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Case Report

Enormous Aneurysm in Coronary Artery Fistula With Immunoglobulin G4–Related Disease

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ABSTRACT

We report the first case of coronary artery fistula with aneurysmal change in a patient with immunoglobulin G4–related disease (IgG4-RD). This case revealed concomitant coronary artery dilation, pericardial inflammatory nodules, and coronary–pulmonary fistula aneurysm in addition to several IgG4-RD lesions. Each of these features was located in close proximity to the thickened pericardium. These lesions might result from inflammation of the pericardial space, which extended to the coronary–pulmonary artery vessels, leading to aneurysmal formation. This case will enhance our understanding of the pathological mechanisms of IgG4-RD inflammation.

RÉSUMÉ

Nous rapportons le premier cas de fistule coronarienne accompagnée d'un changement anévrismal chez un patient atteint de la maladie associée aux immunoglobulines G4 (IgG4). L'examen a mis en évidence la présence concomitante d'une dilatation des coronaires, de nodules inflammatoires péricardiques et d'un anévrisme d'une fistule coronaro–pulmonaire, en plus de plusieurs lésions causées par la maladie associée aux IgG4. Chacune de ces anomalies était située à proximité immédiate du péricarde épaissi. Ces lésions pourraient avoir été provoquées par l'inflammation de l'espace péricardique qui se serait propagée au réseau artériel coronaro-pulmonaire, menant à la formation d'un anévrisme. L'étude de ce cas va nous permettre de mieux comprendre les mécanismes pathologiques sous-jacents de l'inflammation observée dans la maladie associée aux IgG4.

A 58-year-old woman with bronchial asthma presented with symptoms of bilateral submandibular gland swelling. Biopsy indicated infiltration of immunoglobulin (Ig)G4-positive plasma cells (IgG4 = 168 cells/high-power field, IgG4/IgG ratio = 69%). Her serum IgG4, IgE, and C-reactive protein levels were persistently elevated (serum IgG4 range, 1540-1970 mg/dL; IgE = 2120 mg/dL; C-reactive protein range, 0.6-1.96 mg/dL). IgG4-related disease (IgG4-RD) was diagnosed in the patient. In addition, she was found to have dacryoadenitis and sialadenitis (Mikulicz disease), paravertebral mass, bilateral pleural thickenings, infrarenal and external iliac aortitis, and retroperitoneal fibrosis, which are known to be associated complications of IgG4-RD. There were no cardiovascular symptoms; however, whole-body computed tomography scan revealed an enormous aneurysm near the left anterior descending artery. Therefore, we performed a detailed examination of all cardiovascular lesions.

Cardiovascular screening revealed a coronary artery fistula from the left anterior descending artery to the main pulmonary artery, part of which exhibited aneurysmal enlargement. The scan also revealed thickening of soft tissue and nodularity of the pericardium in patches, which corresponded to the sites with fluorodeoxyglucose F18 positron emission tomography increased uptake (Fig. 1). Because steroid therapy might carry the risk of aneurysmal rupture by promoting thinning of the aneurysmal wall, we performed a surgical resection of the aneurysmal enlargement of coronary artery fistula before steroid therapy.

