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【 CASE REPORT 】

Improvement of Mass Lesions around Coronary Arteries and Fractional Flow Reserve after Steroid Therapy in Immunoglobulin-G4-related Coronary Periarteritis

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Abstract:
Immunoglobulin-G4-related disease (IgG4-RD) is a multi-organ systemic inflammatory disorder. The ideal treatment of coronary artery involvement in IgG4-RD remains uncertain due to its rarity. We herein report a case of coronary artery involvement with IgG4-RD, wherein mass lesions surrounded the coronary arteries with a moderate stenosis lesion in the right coronary artery (RCA). The fractional flow reserve (FFR) of the RCA was 0.76. After steroid therapy, the mass lesions around the coronary arteries improved. The FFR of the RCA also improved from 0.76 to 0.86. These findings suggest the efficacy of using steroid therapy for coronary artery involvement with IgG4-RD.

Key words: Immunoglobulin-G4-related disease, coronary artery, pseudoaneurysm, steroid

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Introduction

Immunoglobulin-G4-related disease (IgG4-RD) is a multi-organ systemic inflammatory disorder characterized by the infiltration of IgG4-positive plasma cells into target organs and, often but not always, elevated serum IgG4 concentrations (1, 2). IgG4-RD was first reported in 2003 (3). In the dataset of 235 consecutive patients with IgG4-RD, Inoue et al. (4) reported that the most commonly involved organ was the pancreas (60%). There were aortic lesions in 20% and arterial lesions in only 4% of cases. In particular, the involvement of IgG4-RD with coronary arteries is rare. IgG4-RD generally responds to steroid therapy. However, the optimal treatment for coronary artery lesions in IgG4-RD remains uncertain.

We herein report a case of coronary artery involvement in IgG4-RD, in which the mass lesions around the coronary arteries and fractional flow reserve (FFR) improved after steroid therapy.

Case Report

A 72-year-old man had a history of ascending aortic replacement due to acute aortic dissection performed 7 years earlier. He was admitted to our institution because of an enlarged pseudoaneurysm at the anastomosis of the ascending aorta with masses surrounding the coronary arteries. He showed no symptoms. Coronary computed tomography angiography (CCTA) showed that the size of the pseudoaneurysm was 80 mm. The soft masses surrounding the left anterior descending artery (LAD) and the right coronary artery (RCA) were 11 and 10 mm in size, respectively (Fig. 1). There was a moderate stenosis lesion with calcification in the distal RCA. No typical findings indicated IgG4-RD in other organs. Laboratory examinations revealed an extremely high serum IgG4 level (879 mg/dL; normal value: 4.5-117 mg/dL). ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography-computed tomography (PET-CT) revealed an uptake in the pseudoaneurysm at the anastomosis of the ascending aorta. There were masses around the LAD and RCA (Fig. 2). Therefore, we suspected that the pseudoaneu-

