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Case Report

Isolated Giant Right Coronary Aneurysm Associated With IgG4–Related Disease

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Immunoglobulin-4 (IgG4)-related disease (IgG4-RD) is a multisystem fibroinflammatory disease marked by a dense infiltration of plasma cells that are positive for IgG4 in the affected tissue(s), either with or without increased plasma levels of IgG4. Cardiac manifestations of IgG-RD include periaortitis, aneurysms, luminal thrombus or stenosis, multifocal fibrosclerosis, periarteritis, coronary artery disease, pseudotumours, phlebitis, pulmonary vasculopathy, valvulopathy, pericardial disease, myocardial disease, neurological/cerebrovascular disease, and vasculitis. We report a case of a 60-year-old man who presented with atypical chest pain that led to the diagnosis of giant coronary aneurysm associated with IgG4-RD.

A 60-year-old man with history of hypertension presented with atypical chest pain. Physical examination was unremarkable. Echocardiography showed a large thrombus-filled aneurysm behind the right atrium, with normal biventricular function. Valves were normal, and mild mitral regurgitation was noted. Renal function tests were normal. Urine routine analysis showed trace glycosuria.

Cardiac computerized tomography (CT) with angiography (CTA) revealed a large, partially thrombosed irregular lobulated aneurysm originating in the right coronary artery (RCA) in close proximity to the right atrium, atrial appendage, right atrioventricular groove, and a part of the right ventricle (Fig. 1, A and B). The aneurysm and its distal arteries had reduced flow, which resulted in suboptimal perfusion in the RCA area. Significant periarteritis and periarterial soft tissue enlargement were observed at the proximal RCA and left anterior descending artery (LAD). Moderate pericardial effusion with pericardial thickening was noted as well. CT aortogram and intracranial imaging did not reveal any involvement of intracranial vessels, thoracic, abdominal aorta, or their branches. Invasive coronary angiography showed a large aneurysm arising from the proximal RCA with dye swirling inside, and the distal vessel was not visualised. There was ectasia of the LAD and left circumflex artery. Apart from the giant coronary artery aneurysm, baseline CT showed few small solid enhancing mediastinal lymph nodes.

A panel of laboratory tests were done to rule out inflammatory and infectious etiology including vasculitis. Serum IgG4 levels were markedly elevated at 3530 mg/dL (normal range 2-121 mg/dL). The erythrocyte sedimentation rate was 19 mm/h (normal range 5-15 mm/h). Eosinophil count was normal (4%) and antineutrophilic cytoplasmic antibody was negative. The patient underwent aneurysmal resection (Fig. 1, C and D) with a venous graft to the posterolateral branch of the RCA. Histologic examination of the aneurysmal wall and periarterial tissue specimen revealed dense lymphoid infiltrates with plasmacytosis and foci of phlebitis. Immunohistochemistry demonstrated presence of IgG4/IgG positive plasma cell ratio of 0.76 and 251 IgG4-positive cells per high-power field (HPF) (Fig. 2). The histology with immunochemistry was consistent with diagnosis of IgG4-related disease (IgG4-RD). The patient was discharged on low-dose steroid therapy, extrapolating their effectiveness in noncoronary vascular diseases to reduce further inflammation and prevent aneurysm formation. The eosinophil count was mildly elevated after the surgery (11%). Follow-up CT after 1 year revealed a 10-mm-long thin hypodense lesion in the right lobe of the liver. The left adrenal gland was slightly enlarged and nodular. The patient was asymptomatic, so close follow-up was advised.

Discussion

IgG4-RD is an autoimmune condition that affects almost every organ system and is characterised by an early inflammatory phase followed by fibrotic sequelae. It most commonly presents with inflammation of the salivary and lacrimal glands, pancreatitis, tubulointerstitial nephritis, and retroperitoneal fibrosis.[1] Vascular manifestations, particularly, large-vessel involvement, are well described. However, important

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See page 449 for disclosure information.

