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CASE REPORT

INTERMEDIATE

CLINICAL CASE

Severe Aortic Valvular Incompetence From IgG4-Related Disease

An Unusual Entity

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ABSTRACT

IgG4-related disease (IgG4-RD) is a new clinical entity characterized by lymphoplasmacytic lesions rich in IgG4-positive plasma cells. Myocardial involvement is extremely rare and not a typical cardiovascular manifestation of IgG4-RD. We report a rare case of IgG4-RD–associated myocardial mass causing severe aortic incompetence, successfully treated with surgery and corticosteroids. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2023;24:102027)

HISTORY OF PRESENTATION

A 53-year-old woman presented to the emergency department with dyspnea, palpitations, and fatigue over a 6-month period. She remained afebrile with stable vital signs (blood pressure: 134/760 mm Hg; pulse: 89 beats/min; peripheral oxygen saturation: 98%; respiratory rate: 19 breaths/min; temperature: 36.8 °C). Auscultating the precordium revealed an early diastolic murmur at left sternal border. Electrocardiogram showed sinus rhythm with first degree atrioventricular block.

LEARNING OBJECTIVES

- To recognize myocardial involvement as a manifestation of IgG4-RD.
- To understand the radiologic, serologic, and histopathologic diagnostic criteria for IgG4-RD.

PAST MEDICAL HISTORY

Her medical history included hypothyroidism, asthma, hyperlipidemia, and migraine.

DIFFERENTIAL DIAGNOSIS

Differential diagnoses at this stage included valvular heart disease and heart failure.

INVESTIGATIONS

Initial laboratory investigations revealed mild anemia (hemoglobin: 10.9 g/dL), with mildly elevated erythrocyte sedimentation rate (35 mm/h; normal range: ≤20 mm/h) and C-reactive protein (9 mg/dL; normal range: <1.0 mg/dL). Normal values for white blood cell count (6.3 × 10^9/L) as well as renal

