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CASE REPORT

INTERMEDIATE

CLINICAL CASE

Immunoglobulin G4-Related Multiple Giant Coronary Artery Aneurysms and a Single Left Gastric Artery Aneurysm

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ABSTRACT

Coronary artery aneurysm (CAA) is potentially life-threatening. We describe a case of multiple giant CAAs and a single left gastric artery aneurysm caused by immunoglobulin G4-related disease (IgG4-RD). Our case highlights the significance of assessing IgG4-RD in the diagnosis of CAA and screening for other concurrent cardiovascular involvements. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2020;2:769–74) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

A giant coronary artery aneurysm (CAA) measuring more than 50 mm in diameter is extremely rare; however, potentially serious sequelae may occur (1). The diagnosis and management of giant CAAs remain challenging.

HISTORY OF PRESENTATION

A 77-year-old man was referred to our hospital for the evaluation of a suspected mediastinal mass that was incidentally detected on chest radiography (**Figure 1**). His vital signs were stable. All physical and laboratory examination results and the electrocardiogram were unremarkable.

LEARNING OBJECTIVES

- To understand radiological findings in coronary and abdominal artery involvements associated with IgG4-RD.
- To review the causes of CAAs.

MEDICAL HISTORY

The patient had a history of ischemic stroke, diabetes, hypertension, hyperlipidemia, and smoking. He underwent subtotal gastrectomy for a gastric ulcer at 45 years of age and coronary angiography for angina at 49 years of age.

DIFFERENTIAL DIAGNOSIS

We initially suspected atherosclerotic-related CAAs, postintervention coronary pseudoaneurysms, or inflammatory and infectious diseases.

INVESTIGATIONS

Echocardiography revealed 2 huge masses around the heart (**Figure 2**). Contrast-enhanced computed tomography (CT) revealed multiple CAAs severely compressing the cardiac chambers (**Figure 3**). In addition to a left gastric artery aneurysm (LGAA), we

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ABBREVIATIONS AND ACRONYMS

CAA = coronary artery aneurysm

CT = computed tomography

LGAA = left gastric artery aneurysm

IgG4 = immunoglobulin G4

IgG4-RD = immunoglobulin G4-related disease

RCA = right coronary artery

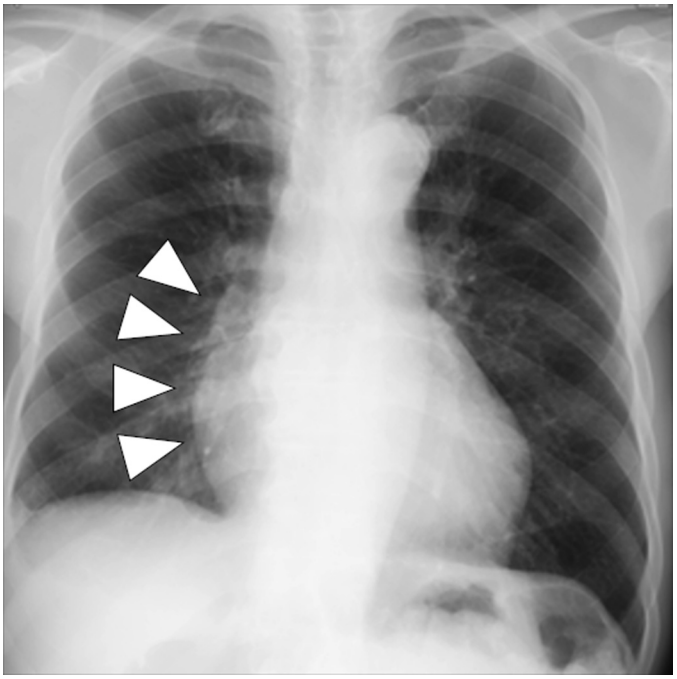
SAM = segmental arterial mediolysis

also identified a severe mural calcification in the main coronary arteries without systemic arterial sclerosis. Coronary CT angiography further characterized multiple CAAs involving the main coronary arteries (Figure 4). Axial and coronal CT scans demonstrated 2 giant CAAs of the proximal and distal right coronary artery (RCA), with the major axes measuring 6.5 × 7.5 cm and 4.8 × 3.5 cm, respectively. Moreover, we detected a proximal RCA with a large lumen and irregular mural thrombus lining; the distal RCA had a circumferential mural calcification and a false lumen filled with mural thrombus. The other CAAs of the proximal left anterior descending and left circumflex arteries with a whole false lumen were filled with a mural thrombus and circumferential mural calcification.

