

Title “Mass Lesions Surrounding Coronary Artery Associated with Immunoglobulin G4-Related Disease”

Type of article; case report

Saburo Kusumoto (MD)<sup>a,\*</sup>, Hiroaki Kawano (MD, PhD, FJCC)<sup>a</sup>, Masayoshi Takeno (MD)<sup>a</sup>, Fumitaka Kawahara (MD)<sup>b</sup>, Kuniko Abe (MD)<sup>c</sup>, Hideyuki Hayashi (MD)<sup>d</sup>, Yuji Koide (MD)<sup>a</sup>, and Koji Maemura (MD, PhD, FJCC)<sup>a</sup>

<sup>a</sup> Department of Cardiovascular Medicine, Nagasaki University Graduate School of Biomedical Sciences, 1-7-1 Sakamoto, Nagasaki, 852-8501, Japan.

<sup>b</sup> Department of Cardiovascular Medicine, Nijigaoka Hospital, Nagasaki, Japan.

<sup>c</sup> Department of Pathology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan.

<sup>d</sup> Department of Radiology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan.

\*Corresponding author. Tel.: +81 95 819 7288; fax.:81 95 819 7290.

E-mail address: ajmtp66@hotmail.com (S. Kusumoto)

## Abstract

Immunoglobulin G4 (IgG4) -related diseases have been reported that they are systemic diseases characterized by elevation of serum IgG4 concentration and infiltration of IgG4-positive plasma cells within the target organ. However, the involvement of coronary artery is very rare. Here, we report a 62-year-old man with the mass lesions surrounding coronary artery and abdominal aorta associated with IgG4 related disease diagnosed by a needle biopsy of the mass lesion surrounding the coronary artery using echocardiography and CT. After we started to treat the patient with prednisolone, his serum IgG4 level decreased, and the mass lesions of coronary and abdominal artery were markedly reduced in size after 4 months. In conclusion, IgG4-related disease should be considered in addition to tumors such as malignant lymphoma when mass lesions surrounding coronary artery are detected.

Key word; IgG4-related disease, CT, arteritis

## Introduction

IgG4-related diseases are systemic and are characterized by elevation of serum IgG4 concentration and infiltration of IgG4-positive plasma cells within the target organ. In particular, autoimmune pancreatitis is thought to be involved in IgG4-related sclerosing disease [1]. Recently other organs such as salivary gland [2], retroperitoneum [3], liver, bile duct [4], and lung [5] have been reported to be involved in IgG4-related disease. They are often sensitive to steroid therapy. The involvement of aorta in IgG4-related disease is relatively common and is often

associated with retroperitoneal fibrosis. However, only several cases of the involvement of coronary artery have been reported so far [6,7,8,9,10]. We report a case of mass lesions surrounding coronary artery associated with IgG4-related disease diagnosed by needle biopsy.

### Case report

A 62-year-old asymptomatic man was admitted to our hospital for further examination because a cardiac tumor was incidentally found by echocardiography.

He had received percutaneous balloon angioplasty in the right coronary artery (RCA) and left circumflex branch (LCx) of the left coronary artery (LCA) because of angina pectoris 18 years previously. In addition, he had undergone coronary bypass surgery (left internal thoracic artery to the left anterior descending branch (LAD) of LCA and saphenous vein grafts to RCA and LCx) 14 years previously. About 7 years ago, the saphenous vein grafts, RCA and LAD were all occluded, although the left internal thoracic artery graft was patent. Because fair collateral flow was observed from LCx to RCA, no further coronary intervention was performed and medical treatment was continued. He has now been treated with inhaled steroid for 3 years due to bronchial asthma.

His echocardiography showed normal left ventricular wall motion and a mass lesion in the atrioventricular sulcus, which compressed the right atrium. Thoracic computed tomography (CT) revealed a mass surrounding the RCA and proximal site of LAD (Figure 1). Abdominal CT revealed a thickened infrarenal abdominal aortic wall (Figure 1). An electrocardiogram showed small Q waves in the inferior leads.