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ABBREVIATIONS AND ACRONYMS

CMR = cardiac magnetic resonance imaging

CT = computed tomography

Ig = immunoglobulin

IgG4-RD = immunoglobulin G4-related disease

LVOT = left ventricular outflow tract

TEE = transesophageal echocardiography

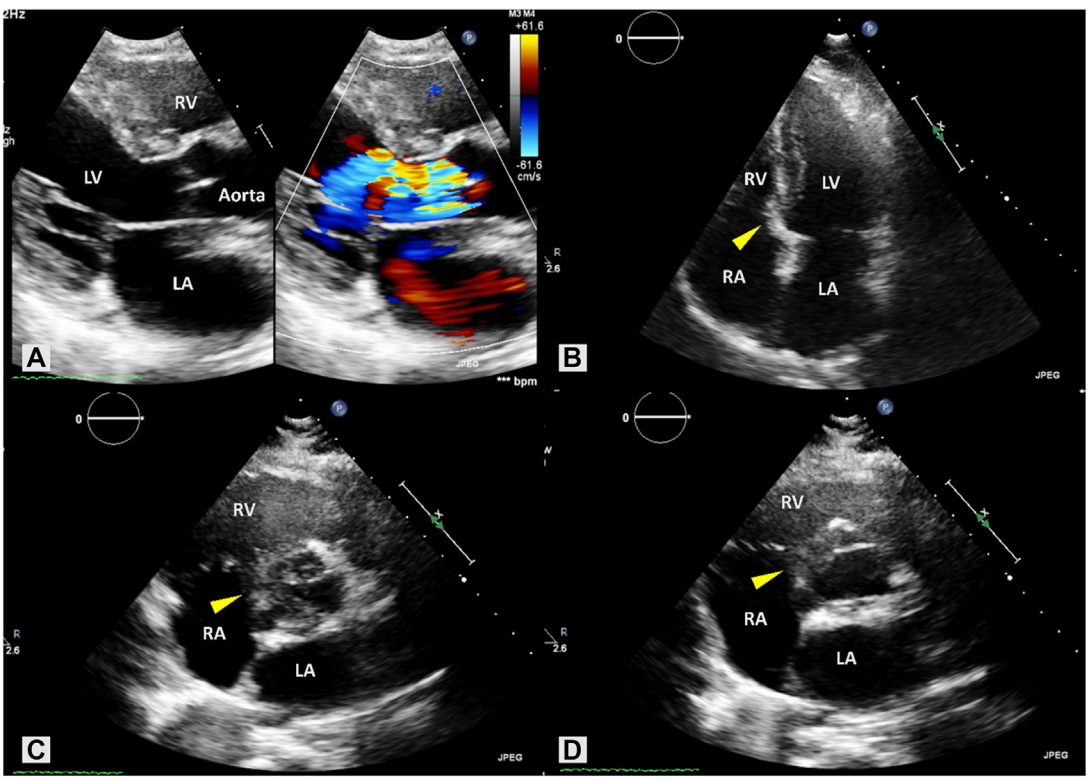
TTE = transthoracic echocardiography

(creatinine: 79 μmol/L) and liver functions (bilirubin: 7.0 μmol/L) were detected while blood cultures remained sterile. Transthoracic echocardiography (TTE) revealed severe aortic incompetence within an abnormal-looking noncoronary cusp of a trileaflet aortic valve (**Figure 1**, Video 1). Left ventricular function was preserved. Transesophageal echocardiography (TEE) revealed an echogenic mass at the base of the noncoronary cusp with severe aortic regurgitation (**Figure 2**). Cardiac computed tomography (CT), optimized for evaluation of the aorta (biphasic contrast injection), revealed a 9 × 7 × 6-mm soft tissue mass surrounding the aortic root, abutting the base of the noncoronary cusp (**Figure 3**). Severe aortic valve incompetence caused by infective endocarditis and complicated by suspected aortic root abscess became the primary working diagnosis. Other extremely rare differentials include inflammatory periaortitis and metastatic cardiac tumors.

MANAGEMENT

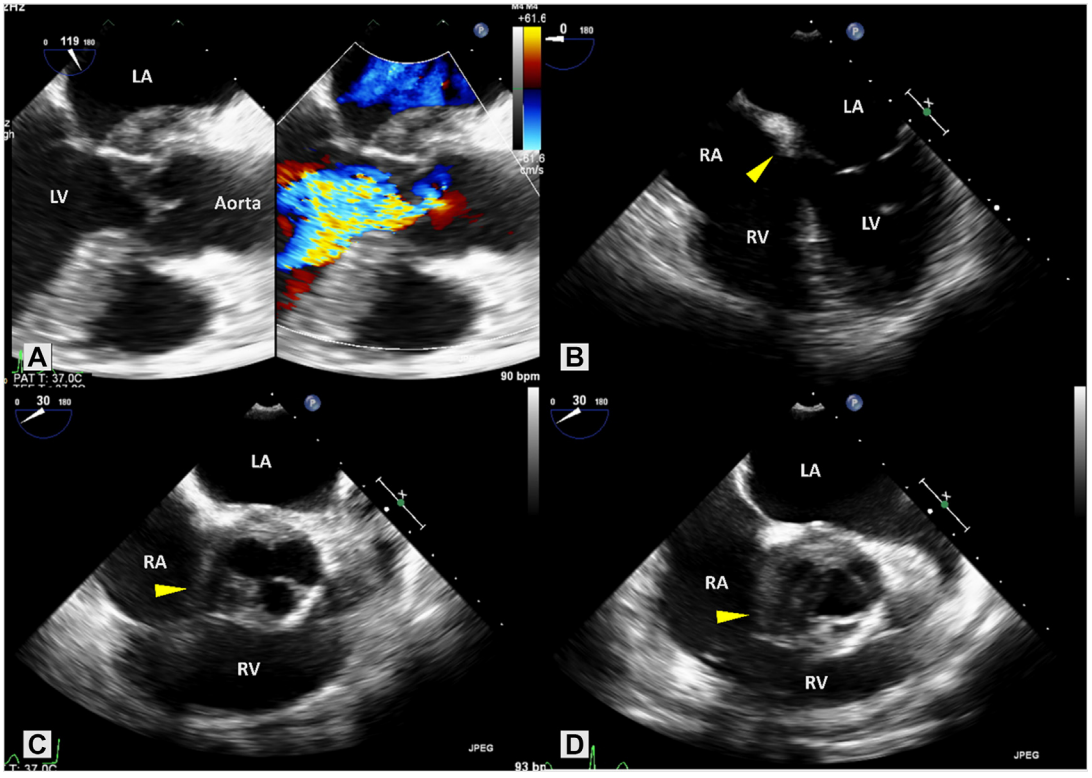
Addressing the working diagnosis, heart team discussion involving the cardiology, radiology, and cardiothoracic surgery departments recommended urgent cardiac surgery with a view to surgical aortic valve replacement and aortic root repair/replacement. Preoperative cardiac magnetic resonance (CMR) was not performed because progressive heart