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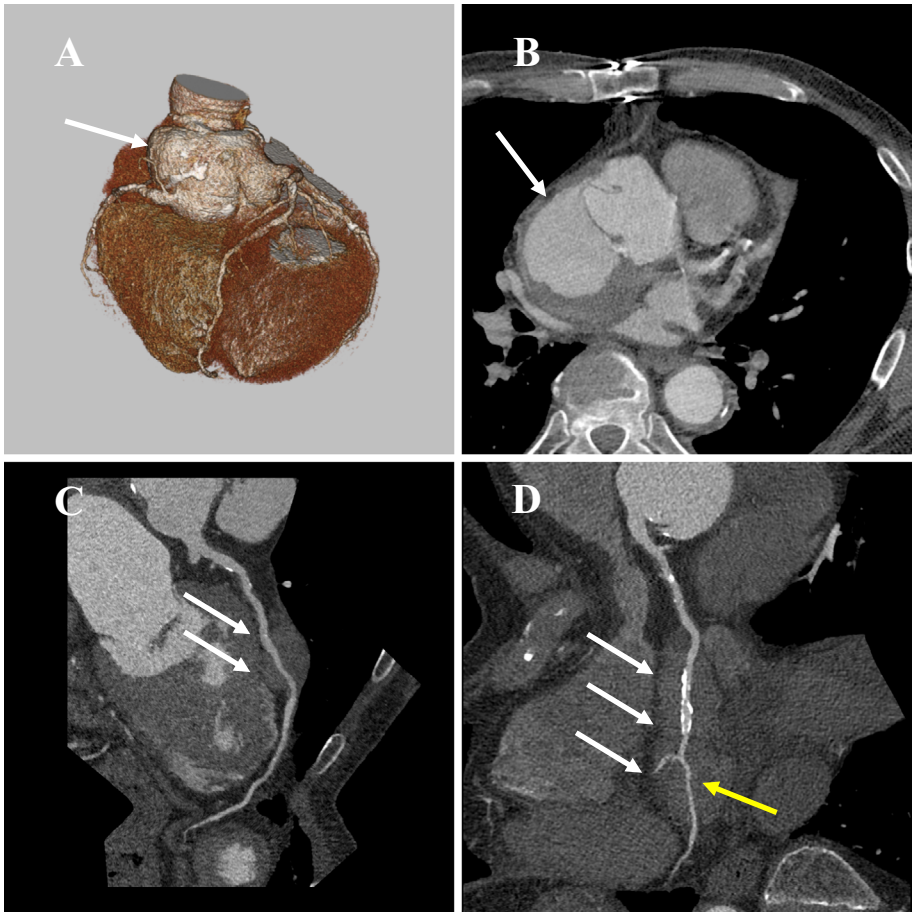

Figure 1. **A: Volume rendering image. The white arrow indicates the pseudoaneurysm at the anastomosis of the ascending aorta. B: Computed tomography short-axis image. The major axis of the pseudoaneurysm was 80 mm. C: Curved planar reformation of the left anterior descending artery (LAD). The white arrows indicate the soft mass surrounding the LAD. D: Curved planar reformation of the right coronary artery (RCA). The white arrows indicate the soft mass surrounding the RCA. The yellow arrow indicates the segment 4 posterolateral branch.**

rysm and soft masses were due to IgG4-RD. Before performing reoperation for the ascending aorta, we conducted coronary angiography (CAG) (Fig. 3), which revealed a mass shadow noted on CCTA around the LAD. However, no significant stenosis appeared in the LAD. There was a moderate stenosis lesion in the RCA, segment 3. The FFR (PressureWire™ X; Abbott Vascular, Abbott Park, USA) of the far distal RCA was 0.76. The FFR values gradually increased toward the proximal end of segment 3, and there was no significant change in the FFR value in RCA segments 1-2. We thus determined that the RCA did not require revascularization before the operation.

We performed the Bentall procedure for the pseudoaneurysm at the anastomosis of the ascending aorta. A pathological examination of the pseudoaneurysm revealed infiltration of IgG4-positive plasma cells. The ratio of IgG4-positive cells/IgG-positive cells was 65%, and the number of IgG4-positive cells was 106/high-power field (HPF). Therefore, we confirmed that the pseudoaneurysm was definitely due to IgG4-RD.

After rehabilitation, the patient received 40 mg/day (0.6 mg/kg/day) of prednisolone, which was reduced gradually and maintained at 5 mg/day. Three months after the initiation of prednisolone, the serum IgG4 level decreased from 879 to 87.5 mg/dL (in the normal range). PET-CT revealed the elimination of the uptake around the ascending aorta and bilateral coronary arteries (Fig. 4). CCTA also demonstrated improvement of mass lesions around the LAD and RCA (Fig. 5). Furthermore, CCTA and CAG revealed slight dilatation, especially at the proximal end of the segment 4 posterolateral branch. The FFR of the RCA improved from 0.76 to 0.86, and the ΔFFR site was similar before and after steroid therapy (Fig. 6).

The patient did not experience chest pain, and there was no relapse of IgG4-RD during an observation period of 12 months.