On laboratory examination, C-reactive protein was 0.43mg/dL (reference range, 0.0-0.17), total protein, 9.0g/dL (6.7-8.3), albumin, 3.5g/dL (4.0-5.0), and N-Terminal pro-brain natriuretic peptide, 177pg/ml (<131). His serum IgG was 3627mg/dl (870-1700), IgG4, 2170mg/dl (4.8-105), IgE, 681IU/ml (<269), IgA, 168mg/dl (110-410), IgM, 85mg/dl (35-220), soluble interleukin-2 receptor 643U/ml (145-518) and antinuclear antibodies were negative. IgG4 subtype made up 60% of the total IgG fraction (usually less than 5-6%).

Gallium-67 scintigraphy revealed no uptake into the mass lesion of coronary artery and abdominal aorta, and bone marrow aspiration showed no abnormal findings. Taken together, we suspected that the tumors surrounding coronary and abdominal artery were associated with IgG4-related disease, although neither swollen pancreas nor significant retroperitoneal fibrosis was observed by abdominal CT. To confirm the diagnosis, we successfully performed a needle biopsy of the mass lesion surrounding the RCA via the epigastric fossa, using echocardiography and CT.

Histological assessment of the coronary mass lesion showed fibrous tissue with infiltration of lymphocytes and plasma cells. Many of the plasma cells were positive for IgG and IgG4. The ratio of IgG4-positive cells / IgG-positive cells was > 60% and this indicated that the mass lesion was associated with IgG4-related disease (Figure 2).

We then started to treat the patient with 40mg (0.6mg/kg) prednisolone daily to reduce the mass lesion and to prevent compression of the right atrium. As a result, his serum IgG4 level decreased to 219mg/dl, and the mass lesions of coronary artery and abdominal aorta were markedly reduced in size after 4 months. The dose of prednisolone was gradually tapered and was maintained at 7.5mg without serious side effects. No recurrence was observed at medical follow-up of 1 year.

## Discussion

The involvement of aorta in IgG4-related disease is relatively common and is often associated with retroperitoneal fibrosis. However, the involvement of coronary artery is very rare. To the best of our knowledge, only 5 cases of IgG4-related tumorous lesions surrounding coronary artery have been previously reported [6,7,8,9,10]. All 6 cases, including the present case, were reported in Japan. Characteristics of the 6 cases are summarized in Table 1. Five cases were elderly men, while one was an elderly woman. Four of the 6 cases had mass lesions surrounding both right and left coronary arteries, one surrounding RCA only, and one surrounding LCA only. Four cases had a coronary artery aneurysm; three of these had a thrombus and one had an acute myocardial infarction associated with an acute thrombus [2]. It was reported that IgG4-related periarteritis mainly occurred in the tunica externa and presented as an aneurysmal lesion rather than as stenosis [6].

At least four cases also had tumorous lesions surrounding the abdominal aorta. Two cases had other IgG4-related glandular diseases.

The diagnosis was confirmed by US and CT guided-needle biopsy in the present case, while the previous cases were diagnosed as follows: 4 cases by open chest biopsy and one indirectly by renal biopsy. We recommended US and CT guided-needle biopsy because it minimizes the risk of coronary artery injury and cardiac tamponade. Moreover, it is less invasive compared with open chest biopsy; this method also has the advantage of permitting therapy to begin as soon as possible after diagnosis, in contrast to open biopsy.

IgG4-related disease is usually sensitive to steroid therapy. The present case and the previous 2 cases were treated with oral prednisolone [7,8], and 2 cases were treated with

surgical resection of the coronary aneurysm and/or abdominal aneurysm without steroid therapy [6,9], and one case was finally treated with surgical resection of the coronary aneurysm because steroid therapy was not fully effective for the coronary lesion [10].

Both of these therapies achieved a marked reduction in serum IgG4 levels, and the steroid treatment reduced mass lesion size surrounding coronary artery and aorta in 3 of 4 cases with steroid therapy. One case died of aortic rupture after corticosteroid therapy. Although an association between rupture and corticosteroid therapy was previously unknown, we should treat patients with corticosteroids carefully because such therapy for IgG4-related periarteritis may induce thinning of the aortic wall.