FIGURE 1 Transthoracic Echocardiographic View of Aortic Root Mass



The yellow arrowheads indicate the aortic root mass. (A) Parasternal long-axis view demonstrating severe aortic incompetence on color Doppler. (B) Apical 4-chamber view. (C) Parasternal short-axis view in end diastole. (D) Parasternal short-axis view in midsystole. LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle.

FIGURE 2 **Transesophageal Echocardiographic View of Aortic Root Mass**



The yellow arrowheads indicate the aortic root mass. (A) Midesophageal long-axis view demonstrating severe aortic incompetence on color Doppler. (B) Midesophageal 4-chamber view. (C) Midesophageal short-axis view in end diastole. (D) Midesophageal short-axis view in midsystole. Abbreviations as in Figure 1.

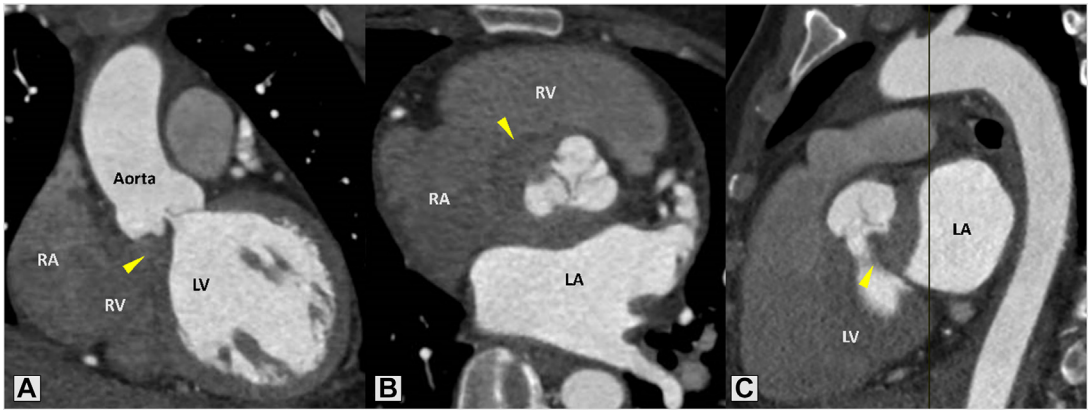
block and strong suspicion for aortic root abscess accentuated the urgency of the case, requiring emergent surgical intervention.

Intraoperative findings revealed a smooth obstructing myocardial mass in the left ventricular outflow tract (LVOT) with abnormally thickened aortic valves. This occurred at the level of the noncoronary sinus, disrupting the valve anatomy with consequent aortic incompetence. There was no macroscopic evidence of infective endocarditis: intact endothelium and no evidence of vegetations or aortic root abscesses.