MANAGEMENT

Owing to the increased risk of an aneurysmal rupture or the thrombotic occlusion of the CAAs, proximal and distal RCA aneurysmectomy with simultaneous coronary artery bypass grafting (using a saphenous vein graft) was performed (Figure 5A). The resected aneurysms were filled with a massive organized thrombus (Figure 5B). Pathological examination of the resected aneurysmal wall revealed lymph follicles of the adventitia and storiform fibrosis amid a prominent lymphoplasmacytic infiltrate, mainly in the adventitia, concomitant with the destruction of the normal structures of the majority of the media. Immunostaining revealed numerous immunoglobulin G4 (IgG4)-positive plasma cells (Figures 5C and 5D); the average number of IgG4-positive plasma cells was 629/high-power field (range: 234 to 1,043/high-power field). The IgG4/IgG ratio was 97%, which suggested IgG4-related coronary periarteritis. The serum IgG4 level was elevated at 353 mg/dl (normal range: 4 to 108 mg/dl). These findings fulfilled all comprehensive diagnostic criteria for immunoglobulin G4-related disease (IgG4-RD) because of the clinical exclusion of all other disorders that may mimic IgG4-RD, including malignancies and inflammatory, infectious, and autoimmune diseases.

FIGURE 1 Chest Radiograph



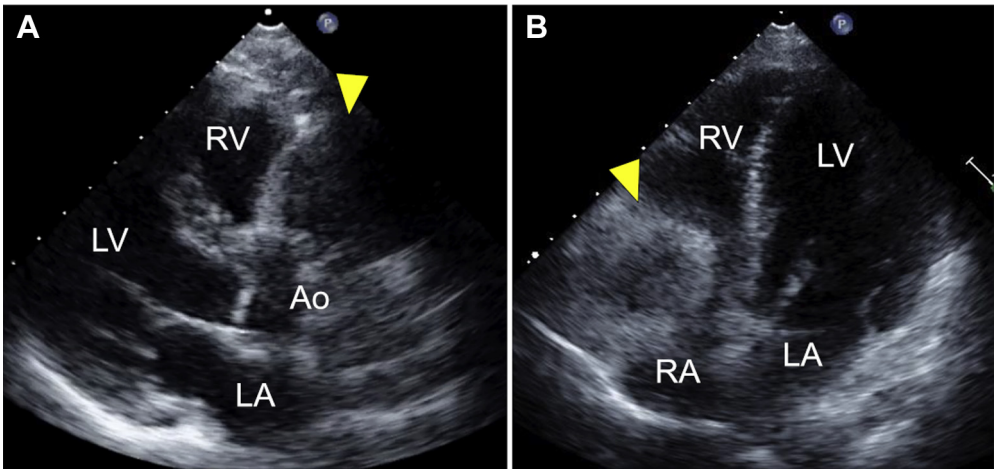
A convex contour of the right cardiac border is observed **(arrowheads)**.

DISCUSSION

IgG4-RD is a systemic immune-mediated fibroinflammatory disease with multiorgan involvement (2); coronary artery involvement presents with various clinical phenotypes, including inflammatory pseudotumors, fibrotic diffuse thickening, and coronary artery stenosis. Multidetector row CT can clearly characterize the perivascular tissue and be useful for the diagnosis of IgG4-RD (3). Typically, coronary artery involvements are characterized by periarterial fibrosclerotic thickening without atherosclerotic changes (e.g., calcification). However, the strong association between IgG4-RD and atherosclerotic coronary artery disease is gaining considerable attention (4). Chronic inflammation, secondary to IgG4-RD, may be involved in the development and progression of atherosclerotic coronary artery disease (5). Epidemiologically, IgG4-RD is common in middle-aged to elderly men with multiple risk factors of atherosclerosis. Thus, IgG4-related CAAs must be clinically differentiated from atherosclerotic-related CAAs. In the present case, coronary artery calcifications were severe despite the less-severe systemic arteriosclerosis. These mismatched findings might be key to the consideration of this rare entity.