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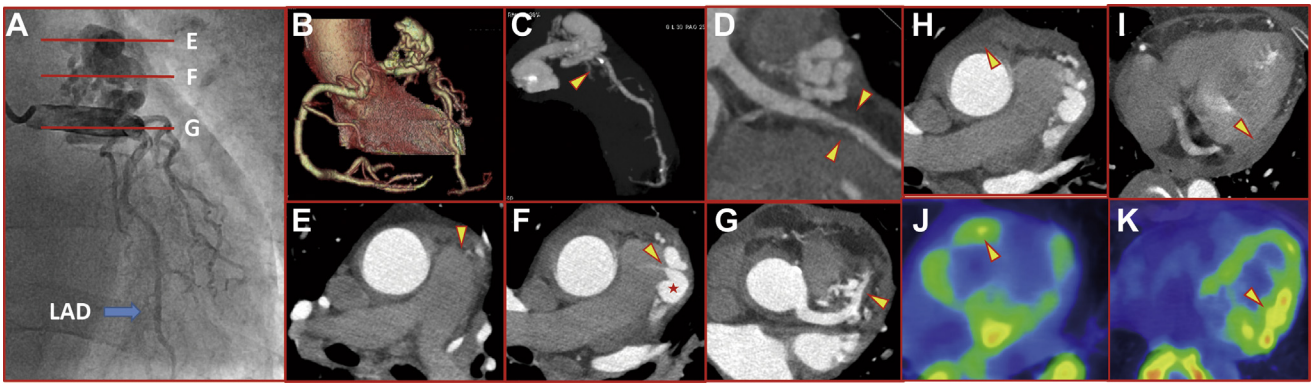

Figure 1. Various images of the coronary artery fistula from the left anterior descending (LAD) artery to the main pulmonary artery were acquired by coronary angiography (**A**). Computed tomography (CT) scan (**B-G**) and fluorodeoxyglucose F18 positron emission tomography are lined up in each corresponding slice (**H-K**). **Arrowhead** in (**C**) indicates calcified plaque and 50% stenosis of the patient's proximal LAD. Detailed analysis of coronary angiography and CT scan images revealed no other atherosclerotic changes in her coronary arteries. **Arrowhead** in (**D**) indicates circumferential mural thickening of the LAD. Axial imaging of the CT scan demonstrates inflow and outflow of the fistula in each corresponding slice (**E-G**). The fistula had a single inflow from the LAD and double outflow to the left pulmonary artery (**E-G**). The **red star** in (**F**) shows the aneurysm. The area of thickened pericardium corresponded to the lesion revealed on fluorodeoxyglucose F18 positron emission tomography with increased uptake (**arrowhead** in **H-K**).

During surgery, many white nodules were observed on the surface of the right ventricle, extending to the aneurysmal lesions of the fistula. Histopathological investigation revealed lymphoplasmacytic infiltrate with IgG4 deposits in the pericardial nodules and resected aneurysmal fistula lesions (Fig. 2). After fistula resection, the patient received prednisolone (0.5 mg/kg), which markedly improved swelling in her bilateral submandibular glands. Her serum IgG4 level decreased to 129 mg/dL, and the prednisolone dosage was reduced to 5 mg/d without IgG4 RD relapse.

Discussion

IgG4-RD is a recently recognized systemic disorder characterized by mass-forming lesions or enlarged organs resulting from infiltration of IgG4-positive plasma cells.[1] The current