Because the diagnosis was unclear, a strategy to restore normal anatomy was adopted. The LVOT mass was excised to restore a normal LVOT diameter. Akin to performing a myomectomy in patients with hypertrophic obstructive cardiomyopathy, myocardium in the LVOT was progressively excised until an adequate LVOT area was achieved. There was not a circumscribed mass with clear abnormal margins; instead, it resembled hypertrophic obstructive cardiomyopathy with an abnormal inflammatory appearance. The regurgitant valve was excised, and a mechanical aortic prosthesis was inserted. Because the aortic root was normal, aortic root repair was not indicated. The patient recovered uneventfully after surgery. Postoperative TEE revealed a functioning prosthetic valve without an abnormal gradient across the LVOT.

Pathologic investigations raised the possibility of alternative diagnoses. Microscopic examination revealed prominent plasma cell infiltrations with admixed small lymphoid cells. The infiltrations were associated with increased fibrosis with focal vascular endothelial prominence, inflammation, and obliterative features seen with myxoid changes to vascular

FIGURE 3 Aortic Root Mass Evaluation Using Cardiac Computed Tomography

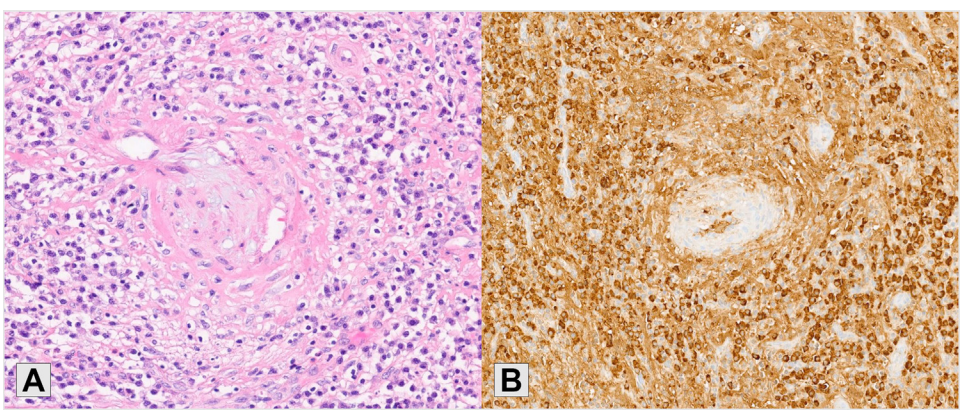


The yellow arrowheads indicate the aortic root mass. (A) Coronal plane. (B) Axial plane. (C) Sagittal plane. Abbreviations as in Figure 1.

walls (Figure 4). Immunohistochemical staining demonstrated plasma cells of immunoglobulin (Ig) G4-positive predominant pattern, with many areas showing >50 IgG4-positive plasma cells per high-power field. With features of chronic endocarditis involving the valve and septum as well as conditions such as rheumatic heart disease also exhibiting increased IgG4-positive plasma cell infiltration, current differentials included IgG4-related disease (IgG4-RD) along with an autoimmune phenomenon and chronic endocarditis.

Further serologic investigations performed demonstrated that serum IgG4 was significantly elevated (2.603 g/L; normal range: 0.039-0.864 g/L) while levels from other subclasses remained normal. Apart from carrying the HLA-B27 allele, an extended autoimmune screen tested negative for all serologic parameters, including rheumatoid factor, antinuclear antibody, anti-cardiolipin, anti-Ro, anti-La, anti-centromere, anti-Scl70, anti-Jo1, anti-SM, anti-ribosomal-PP, antineutrophilic cytoplasmic antibody, and anti-B2GP-1. The infective screen result was negative

FIGURE 4 Histopathology of Tissue From Noncoronary Sinus



(A) Hematoxylin and eosin stain demonstrating dense plasma cell-rich infiltrate associated with damage to vascular walls, with myxoid change and obliterative features. (B) Immunoglobulin G4 immunohistochemical stain demonstrating plasma cell infiltrate with diffuse immunoglobulin G4 positivity.

for acute, chronic, and bloodborne infections (hepatitis B, hepatitis C, HIV), with sterile blood cultures and normal serum complement levels. Based on the clinical finding of a tumefactive lesion alongside histologic and serologic evidence, the diagnosis of IgG4-RD was made, and corticosteroid therapy was initiated postoperatively.