IgG4-RD can simultaneously affect large and/or medium vessels; this frequently occurs in the infrarenal segment of the abdominal aorta (6,7). To the best of our knowledge, the present report is the first on IgG4-RD-associated LGAA. Segmental arterial mediolysis (SAM), which occurs in the middle to advanced ages, is

FIGURE 2 Transthoracic Echocardiography



(A) Parasternal long-axis view showing an echolucent mass **(arrowhead)** outside the right coronary cusp. **(B)** Apical 4-chamber view showing a heteroechogenic mass **(arrowhead)** in the right atrioventricular groove. See Videos 1 and 2. Ao = aorta; LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle.

a life-threatening, nonatherosclerotic, and noninflammatory vasculopathy. It often causes intra-abdominal bleeding resulting from the formation and rupture of aneurysms in the abdominal arteries, and requires prompt treatment by vascular embolization or surgical resection (8). In addition to the superior mesenteric, hepatic, celiac, and splenic arteries, the left gastric artery is also affected. The CT findings for LGAA are similar between IgG4-RD and SAM. Thus, it is important to distinguish between the 2 because although they are similar in terms of the age of onset and radiological findings, they differ in the requisite treatment approaches. IgG4-RD and SAM can also be differentiated based on the histopathological findings (9).

Although corticosteroid therapy is the gold standard treatment for IgG4-related cardiovascular involvements, its effectiveness for luminal dilatated lesions is controversial (6,7); there are concerns regarding acute progression or rupture of the existing CAAs and the development of new aortic aneurysmal lesions after therapy. Thus, care must be taken with the indication or timing and the dose of the corticosteroid treatment for CAAs or LGAA. Rituximab is considered a second option in maintenance therapy after steroid tapering or in high-risk patients with steroid intolerance (6). Immunomodulators, such as cyclophosphamide, may be an additional treatment option (10). In some cases, long-term spontaneous remission was achieved without an aggressive drug treatment for IgG4-RD (11). Further investigation is necessary to devise proper treatment strategies for patients with IgG4-RD. Our patient refused the aforementioned drug treatments and received close monitoring with outpatient follow-up.

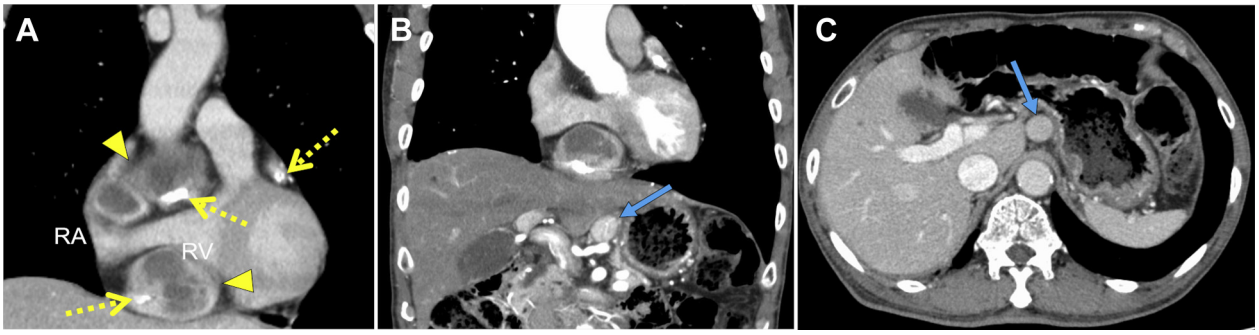
FOLLOW-UP

The postoperative course was uneventful. With no medical treatment, the remaining coronary artery lesions showed no exacerbation. Spontaneous regression of the LGAA was observed at the 6-month follow-up (**Figure 6**). He remained clinically stable with a 48-month follow-up. Although the serum IgG4 levels remained elevated (584 mg/dl), other serological inflammatory biomarkers were within the normal range: erythrocyte sedimentation rate, 12 mm/h (reference: 0 to 15 mm/h) and C-reactive protein level, 0.01 mg/dl (reference: 0 to 0.30 mg/dl). The serum complement levels, including those of C3, C4, and CH50, were within the normal range.