Discussion

We encountered a case of coronary artery involvement in IgG4-RD, in which the mass lesions around the coronary arteries and FFR improved after steroid therapy. IgG4-RD is a

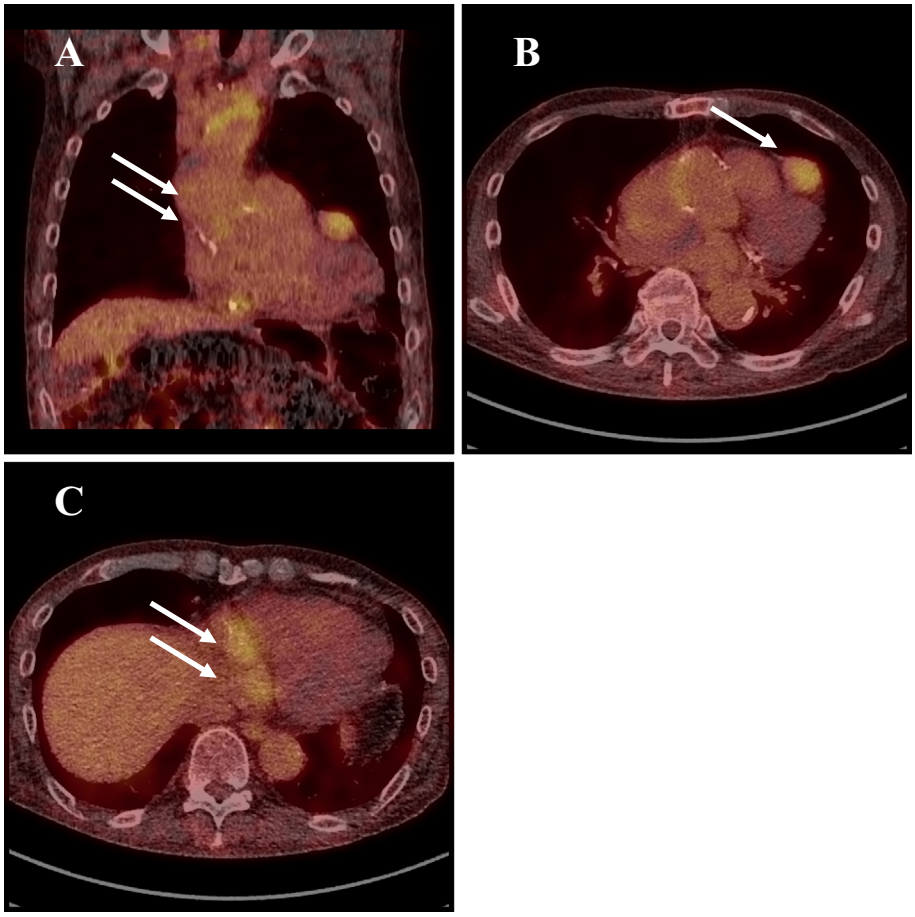

Figure 2. **^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography-computed tomography (PET-CT) revealed an uptake in the pseudoaneurysm at the anastomosis of the ascending aorta (A) and masses around the LAD (B) and RCA (C).**

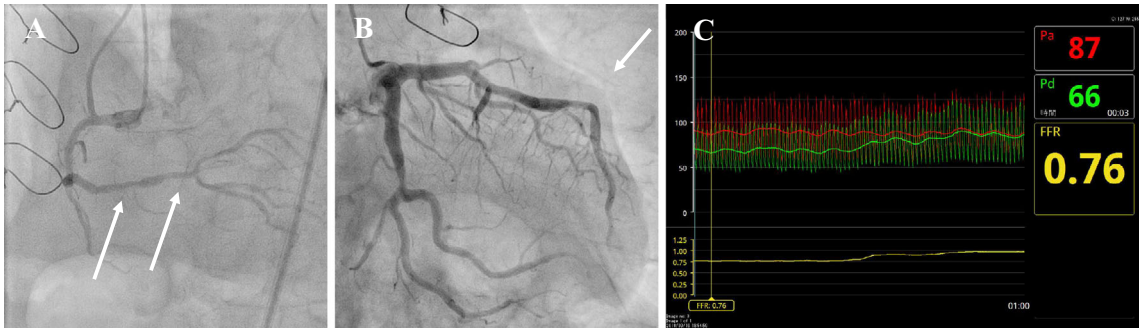

Figure 3. **Coronary angiography (CAG) revealed a moderate stenosis lesion in the RCA, segment 3 (A). CAG also revealed a mass shadow noted on CCTA around LAD (B, white arrow). The fractional flow reserve (FFR) of the far distal RCA was 0.76 (C).**

