CASE REPORT

Immunoglobulin G4-related Coronary Periarteritis and Luminal Stenosis in a Patient with a History of Autoimmune Pancreatitis

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Abstract:
Immunoglobulin G4 (IgG4)-related disease is a systemic inflammatory disorder that was first described in patients with autoimmune pancreatitis. Although IgG4-related disease is thought to involve the cardiovascular system, case reports describing coronary artery involvement are relatively rare. We describe a patient who was previously diagnosed with autoimmune pancreatitis and found to have coronary periarteritis and luminal narrowing. After the initiation of steroid treatment, the patient’s coronary periarteritis and luminal stenosis were both ameliorated with an improvement in the serum IgG4 concentration. The present findings collectively suggest that IgG4-related immuno-inflammation may have a role in the development of coronary periarteritis and luminal atherosclerosis.

Key words: IgG4, coronary periarteritis, coronary artery stenosis, atherosclerosis

(Intern Med 56: 2445-2450, 2017)
(DOI: 10.2169/internalmedicine.8259-16)

Introduction

Immunoglobulin G4 (IgG4)-related disease is a newly proposed systemic inflammatory disorder that is characterized by the infiltration of IgG4-positive plasma cells, diffuse fibrosis, and often, but not always, an increased serum IgG4 concentration (1, 2). Since IgG4-related disease was first reported in patients with autoimmune pancreatitis (3), similar clinicopathological conditions have been identified in various organs, including the lung, kidney, and thyroid (4-6). In addition, it has been recently suggested that IgG4-related disease may involve the cardiovascular system (7, 8). Although IgG4-related perivascular immuno-inflammation has been observed not only in large vessels but also in smaller vessels, including the coronary arteries (9, 10), the association of IgG4-related disease with coronary periarteritis and coronary luminal narrowing has not been fully demonstrated. We herein describe a case of coronary periarteritis at the site of coronary artery stenosis in a patient who was previously diagnosed with autoimmune pancreatitis. The initiation of steroid treatment resulted in the improvement of the patient’s coronary artery lesions.

Case Report

A 67-year-old Japanese man was referred to the Department of Cardiovascular Medicine to undergo assessment for an abnormal electrocardiogram (ECG) prior to orthopedic surgery. He had been diagnosed with autoimmune pancreatitis at 58 years of age based on abdominal computed tomography (CT) images showing a diffusely enlarged pancreas, endoscopic retrograde cholangiopancreatography (ERCP) images showing the irregular narrowing of the main pancreatic duct, and an elevated serum IgG4 concentration (481 mg/dL). Extrapancreatic lesions, which may be associated with IgG4-related disease, were not detected. Oral steroid therapy (prednisolone, 30 mg/day) was initiated, and then tapered off when the patient was 65 years of age as he showed clinical im-

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Received: September 12, 2016; Accepted: February 9, 2017; Advance Publication by J-STAGE: August 21, 2017
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The treatment of coronary periarteritis. The patient continued the recurrence prevention of autoimmune pancreatitis and assumed for management of IgG4-related disease, including expected, steroid treatment (prednisolone, 25 mg/day) was re-examined 4 months after the initiation of steroid therapy, coronary CT angiography showed both a resolution of the coronary stenosis of the LAD and a reduction in the volume of soft tissue with a thickness of 2 to 3 mm (Fig. 4A, D, G). When the steroid dose was tapered to 5 mg/day, however, the patient’s serum IgG4 concentration became elevated again (116 mg/dL) and coronary periarteritis of the LAD (thickness, 3 - 4 mm) was found to have worsened by coronary CT angiography. The luminal narrowing was also found to have slightly progressed (Fig. 4B, E, H). After the dose of steroid was increased to 7.5 mg/day, an improvement in both the serum IgG4 concentration (73.9 mg/dL) and the coronary CT angiography findings (Fig. 4C, F, I) was observed. The thickness of soft tissue around the LAD was 1 to 2 mm. The patient has remained under observation at a steroid dose of 7.5 mg/day without apparent changes in his coronary artery lesions or the development of new lesions in other organs.

Discussion

We described the case of a patient with a history of autoimmune pancreatitis who presented with coronary periarteritis around a coronary luminal stenotic lesion, and showed that both of these coronary artery findings improved after the initiation of steroid treatment.

IgG4, which is the least common of the four subclasses of IgG, may contribute to certain immune-mediated conditions (1). In 2009 in Japan, the total number of patients with IgG4-related disease, such as autoimmune pancreatitis and Mikulicz’s disease, was reported to be approximately 8,000, indicating that IgG4-related disease is not such a rare disease (12). Furthermore, several recent reports have shown that IgG4-related disease can involve the cardiovascular system; however, IgG4-related cardiovascular disorders remain relatively uncommon among patients with IgG4-related disease. For example, a case of inflammatory abdominal aortic periarteritis could not be demonstrated (13). As the relapse of IgG4-related disease was suspected, betablockers (AUC, 31% per day) were resumed for management of IgG4-related disease, including the recurrence prevention of autoimmune pancreatitis and the treatment of coronary periarteritis. The patient continued to receive drug therapy without coronary intervention, because invasive coronary angiography, which was performed 1 week after the reinstatement of steroid treatment, showed moderate, but not severe, stenosis of the LAD (Fig. 3E, F).

