Multiple Coronary Artery Aneurysms and Thoracic Aortitis Associated with IgG4-related Disease

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Abstract

A 60-year-old man was admitted due to the onset of right coronary artery (RCA) aneurysms. Coronary angiography showed two RCA aneurysms and focal stenosis with limitations in the blood flow. Balloon angioplasty was performed. However, the follow-up coronary angiography showed restenosis, an enlarged proximal aneurysm and a newly formed aneurysm. The serum immunoglobulin G4 level was elevated to 1,350 mg/dL and fluorodeoxyglucose positron emission tomography showed increased uptake in the ascending aorta, so the patient was diagnosed with immunoglobulin G4-related vascular disease. The prevention of further enlargement of the aneurysms and an improvement in the RCA flow were achieved with steroid therapy. Steroid therapy may therefore be effective for immunoglobulin G4-related vascular disease.

Key words: immunoglobulin G4-related disease, coronary artery aneurysm, steroid, aortitis, vascular disease

(intern med 55: 1605-1609, 2016)
(DOI: 10.2169/internalmedicine.55.6314)

Introduction

Immunoglobulin G4-related disease (IgG4RD) is a systemic inflammatory disease that is characterized by the elevation of serum IgG4 levels and IgG4-positive plasmacyte infiltration in tissues (1). It is common in middle-aged or older men (2) and may affect various organs, such as the pancreas (3), biliary tree (4), salivary glands (5) and retroperitoneum (6) either synchronously or metachronously. Recently, IgG4RD has been recognized as one of the causes of vascular disease (7, 8), but the optimal treatment strategy for IgG4-related vascular disease remains unclear.

We herein report a case of IgG4-related multiple coronary artery aneurysms and ascending aortitis that was treated with a steroid.

Case Report

A 60-year-old man was admitted to our hospital for recurrent cerebral infarction. At 59 years of age, he suffered a cerebral infarction, showing right hemiplegia, and antiplatelet drug therapy was started. A few months after the first episode, a second cerebral infarction occurred despite administering appropriate antiplatelet therapy. On admission, magnetic resonance angiography showed a stenotic lesion of the left middle cerebral artery and stenotic and dilated lesions of the right middle cerebral artery (Fig. 1). An electrocardiogram showed a sinus rhythm and no significant ST-T change. However, transthoracic echocardiography showed mild hypokinesis in the inferior region and an aneurysm of the right coronary artery (RCA) ostium, with a diameter of 9 mm. Contrast-enhanced coronary computed tomographic angiography (CCTA) showed multiple RCA aneurysms with a maximum minor axis diameter of 11 mm, and a diffusely dilated left coronary artery, and there were no tumorous lesions surrounding the coronary artery. Therefore, he was referred to our department.

He had no history of Kawasaki disease, autoimmune disease or allergy. Laboratory data showed the following: a C-
nary angiography and CCTA were performed, although the patient was observed without administering steroid therapy. Therefore, we decided to elevate serum IgG4 levels and erythrocyte sedimentation rate might have been IgG4-related vascular disease due to the cause of the coronary artery aneurysms and coronary flow improved to TIMI grade 3 (Fig. 2b). We considered that the cause of the recanalized lesion which developed after thrombotic occlusion.

Coronary angiography also showed two RCA aneurysms and focal stenosis between these two aneurysms with a limitation of the blood flow [thrombolysis in myocardial infarction (TIMI) grade 2] (Fig. 2a). The left coronary artery was diffusely ectatic, without a coronary fistula. Optical coherence tomography showed the presence of aneurysms in the proximal RCA and a lotus root-like appearance with multiple channels at the focal stenosis in the mid-RCA (Fig. 3). This was considered to be a recanalized lesion which developed after thrombotic occlusion.