CONCLUSIONS

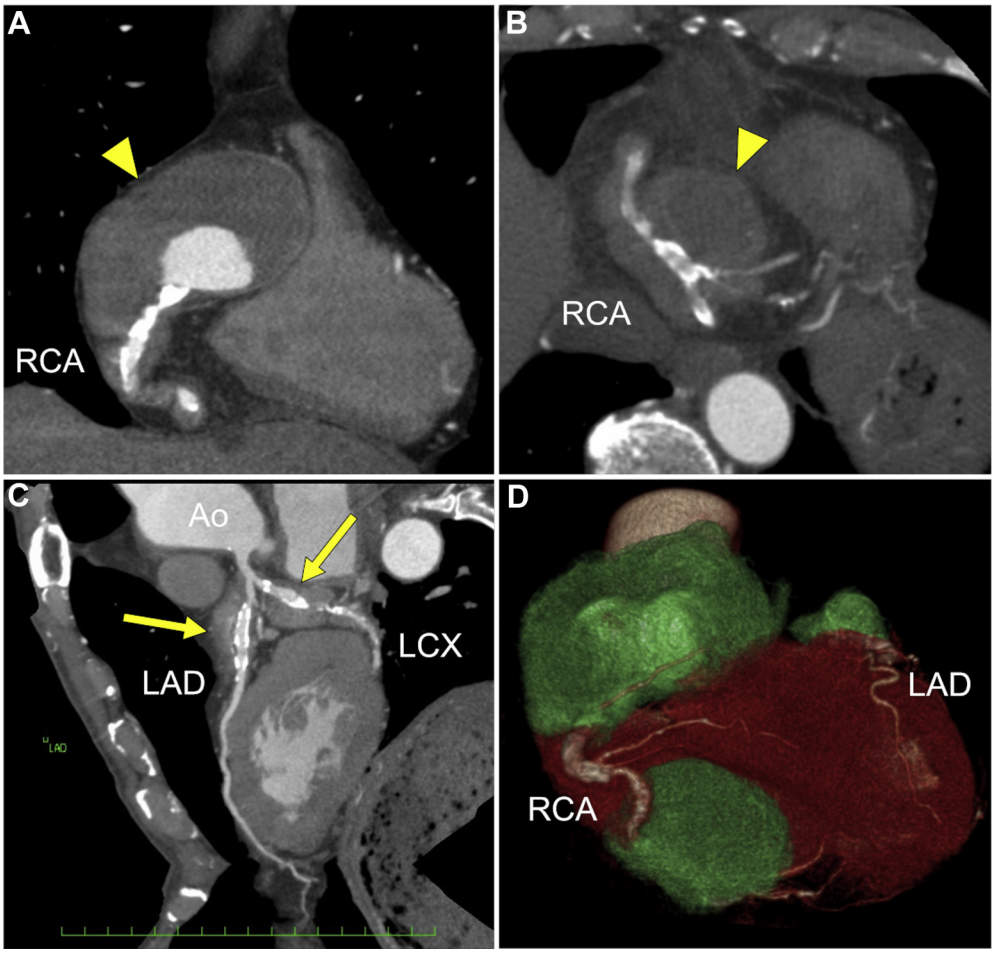
We described a case of multiple giant CAAs and a single LGAA resulting from IgG4-RD. Clinicians