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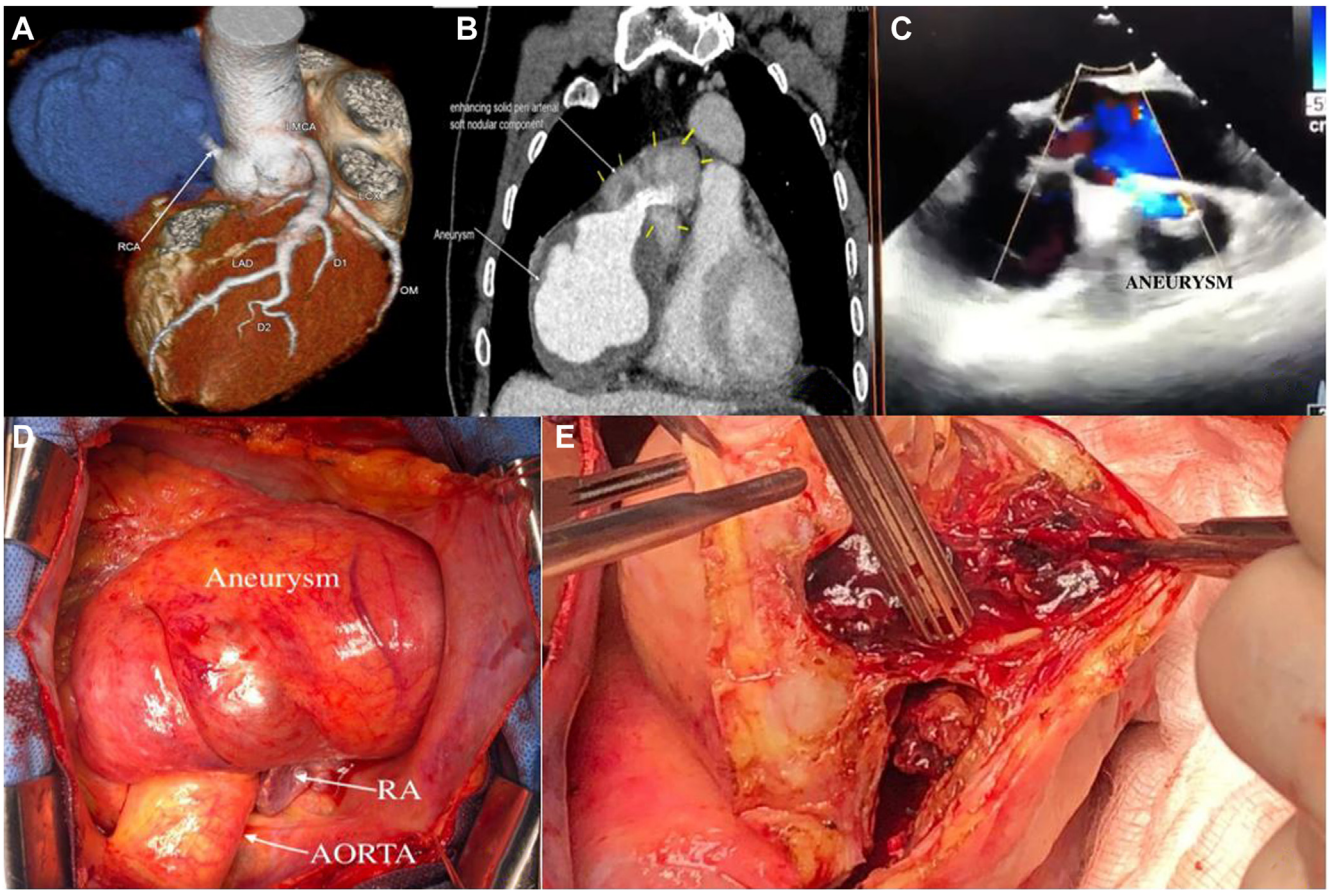

Figure 1. (**A**) Cardiac computed tomographic (CT) three-dimensional volume-rendering image, showing giant aneurysm (**blue**) arising from the proximal right coronary artery (RCA). (**B**) Cardiac CT angiography, showing irregular lobulated thrombosed giant aneurysm and periarterial soft nodular components. (**C**) Intraoperative transesophageal echocardiography, showing flow into the aneurysm. (**D**) Intraoperative image after pericardial reflection, showing giant aneurysm compressing the right atrium (RA). (**E**) Intraoperative image of the opened coronary aneurysm. D1, diagonal artery 1; D2, diagonal artery 2; LMCA, left main coronary artery; OM, obtuse marginal artery.

IgG4-related effects on medium-size arteries and the pericardium are less well recognised.