multi-organ systemic inflammatory disorder (1, 2). The diagnosis of IgG4-RD is based on the comprehensive diagnostic criteria for IgG4-RD, established in 2011 (5) (Table). In the present case, we diagnosed IgG4-RD because the patient met the following criteria: (1) coronary artery swelling and inflammatory aneurysm in the thoracic aorta, (2) elevated serum IgG4 concentrations and (3) infiltration of IgG4-positive plasma cells on a pathological examination of the pseudoaneurysm and the ratio of IgG4-positive cells/IgG-positive cells was 65%, and the number of IgG4-positive cells was 106/HPF. Although several reports (6-29) have described IgG4-related coronary artery involvement, the prevalence and treatment of coronary artery involvement in IgG4-RD remain uncertain. Thickening of the coronary artery walls and soft tissues surrounding the arteries observed as IgG4-positive cells infiltrating the adventitia are reported features of coronary artery involvement in IgG4-RD, resulting in the formation of stenosis (7, 8, 12, 14, 15, 17, 19-24,

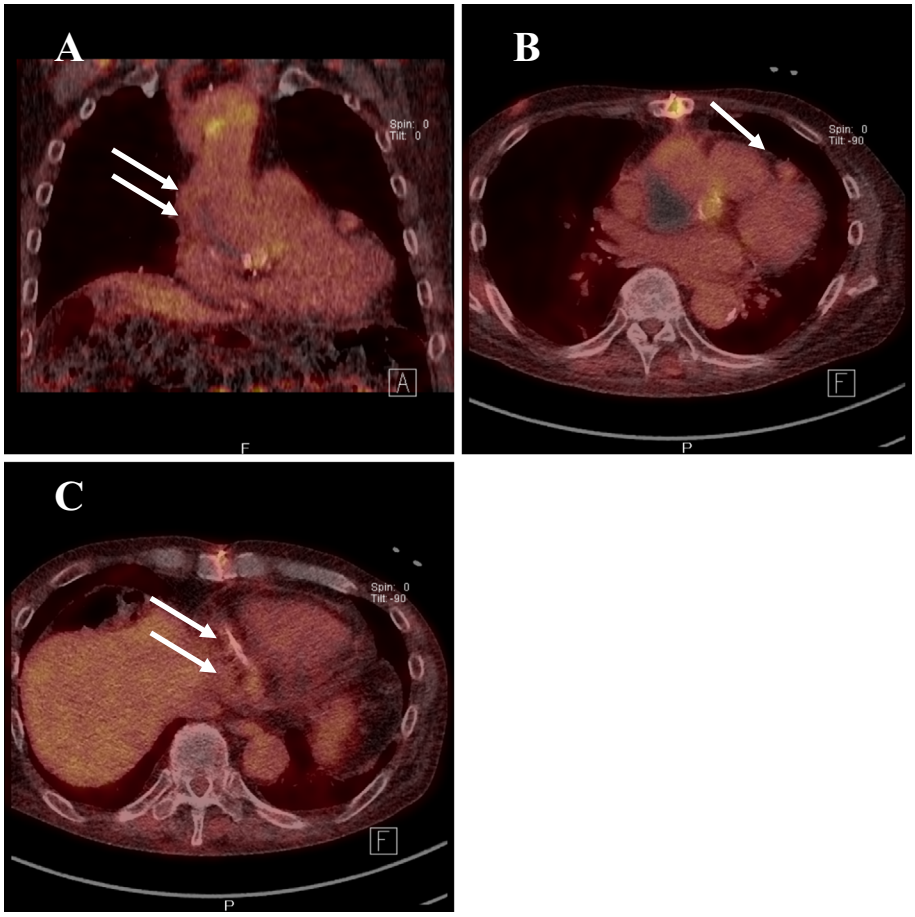

Figure 4. **PET-CT after steroid therapy. PET-CT revealed an improved uptake around the ascending aorta (A) and coronary arteries (B, C).**