FIGURE 3 Contrast-Enhanced Computed Tomography



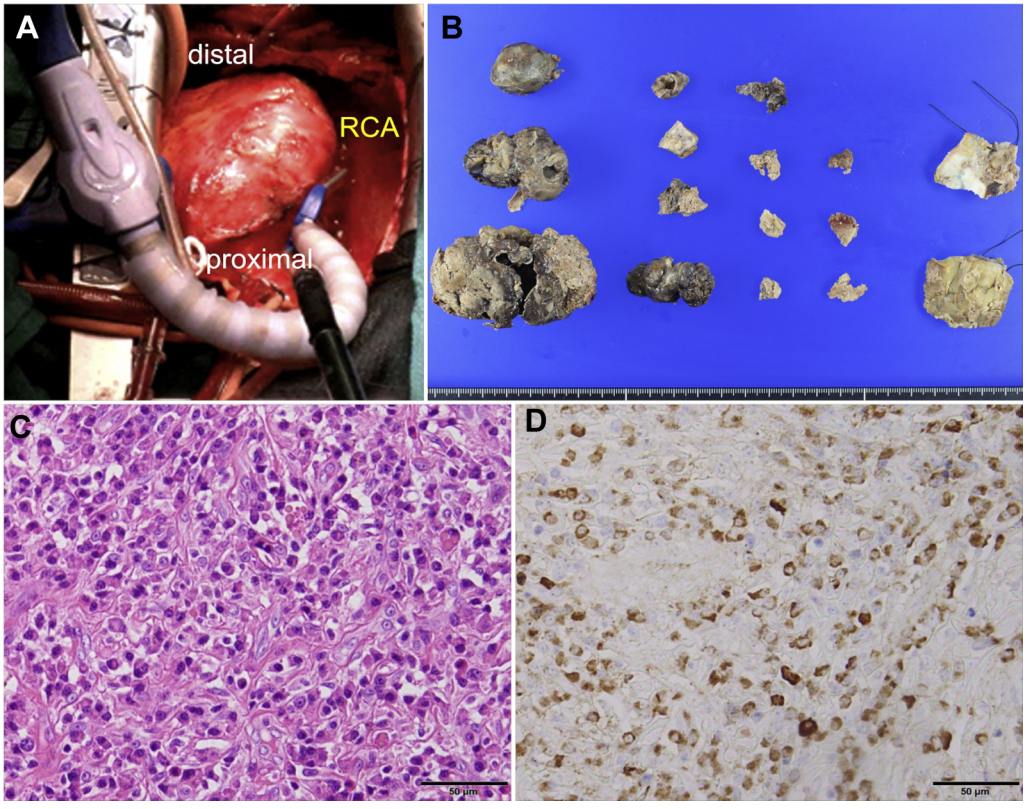
(A,B) Coronal and **(C)** axial images. Computed tomography images show multiple CAAs **(arrowheads)** severely compressing the cardiac chambers, with severe mural calcification in the main coronary arteries **(dashed arrows)** and a single LGAA **(arrow)**, with a maximum diameter of 18 mm in the lesser curvature of the postoperative stomach. CAA = coronary artery aneurysm; LGAA = left gastric artery aneurysm; RA = right atrium; RV = right ventricle.

FIGURE 4 Coronary Computed Tomography Angiography



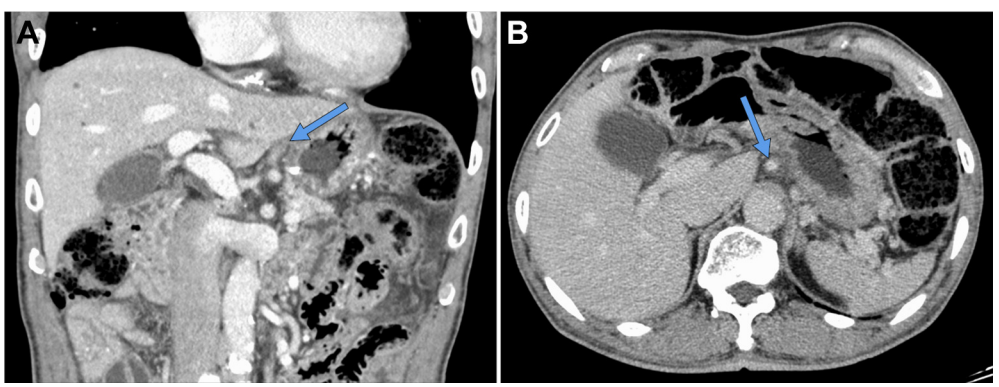
(A) Coronal and **(B)** axial images. **(C)** Curved planar reconstruction and **(D)** volume-rendering reconstruction. The extracoronary luminal lesion appears in green. Two giant CAAs of the proximal and distal RCA **(arrowheads)** and other CAAs of the proximal LAD and LCX **(arrows)** are visible. Ao = aorta; CAA = coronary artery aneurysm; LAD = left anterior descending artery; LCX = left circumflex artery; RCA = right coronary artery.

FIGURE 5 Intraoperative and Pathological Findings



(A) Surgeons' intraoperative view of the RCA aneurysms. **(B)** Resected aneurysms. **(C)** Photomicrograph with hematoxylin and eosin staining (scale bar: 50 μm). **(D)** Photomicrograph with immunostaining for immunoglobulin G4 (scale bar: 50 μm). RCA = right coronary artery.

FIGURE 6 Follow-Up Contrast-Enhanced Computed Tomography Image



(A) Coronal and **(B)** axial images. Spontaneous regression of the left gastric artery aneurysm observed at the 6-month follow-up **(arrows)**.

should be aware of this new clinicopathological entity, considering the possibility of this disease as a differential diagnosis of CAA in adults. Radiological screening for any other concurrent cardiovascular involvements is warranted.

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KEY WORDS coronary artery aneurysm, coronary artery calcification, immunoglobulin G4-related disease, left gastric artery aneurysm

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