing pericarditis in a young man with recurrent chest pain. Ann Thorac Surg 108(4):e261–e263
39. Tong X, Bai M, Wang W, Han Q, Tian P, Fan H (2017) IgG4-related disease involving polyserous effusions with elevated serum interleukin-6 levels: a case report and literature review. Immunol Res 65(4):944–950
40. González-Moreno J, Losada-López I, Gállego-Lezaun C, García-Gasalla M, Gómez Bellvert C, Ortego CN (2016) Serosal involvement in IgG4-related disease: report of two cases and review of the literature. Rheumatol Int 36(7):1033–1041
41. Nayar M, Charnley R, Scott J, Haugk B, Oppong K (2009) Autoimmune pancreatitis with multiorgan involvement. A case of pericardial involvement. J Pancreas 10(5):539–542
42. Atallah PC, Kassier A, Powers S (2014) IgG4-related disease with effusive-constrictive pericarditis, tamponade, and hepatopathy: A novel triad. Int J Cardiol 176(2):516–518
43. Gorecka MM, Armstrong R, Daly C (2019) Unusual cause of pericardial effusion: IgG4-related disease. BMJ Case Rep 12(6):1–3
44. Sendo S, Saegusa J, Morinaga Y, Kawakami F, Kogata Y, Kageyama G et al (2017) IgG4-related disease manifesting as pericarditis with elevated adenosine deaminase and IL-10 levels in pericardial fluid. Mod Rheumatol 27(5):894–897
45. Hajsadeghi S, Pakbaz M, Hassanzadeh M, Sadeghipour A (2020) A challenging case report of IgG4-related systemic disease involving the heart and retroperitoneum with a literature review of similar heart lesions. Echocardiography 37(9):1478–1484
46. Vu K, Gupta R, Frater J, Atkinson J, Ranganathan P (2017) A 55-year-old man with periorbital and inguinal masses, pericarditis, and pleuritis. Arthritis Care Res 69(5):730–736
47. Kondo T, Uehara T (2016) Immunoglobulin G4-related disease with fibroinflammatory lesions in the pleura, bile ducts and pericardium. CMAJ 188(13):972
48. Yuriditsky E, Dwivedi A, Narula N, Axel L, Horowitz JM, Vaynblat M (2020) Constrictive pericarditis caused by IgG4-related disease requiring pericardiectomy after partial response to corticosteroids. JACC Case Rep 2(10):1558–1563
49. Ishida M, Hodohara K, Furuya A, Fujishiro A, Okuno H, Yoshii M et al (2014) Concomitant occurrence of IgG4-related pleuritis and periaortitis: a case report with review of the literature. Int J Clin Exp Pathol 7(2):808–814