Internal Medicine
The Japanese Society of Internal Medicine
doi: 10.2169/internalmedicine.9017-17
Intern Med 56: 2385-2386, 2017
http://internmed.jp

【 EDITORIAL 】

IgG4-related Coronary Periarteritis - In Search of an Optimal Diagnosis and Management Method

Koichi Sohmiya and Nobukazu Ishizaka

Key words: IgG4-related coronary periarteritis, diagnosis, steroid therapy, luminal narrowing

(Intern Med 56: 2385-2386, 2017)
(DOI: 10.2169/internalmedicine.9017-17)

Immunoglobulin G4 (IgG4)-related disease is an immune-mediated fibroinflammatory condition that can affect various organs, including the pancreas, lacrimal and salivary glands, thyroid, kidney, and lung (1). IgG4-related disease can cause formation of tumefactive and tissue-destructive lesions, which might present as visible organ swelling or functional impairment. The cardiovascular system is also a target of IgG4-related disease, which may be diagnosed incidentally or based on the cardiovascular symptoms (1, 2).

In Japan, at present, for the definitive diagnosis of IgG4-related disease in the cardiovascular system, both clinical and histopathological findings - namely, elevation of serum IgG4 levels and tissue infiltration of IgG4-positive cells - should be demonstrated. Although potential risks due to sampling cardiovascular tissue with suspected disease may represent a diagnostic hurdle, it is reasonable to assume that the concomitant presence or a history of definitive IgG4-related disease in other tissues or organs will substantially strengthen the likelihood that IgG4-related disease is involved in the cardiovascular system.

In this issue of *Internal Medicine*, Sakamoto et al. reported a patient who showed coronary periarteritis during a follow-up examination for autoimmune pancreatitis, which is a pancreatic manifestation of IgG4-related disease (3). Of note, they showed that restarting corticosteroid therapy ameliorated not only the periarterial thickening but also luminal narrowing of the affected coronary arteries. The beneficial effects of steroid therapy on IgG4-related coronary periarteritis have also been reported by other investigators (4); however, for several reasons, it seems that more detailed discussions are needed before steroid treatment can be regarded as a therapeutic option for IgG4-related coronary periarteritis.

First, the mechanism underlying the effectiveness of steroid therapy remains unclear. For example, whether or not steroid treatment led to plaque regression and, if so, whether or not the coronary plaque had massive infiltration of inflammatory cells, including IgG4-positive plasma cells, should be clarified. The infiltration of IgG4-positive cells is, in general, considered to occur within the adventitial or perivascular regions, although it may also be seen in the intimal layer of the atherosclerotic vessel (5).

Second, the presence of IgG4-related coronary periarteritis is not always confirmed histopathologically, and it is possible that the appearance of IgG4-related periarteritis-like regions demonstrated by imaging modalities in patients with proven IgG4-related disease in other tissues or organs might not necessarily indicate IgG4-related periarteritis. In a previous case study, for example, Tajima et al. reported a patient with IgG4-related disease that had been diagnosed by elevated serum IgG4 levels and IgG4-positive cell infiltration in the salivary glands (6). This patient had a prominent coronary pericardial pseudotumor, suggestive of IgG4-related coronary periarteritis; however, the ratio of IgG4-poisitve to IgG-positive cells in the coronary periarterial tissue was low and did not reach the cut-off value for the diagnosis of IgG 4-related disease (7). Although this relatively low prevalence of periarterial IgG4-positive cell infiltration might be due to the six-month period of corticosteroid treatment, the possibility remains that the clinical picture may mimic IgG4-related periarteritis even when there is no prominent IgG4-positive cell infiltration (8). When IgG4-related periarteritis-like regions are observed by imaging in patients with a definitive diagnosis of IgG4-related disease in non-vascular tissue, should such lesions be called “IgG4-related periarteritis” or “IgG4-related disease-associated perivascular lesions”?

Third, we may have to clarify the subset of patients with IgG4-related periarteritis who will benefit from corticosteroid therapy. This therapy is known to be extremely potent in resolving IgG4-related immune inflammation; however, it can also facilitate the rupture or dilatation of arteries, which

Department of Cardiology, Osaka Medical College, Japan
Received: February 13, 2017; Accepted: February 28, 2017; Advance Publication by J-STAGE: August 21, 2017
Correspondence to Dr. Nobukazu Ishizaka, ishizaka@osaka-med.ac.jp

might lead to a critical condition (9, 10). Whether or not the amelioration of luminal narrowing of the coronary artery by corticosteroid therapy observed in Sakamoto et al.'s study was due to the regression of plaque or to unexpected remodeling of the arterial wall remains unclear.

Needless to say, we should continue accumulating knowledge regarding IgG4-related periarteritis and analyzing its clinical course to determine the optimal therapeutic strategy as well as pursue the pathogenesis of this disorder, especially since IgG4-related disease was specified as an intractable disease by the Japanese government in 2015.

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

References

1. Perugino CA, Wallace ZS, Meyersohn N, et al. Large vessel involvement by IgG4-related disease. Medicine (Baltimore) **95**: e3344, 2016.
2. Mavrogeni S, Markousis-Mavrogenis G, Kolovou G. IgG4-related cardiovascular disease. The emerging role of cardiovascular imaging. Eur J Radiol **86**: 169-175, 2017.
3. Sakamoto A, Tanaka T, Hirano K, et al. Immunoglobulin G4-related coronary periarteritis and luminal stenosis in a patient with a history of autoimmune pancreatitis. Intern Med **56**: 2445-2450, 2017.
4. Higashi H, Inaba S, Azuma T, et al. Effects of steroid therapy for IgG4-related coronary periarteritis. Intern Med **55**: 1935-1936, 2016.
5. Fujita S, Nishioka N, Ito T, et al. Increased serum IgG4 levels and intimal IgG4-positive cell infiltration in rapidly growing aortic aneurysm. SAGE Open Med Case Rep **1**: 2050313X13496504, 2013.
6. Tajima M, Hiroi Y, Takazawa Y, et al. Immunoglobulin G4-related multiple systemic aneurysms and splenic aneurysm rupture during steroid therapy. Hum Pathol **45**: 175-179, 2014.
7. Umehara H, Okazaki K, Masaki Y, et al. Comprehensive diagnostic criteria for IgG4-related disease (IgG4-RD), 2011. Mod Rheumatol **22**: 21-30, 2012.
8. Kasashima S, Zen Y, Kawashima A, et al. A new clinicopathological entity of IgG4-related inflammatory abdominal aortic aneurysm. J Vasc Surg **49**: 1264-1271; discussion 1271, 2009.
9. Ikutomi M, Matsumura T, Iwata H, et al. Giant tumorous lesions (correction of legions) surrounding the right coronary artery associated with immunoglobulin-G4-related systemic disease. Cardiology **120**: 22-26, 2011.
10. Kasashima S, Kawashima A, Kasashima F, et al. Immunoglobulin G4-related periaortitis complicated by aortic rupture and aortoduodenal fistula after endovascular AAA repair. J Endovasc Ther **21**: 589-597, 2014.