We performed balloon angioplasty for the RCA, and the coronary flow improved to TIMI grade 3 (Fig. 2b). We considered that the cause of the coronary artery aneurysms and stenosis might have been IgG4-related vascular disease due to elevated serum IgG4 levels and erythrocyte sedimentation rate. However, contrast-enhanced computed tomography did not show any other invasive lesions. Therefore, we decided to observe the patient without administering steroid therapy.

Two years after the balloon angioplasty, follow-up coronary angiography and CCTA were performed, although the patient had no chest pain. The proximal aneurysm had become larger during this period. An intraluminal thrombus had formed in the distal aneurysm. Therefore, the distal aneurysm appeared to have angiographically disappeared. Furthermore, an aneurysm had newly developed at the distal site of the previous balloon dilation site and restenosis was detected with a TIMI 2 flow (Fig. 2c). Moreover, during the follow-up, the patient suffered recurrent cerebral infarctions twice, despite the administration of antiplatelet and anticoagulant drug therapies.

Fluorodeoxyglucose positron emission tomography (FDG-PET) showed an increased uptake in the ascending aorta, as well as the salivary glands and pancreas (Fig. 4a-c).

Therefore, IgG4-related vascular disease, including the coronary artery and the ascending aorta, was clinically diagnosed using the laboratory data, FDG-PET findings and chronological changes in coronary artery aneurysms, although contrast-enhanced computed tomography did not show aneurysmal formation or wall thickening in the ascending aorta.

We decided to treat this patient with a steroid, without either additional percutaneous coronary intervention or cardiac surgery, despite limitations in the blood flow. This is because he was asymptomatic and the previous balloon angioplasty might have caused the formation of a new aneurysm. Moreover, there was also a possibility that a saphenous vein graft might detach from an inflammatory ascending aorta, and the coronary artery aneurysm was not large enough to be indicated for surgical intervention. Steroid therapy was started with prednisolone at 20 mg per day, which was tapered to 10 mg per day for six months.

During the one-year follow-up with steroid therapy, he did not experience any cerebral infarctions again and his neurological symptoms also dramatically recovered, thus allowing him to return to his daily life without disability. The serum IgG4 levels decreased from 1,350 mg/dL to 187 mg/dL and the erythrocyte sedimentation rate at 1 hour decreased from 100 mm to 12 mm. Follow-up coronary angiography and CCTA showed that the flow of the RCA considerably improved to TIMI grade 3, and the sizes of the proximal and distal RCA aneurysms had not enlarged (Fig. 2d). FDG-PET also demonstrated a reduction in the uptake in the ascending aorta and pancreas (Fig. 4d, e). Steroid therapy was considered to be effective for IgG4-related vascular disease. Therefore, the patient is currently receiving oral treatment with prednisolone at a dose of 10 mg per day.

Discussion

We herein present a rare case of IgG4-related vascular disease including the coronary artery and the thoracic aorta. Currently, IgG4RD is recognized as one of the causes of vasculitis, and aneurysmal formation is thought to be the principle feature of IgG4-related vascular disease (9). In our case, not only aneurysmal formation but also stenotic lesions were observed, and these were thought to be uncommon. Patel et al. (10) reported sudden cardiac death due to coronary artery involvement by IgG4RD, and the coronary artery showed luminal stenosis due to encasement and transmural infiltration by plasmacytes. In the present case, transmural infiltration, in combination with concomitant atherothrombosis, might have resulted in severe stenosis of the coronary artery.

Figure 1. Magnetic resonance angiography on admission. Magnetic resonance angiography showed stenotic (white solid arrow) and dilated (white dotted arrow) lesions of the right middle cerebral artery and a stenotic lesion of the left middle cerebral artery (white arrowhead).
IgG4-related vascular disease can occur at multiple sites including the coronary artery, but histological findings are often difficult to obtain in clinical settings. Matsumoto et al. (11) reported IgG4-related periarteritis presenting with an aneurysmal lesion of the coronary artery and abdominal aorta. Tanigawa et al. (12) reported a patient with myocardial infarction who was found to have focal stenosis in the left circumflex branch and increased serum IgG4 levels. In both previous cases, cardiac surgery was performed. Therefore, histological findings were obtained. On the other hand, a prospective cohort study reported the utility of FDG-PET in IgG4RD (13). FDG-PET is considered to be a useful tool for assessing organ involvement and monitoring the therapeutic response (13, 14). In our case, the coronary artery aneurysms were not large enough to warrant surgical intervention. Thus, the FDG-PET findings contributed to the diagnosis of IgG4-related vascular disease.