A comprehensive analysis of the literature found cardiac involvement in 219 cases (140 patients) as of 2019. Out of these, 24 aneurysms were documented in 18 cases.[2] Giant coronary artery aneurysms of > 2 cm in diameter are rare. Patients typically present with angina, myocardial infarction, congestive heart failure, or sudden cardiac death, or with a

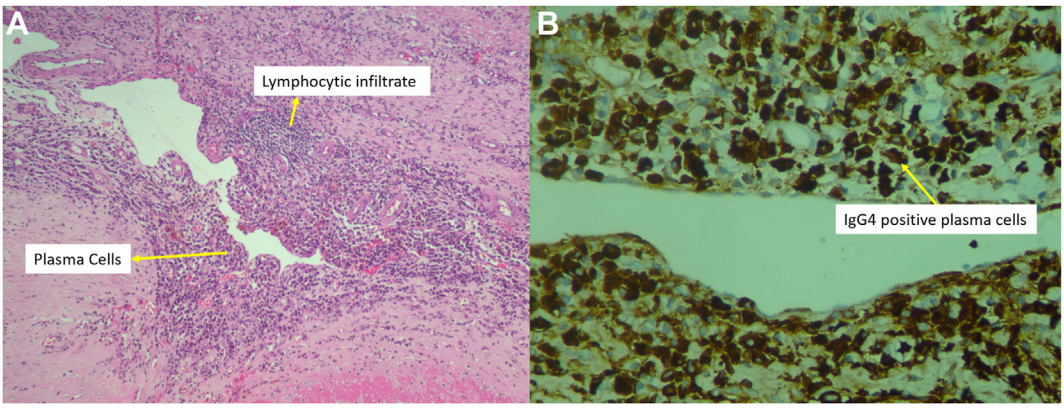

Figure 2. (**A**) Histopathologic examination of periarterial tissue and aneurysmal wall, showing wall of artery with thickened media and dense lymphoplasmacytic infiltrate with phlebitis. (**B**) Immunohistochemistry, demonstrating increased immunoglobulin-4 (IgG4)-positive plasma cells per high power field.

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mediastinal mass having compressive symptoms.[3] The largest aneurysm in the present patient, which involved the RCA, measured 8.5 cm in length and 8.7 cm in diameter. The isolated RCA aneurysm had a compressive impact. In addition, the baseline CT revealed a few small solidly enhanced mediastinal lymph nodes that may have been related to inflammatory response.

Although the range varies greatly, most individuals with IgG4-related diseases have high serum IgG4 concentrations. Our patient had an almost 29-fold increase in serum IgG4 levels. It should be highlighted that tissue or serum IgG4 levels have low specificity for the diagnosis of IgG4-RD, because up to 30% of individuals may have normal levels.[2] The key in the diagnosis of IgG4-related disease continues to be the histopathologic examination of biopsy samples. The primary morphologic characteristics of IgG4-related disease include an obliterative phlebitis, a mild-to-moderate eosinophil infiltrate, and a thick lymphoplasmacytic infiltration structured in a storiform pattern.[4] The arterial samples from our patient painted a similar picture with dense inflammatory infiltration, plasmacytosis, and phlebitis confirming the diagnosis. The diagnosis of IgG4-related aneurysmal change is determined with the use of immunohistochemistry with more than 50% IgG4-positive cells, an IgG4/IgG cell ratio greater than 0.4, and more than 10 IgG4-positive cells per HPF.[5] Our patient had an IgG4/IgG ratio of 0.76 and 251 IgG4-positive cells per HPF. Histopathology of the aneurysmal wall in our patient showed lymphocytic/IgG4 infiltration unlike in Kawasaki disease, which has monocytes/macrophages, thus ruling out the possibility of preexisting Kawasaki disease.

The pathophysiology of IgG4-RD has a waxing and waning pattern during the acute inflammatory phase. Early diagnosis and prompt treatment are essential before the fibrotic phase, which has irreversible adverse consequences. Corticosteroids are the first line of medical treatment for active IgG4-RD. However, there is no consensus regarding optimal management of coronary aneurysms. IgG4-RD is a multisystem inflammatory disease. Pericardial effusion is probably a part of the systemic inflammatory process. Our patient was initiated on steroids after the surgery. Studies on coronary artery aneurysms associated with other disorders have demonstrated the use of covered stents for smaller coronary artery aneurysms and surgery for larger aneurysms (aneurysm resection, aneurysmal thrombectomy, or bypass grafting).[3] Our patient underwent aneurysmal resection along with a venous graft to the posterolateral branch of RCA in view the of compressive effect on the adjacent structures associated with reduced distal perfusion in the RCA territory of the myocardium.

Conclusion

This report describes a novel case wherein a patient developed cardiac symptoms after a protracted asymptomatic period, which resulted in the very unusual diagnosis of IgG4-RD with giant coronary aneurysm with minimal involvement of other organs.

Data Availability

Additional information related to the case report is available from the corresponding author on reasonable request.

Ethics Statement

This is a case report and therefore ethical approval was not required.

Patient Consent

Patient consent was obtained to use deidentified images for publication purpose.

Funding Sources

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Disclosures

The authors have no conflicts of interest to disclose.

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