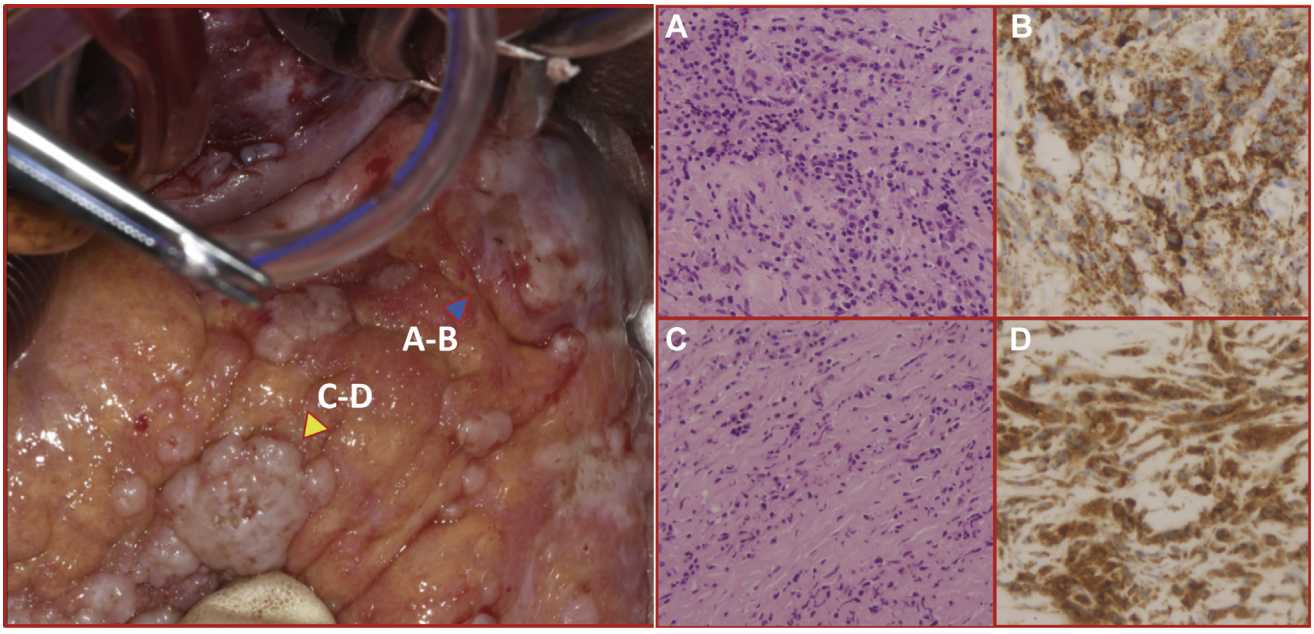

Figure 2. Numerous white nodules (**yellow arrowhead**) were observed on the surface of the patient's right ventricle, with some surrounding the fistula (**blue arrowhead**). Histopathological investigation of the resected coronary pulmonary fistula aneurysm (**A**, **B**) and the resected white nodule located on the surface of pericardium (**C**, **D**). (**A**) Massive lymphoplasmacytic infiltrates were shown mainly in the adventitia side to the middle layer of the vasculature, as demonstrated by hematoxylin–eosin staining. (**B**) Immunohistological analysis using an anti-immunoglobulin (Ig)G4 antibody revealing that most of the infiltrated cells were IgG4-positive plasma cells with IgG4+/IgG+ ratio of 40% to 80%. (**C**) Lymphoplasmacytic infiltrate was observed within the fibroelastic tissue. (**D**) Immunohistological analysis using an anti-IgG4 antibody revealing that most infiltrated cells were IgG4-positive plasma cells with IgG4+/IgG+ ratio greater than 80%.

case did not exhibit any symptoms of cardiac dysfunction; however, an aneurysm of the coronary artery fistula was found during screening in addition to the other IgG4-RD–related complications. Considering the risk of aneurysmal rupture during steroid treatment, surgical resection of the aneurysm was selected before steroid administration.[2]

Coronary artery fistulas are rare congenital or acquired coronary artery anomalies that drain each of the cardiac chambers or great vessels. We believe our patient had a congenital fistula; however, IgG4-RD–associated inflammation spread to the fistula, producing luminal dilatation and aneurysmal changes.

In patients with IgG4-RD, vasculature is commonly affected with the abdominal aorta as the most common site of cardiovascular lesions. Aortic abnormalities comprise some of the pathophysiological effects of IgG4-RD,[3] and a possible role of atherosclerotic plaque in the pathogenesis of IgG4-related periaortitis has been suggested.[4] Similar mechanisms may affect the coronary arteries in patients with IgG4-RD.[5] The pericardium also can be affected by IgG4-RD. Closed cavity spaces, like the retroperitoneal space, seem to be preferred lesion sites for IgG4-RD. In this case, we also observed circumferential mural thickening of the left anterior descending artery, pericardial nodular inflammation, and an aneurysm of the coronary–pulmonary fistula. Each of these features was located in close proximity to the thickened pericardium. These lesions might result from inflammation of the pericardial space, which extended to the coronary–pulmonary artery vessels. This case will enhance our understanding of the pathological mechanisms of IgG4-RD inflammation.

Disclosures

The authors have no conflicts of interest to disclose.

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