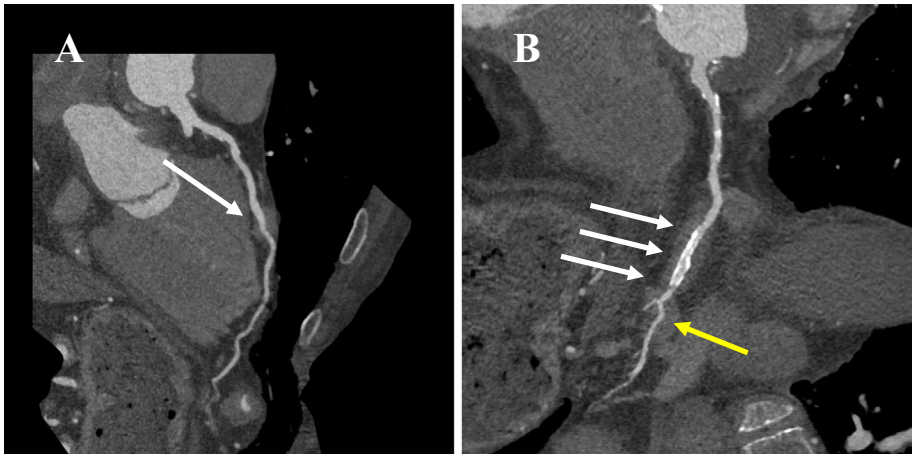

Figure 5. **CCTA after steroid therapy revealed the improvement of mass lesions around the LAD (A) and RCA (B). The yellow arrow indicates the segment 4, posterolateral branch.**

28, 29) and aneurysm (8, 9, 11, 16, 17, 20, 22, 29) in the coronary artery. In some cases, coronary artery involvement in IgG4-RD can lead to an acute coronary syndrome that necessitates percutaneous coronary intervention or coronary artery bypass grafting (8, 12, 19, 22, 24, 26). Although there are no randomized treatment trials, steroids are typically the first-line therapy for IgG4-RD (30). Some reports (10, 17-20, 25, 28, 29) have described steroid therapy as being effective for coronary artery involvement in IgG4-RD. There was an improvement in the thickening of the coronary artery walls and soft tissues surrounding the arteries. The mechanisms underlying coronary stenosis at the site of IgG4-related coronary involvement have not been completely elucidated. However, Sakamoto et al. reported that increased

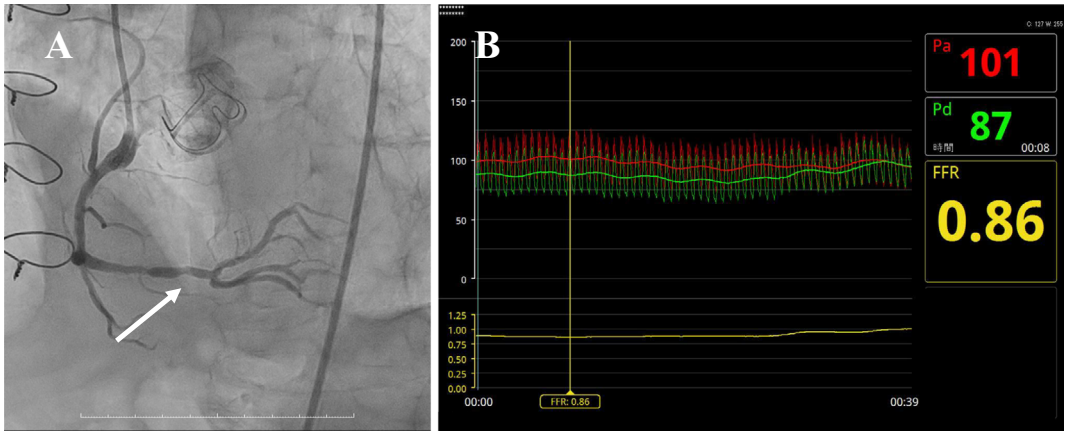

Figure 6. **CAG of the RCA showed no change from pre-steroid-therapy (A), but the FFR of the RCA far distal increased to 0.86 (B).**