Follow-up abdominal ultrasound and CMR did not detect any extramyocardial manifestations of IgG4-RD such as pericarditis, coronary arteritis/aneurysms, intra-abdominal pseudotumors, or biliary strictures.

DISCUSSION

IgG4-RD was first described by Japanese researchers as a systemic fibroinflammatory condition in 2003.[1] According to the Japanese IgG4 Group 2020 IgG4-RD diagnostic criteria, a definite diagnosis of IgG4-RD required radiologic (tumefactive mass), serologic (serum IgG4 levels: >1.35 g/L), and histopathologic (>10 IgG4-positive plasma cells per high-power field and typical fibrosis pattern) correlation.[2]

Known to affect multiple organ systems, cardiovascular manifestations of IgG4-RD include periaortitis, coronary arteritis, and pericarditis.[3,4] Because myocardial involvement remains extremely rare, consensus is lacking on the optimal approach to diagnosis. This case report highlights myocardial involvement as a rare presentation of IgG4-RD and the steps taken to reach a diagnosis of IgG4-RD-associated myocardial mass causing severe aortic incompetence.

The workup for any intracardiac mass involves multimodal imaging to characterize the lesion. Combined use of TTE, TEE, cardiac CT, and CMR allows the noninvasive assessment of the type, location, and hemodynamic significance of the cardiac lesion. In our case, symptomatic severe aortic incompetence with progressive heart block made urgent surgical intervention a reasonable approach and provided histologic analysis. Although this approach remains the commonest method for obtaining a histologic diagnosis for IgG4-RD-associated myocardial mass, less invasive transcatheter approaches or superficial site biopsies have previously been demonstrated.[5,6] Positron emission tomography may be used to identify extracardiac involvement of IgG4-RD, providing easier alternative biopsy sites.[6]

The excellent response to corticosteroids make them the first-line recommended therapy for IgG4-RD by international consensus.[7] Although we performed urgent surgical intervention because of the sinister signs of severe aortic incompetence and aortic root abscess, less invasive strategies can be useful in potentially avoiding high-risk surgery. Yano et al[5] previously demonstrated that a transcatheter approach to obtaining a biopsy diagnosis of IgG4-RD-associated myocardial mass, followed by corticosteroid therapy, can be effective in achieving remission without surgery.[5] Postoperative patients are also at risk of recurrence if not on corticosteroids. Ishida et al[8] demonstrated growth of a previously excised IgG4-RD-associated myocardial mass on cardiac CT in a steroid-naive patient at 1 year from surgery that responded well to the initiation of corticosteroids. With such a response to corticosteroids, conservative strategies to diagnose the cardiac mass should be considered first in hemodynamically stable patients with no sinister signs and symptoms or severe valvular lesions that require surgical intervention.

FOLLOW-UP

The patient remained asymptomatic with a normally functioning mechanical aortic valve on TTE at 1, 6, and 24 months postsurgery. Because no recurrence was detected on TTE at the 2-year follow-up, surgery and corticosteroid therapy were deemed curative.

CONCLUSIONS

Myocardial involvement in IgG4-RD remains extremely rare but should be considered in the differential diagnosis of a cardiac mass.

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KEY WORDS cardiac mass, IgG4-RD, IgG4-related disease, multimodal imaging

APPENDIX For a supplemental video, please see the online version of this paper.