The steroid treatment was effective and the patient’s laboratory data gradually improved (C-reactive protein, 0.19 mg/dL; IgG, 1,132 mg/dL; IgG4, 88.3 mg/dL). Furthermore, at 4 months after the initiation of steroid therapy, coronary CT angiography showed both a resolution of the coronary stenosis of the LAD and a reduction in the volume of soft tissue with a thickness of 2 to 3 mm (Fig. 4A, D, G). When the steroid dose was tapered to 5 mg/day, however, the patient’s serum IgG4 concentration became elevated again (116 mg/dL) and coronary periarteritis of the LAD (thickness, 3 - 4 mm) was found to have worsened by coronary CT angiography. The luminal narrowing was also found to have slightly progressed (Fig. 4B, E, H). After the dose of steroid was increased to 7.5 mg/day, an improvement in both the serum IgG4 concentration (73.9 mg/dL) and the coronary CT angiography findings (Fig. 4C, F, I) was observed. The thickness of soft tissue around the LAD was 1 to 2 mm. The patient has remained under observation at a steroid dose of 7.5 mg/day without apparent changes in his coronary artery lesions or the development of new lesions in other organs.

Figs. 1 and 2. Abdominal contrast-enhanced computed tomography image showing no evidence of an enlarged pancreatitis, periarteritis soft tissue, or aortic dilation.

Figure 1. An electrocardiogram at the time of admission. A slight ST segment depression was observed in leads II, aVF, and V5-6.
tery lesions caused by IgG4-related disease have been re-
cases of sudden cardiac death in patients with coronary ar-
acute coronary syndrome, coronary periarteritis, in the lesion
nosed with IgG4-related disease (17, 18). In a case of
arteritis and/or aneurysms has been identified in patients di-
around the patient’s coronary and abdominal arteries. Fur-
the coronary arteries and the abdominal aorta who was diag-
nosed with IgG4-related disease by a needle biopsy of a
specimen (15) and a patient with mass lesions surrounding
the coronary arteries who was diagnosed as having IgG4-
related periaortitis (23, 24). Castelein et al. recently raised the pos-
sibility that the reaction of IgG4 autoantibodies against anti-
gens in intimal atherosclerotic plaques might cause IgG4-
related periaortitis (25). In our previous analyses, we found
that, among patients who underwent invasive coronary angi-
ography, the serum IgG4 concentrations of patients with
CAD were significantly higher than those without
CAD (26). Additionally, by analyzing the data from patients
who underwent coronary CT angiography, the serum IgG4
concentrations of patients with low-density coronary plaques
were found to be significantly elevated in comparison to
those without low-density coronary plaques (27). In both
analyses, increased serum IgG4 concentrations had a signifi-
cant association with CAD or low-density coronary plaques,
independent of traditional cardiovascular risk factors, even
though the serum IgG4 concentrations did not exceed the
upper normal limit. These findings may partly explain why
the coronary artery lesions of the patient in the present case
worsened again without a marked elevation in the patient’s
serum IgG4 concentration. Careful follow-up may be re-
quired in patients with IgG4-related cardiovascular lesions,
even when their serum IgG4 concentrations are maintained to within almost normal limits.

The mechanisms underlying luminal narrowing at the site of IgG4-related coronary periarteritis have not been fully elucidated. On the one hand, intimal inflammation is increasingly recognized to be cross-linked to a distinct inflammatory reaction in the adjacent adventitia (28). Epicardial adipose tissue, which is a source of various inflammatory mediators surrounding the coronary arteries, may have paracrine effects on coronary atherogenesis (29, 30). We previously demonstrated that elevated serum IgG4 concentrations were significantly associated with an increased epicardial fat volume in patients who underwent coronary CT angiography (31). Taken together, we hypothesize that IgG4-related immuno-inflammation may, at least in part, play a certain role in the development of luminal stenosis as well as coronary periarteritis. On the other hand, among patients with IgG4-related vascular disorders, it was reported that luminal stenosis of the LAD may not have had a close association with the ECG findings, which were recognized as almost nonspecific ST changes. It can be considered fortuitous that coronary periarteritis was found during the assessment of the ECG findings. Patients with coronary periarteritis and/or aneurysms are frequently asymptomatic, and recent developments and the spread of various imaging techniques have increased the number of IgG4-related cardiovascular lesions that are detected by chance (18, 33). As multiple organ involvement is often identified in patients with IgG4-related disease (32, 34), other organ lesions, including lesions of the coronary arteries, should not be overlooked.

Coronary periarteritis at the site of luminal narrowing in the present case was recognized as IgG4-related based on the coronary CT angiography images, the elevated serum IgG4 concentration, the effects of steroid treatment, and the
patient’s history of autoimmune pancreatitis. However, pathological and immunohistochemical analyses were not performed, because the coronary artery findings were managed by drug therapy and surgery was not performed. Thus, we could not demonstrate the infiltration of IgG4-positive plasma cells in the coronary artery lesions, which may be a limitation of this report. In comparison to other organs, it is often difficult to obtain samples of vascular tissues, such as coronary artery tissue, for histological examination (18, 25); therefore, clinical features that are useful for the diagnosis of IgG4-related periarteritis, such as serum biomarkers and imaging findings, should be established. On the other hand, as the clinical characteristics of patients with chronic periarteritis, including inflammatory abdominal aortic aneurysm and retroperitoneal fibrosis, are frequently similar in patients with IgG4-related and non-IgG4-related disease (2, 7, 8), the histological analysis of other organs may be necessary to make an accurate diagnosis of IgG4-related cardiovascular disorder.

In summary, we have described a case of coronary periarteritis and luminal stenosis in a patient who was previously diagnosed with autoimmune pancreatitis, suggesting the cardiovascular involvement of IgG4-related disease. To our knowledge, this is the first detailed case report to demonstrate an improvement in coronary artery lesions, including both periarteritis and luminal narrowing, after the initiation of steroid treatment. Further studies will be needed to determine the appropriate management of IgG4-related cardiovascular disease.

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

Acknowledgement

We are appreciative of Dr. Kouhei Kamiya for his comments on the preparation of the curved multiplanar reformatted images in this report.

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