Table. **Comprehensive Diagnostic Criteria for IgG4-related Disease (IgG4-RD), 2011 (5).**

(1) Clinical examination shows characteristic diffuse/localized swelling or masses in single or multiple organs.
(2) Hematological examination shows elevated serum IgG4 concentrations (≥135 mg/dL).
(3) Histopathologic examination shows; (1) marked lymphocyte and plasmacyte infiltration and fibrosis (2) infiltration of IgG4-positive plasma cells: ratio of IgG4/IgG positive cells > 40% and > 10 IgG4-positive plasma cells/HPF.
Definite: (1) + (2) + (3), Probable: (1) + (3), Possible: (1) + (2)

serum IgG4 concentrations were significantly associated with coronary artery disease, independent of traditional cardiovascular risk factors (31). They hypothesized that IgG4-related immune-inflammation plays a certain role in the development of luminal stenosis and coronary periarteritis.

In the present case, CAG revealed slight dilatation of the distal RCA, and the FFR of the RCA improved after steroid therapy. The FFR is an invasive index of the functional severity of stenosis determined from the coronary pressure during cardiac catheterization. It represents the maximum achievable blood flow to the myocardium supplied by a stenotic artery as a fraction of the normal maximum flow. An FFR value of ≤0.75 (i.e. a decrease in maximal blood flow of ≥25% due to stenosis) indicates the potential of stenosis to induce myocardial ischemia (32, 33). In our case, the FFR of the RCA was 0.76 before the operation. After steroid therapy, the mass lesions around the RCA improved and the FFR of the RCA also improved from 0.76 to 0.86. These findings suggest that mechanical compression by adventitial thickening due to coronary artery involvement in IgG4-RD affects blood flow, or steroid therapy improved the microvascular dysfunction in IgG4-RD.

The indication of steroid therapy for IgG4-RD such us autoimmune pancreatitis and sclerosing cholangitis has been established. However, the indication of steroid therapy for only coronary periarteritis without significant stenosis is uncertain. Our case suggests that coronary periarteritis with IgG4-RD decreases coronary flow by coronary compression. In fact, Deepak et al. (34) reported ST-segment elevation myocardial infarction due to coronary artery compression by cardiac sarcoma. Steroid therapy may improve the coronary flow by improving the coronary compression induced by coronary periarteritis or microvascular dysfunction. Therefore, in patients with IgG4-related coronary periarteritis, intervention for coronary stenosis may be, if clinically stable, deffered depending on the response to steroid therapy.

One limitation associated with the present study is that we were unable to conduct a pathological analysis of the mass lesions around the coronary arteries. It is often difficult to obtain samples of coronary artery tissue. We diagnosed this case with IgG4-RD based on serum IgG4 elevation and a pathological analysis of the pseudoaneurysm. CCTA and PET-CT findings of the coronary artery were also similar to those in previous reports of IgG4-related coronary involvement. Further research is necessary to establish an accurate diagnosis of IgG4-related coronary involvement. The lack of a coronary microcirculation assessment, such as the index of microvascular resistance or coronary flow reserve, is also a limitation of this case report. The FFR is influenced by many factors, and a careful assessment is needed. Intravascular imaging, e.g. intravascular ultrasound, might also aid in evaluating IgG4-related coronary involvement.

In conclusion, steroid therapy was effective for coronary artery involvement in IgG4-RD, and it may improve coronary flow by reducing the masses around arteries or the microvascular dysfunction.

The authors state that they have no Conflict of Interest (COI).

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