The optimal therapeutic approach for IgG4-related vascular disease has not yet been clearly established. Steroid therapy is considered to be the first-line treatment for it (15). This therapy is expected to prevent the further development of vascular lesions by reducing inflammation with the suppression of lymphocyte activation. A retrospective, multicenter study showed that steroid therapy prevented new aneurysmal formation, but it could not heal any aneurysms that had already developed (15). Furthermore, in patients with IgG4-related vascular disease, the infiltration of IgG4-positive plasmacytes is sometimes involved in the intima (10). The inflammation may cause endothelial dysfunction. It leads to a reduction in the release of nitric oxide and the induction of ischemia (16). A previous study reported that endothelial dysfunction in patients with vasculitis improved after the suppression of inflammation (17). In the present case, an aneurysm newly developed at the distal site of the balloon angioplasty and restenosis in the mid-RCA with a limited blood flow (TIMI grade 2) occurred (white solid arrow). (d) One year after the steroid therapy, the size of the aneurysms remained unchanged and the RCA flow improved to TIMI grade 3.

Figure 2. Serial changes in right coronary artery (RCA) angiography and contrast-enhanced coronary computed tomography angiography (CCTA). (a) In initial coronary artery angiography and CCTA, two aneurysms and focal stenosis (white solid arrow) between these two aneurysms, with a limited blood flow [thrombolysis in myocardial infarction (TIMI) grade 2] (white dotted arrow), could be seen. (b) Just after the balloon angioplasty, an improvement in the RCA flow (TIMI grade 3) was observed. (c) Two years after the balloon angioplasty, the size of the proximal aneurysm increased and the distal aneurysm seemed to disappear angiographically because of the intraluminal formation of a thrombus. However, a new aneurysm developed at the distal site of the previous balloon dilation site (white dotted arrow), and restenosis in the mid-RCA with a limited blood flow (TIMI grade 2) occurred (white solid arrow).
Figure 3. Optical coherence tomography. (a) A coronary artery aneurysm could be seen at the proximal right coronary artery (RCA). (b) At the site of focal stenosis between the two aneurysms, a lotus root-like appearance with multiple channels could be seen.

Figure 4. Fluorodeoxyglucose positron emission tomography. An increased uptake (white solid arrows) in the salivary glands (a), ascending aorta (b) and pancreas (c) could be seen. One year after the steroid therapy, a reduction in the uptake (white dotted arrows) in the ascending aorta and pancreas (d, e) could be seen.
There are no reports on IgG4-related cerebral infarction. In our case, magnetic resonance angiography showed stenotic and dilated lesions of the middle cerebral artery. We could not clarify whether these invaded lesions were associated with IgG4-related vascular disease or not because FDG uptake in the brain was shown physiologically. However, our patient never suffered a cerebral infarction and his basic activities of daily living were greatly improved after the steroid therapy. Therefore, there is a possibility that the recurrent cerebral infarctions were associated with IgG4-related vascular disease and the steroid therapy was effective for preventing the further recurrence of cerebral infarction.

In patients with IgG4-related vascular disease, a pathological specimen is often difficult to obtain in clinical settings. In our case, the FDG-PET findings were helpful for making a diagnosis and for monitoring the therapeutic effect after the steroid therapy. Therefore, FDG-PET is considered to be a useful method for the diagnosis, and steroid therapy should be considered as an alternative treatment to surgical intervention in patients with IgG4-related vascular disease.

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

References