In conclusion, IgG4-related disease should be considered in addition to tumors such as malignant lymphoma when mass lesions surrounding coronary artery are detected, and the steroid therapy is effective for the coronary lesions in at least half of these patients.

## References

- [1] Hamano H, Kasashima S, Horiuchi A, Unno H, Furuya N, Akamatsu T, Fukushima M, Nikaido T, Nakayama K, Usuda N, Kiyosawa K. High serum IgG4 concentrations in patients with sclerosing pancreatitis. *N Engl J Med* 2001;344:732-8.
- [2] Kitagawa S, Zen Y, Harada K, Sasaki M, Sato Y, Minato H, Watanabe K, Kurumaya H, Katayanagi K, Masuda S, Niwa H, Tsuneyama K, Saito K, Haratake J, Takagawa K, Nakanuma Y. Abundant IgG4-positive plasma cell infiltration characterized chronic sclerosing sialadenitis. *Am J Surg Pathol* 2004;28:1193-203.
- [3] A. H. Kardar, S. Kattan, E. Lindstedt and K. Hanash. Steroid therapy for idiopathic retroperitoneal fibrosis: Dose and duration. *J Urol* 2002;168:550-5.
- [4] Zen Y, Harada K, Sasaki M, Sato Y, Tsuneyama K, Haratake J, Kurumaya H, Katayanagi K, Masuda S, Niwa H, Morimoto H, Miwa A, Uchiyama A, Portman B, FRCPath and Nakanuma Y. IgG4-related sclerosing cholangitis with and without hepatic inflammatory pseudotumor, and sclerosing pancreatitis-associated sclerosing cholangitis. *Am J Surg Pathol* 2004;28:1193-1203.
- [5] Zen Y, Kitagawa S, Minato H, Kurumaya H, Katayanagi K, Masuda S, Niwa H, Fujimura M, Nakamura Y. IgG4-positive plasma cells in inflammatory pseudotumor (plasma cell granuloma) of the lung. *Hum Pathol* 2005;36:710-7.
- [6] Matsumoto Y, Kasashima S, Kawashima A, Sasaki H, Endo M, Kawakami K, Zen Y, Nakanuma Y. A case of multiple immunoglobulin G4-related periarteritis: a tumorous lesion of the coronary artery and abdominal aortic aneurysm. *Hum Pathol* 2008;39:975-80.

[7]Fujii T, Tsushima H, Masada K, Kurushima S, Maeda H, Tsujiyama S, Hirabayashi A, Daimaru H. A case report of acute myocardial infarction associated with coronary artery aneurysm and IgG-related periarteritis. Nihon Nousei Igakkai Gakujyutu Soukai Syourokusyu 2010; 59 ; 108 (In Japanese).

[8]Okamoto M, Nagumo M, Goto T, Yoshitake A, Miki T, Osumi K. A case of immunoglobulin G4-related cardiac tumor around the coronary artery. Jpn. J. Cardiovasc. Surg 2010;39:230-3.

[9]Ichihara Y, Tsuchiya K, Nakajima M, Kaku Y, Koyama T. A case report of surgical repair for IgG4-related coronary artery aneurysm. The 155<sup>th</sup> Meeting of The Kanto Koushinetsu area in The Japanese Association for Thoracic Surgery Abstract 2011, pp21 (In Japanese).

[10]Ikutomi M, Matsumura T, Iwata H, et al. Giant tumorous lesions surrounding the right coronary artery associated with immunoglobulin-G4-related systemic disease. Cardiology 2011;120(1):22-26.



## Figure Caption

FIGURE 1. A and B, Contrast material-enhanced CT angiography shows the mass lesion surrounding the right coronary artery and abdominal aorta before corticosteroid therapy (arrowheads). C and D, The mass lesion was markedly reduced in size after corticosteroid therapy (arrows).

FIGURE 2. Microscopic findings of the tumorous lesion surrounding the right coronary artery. A, Many inflammatory cells are infiltrating within the lesion. Several eosinophils are also shown (H and E, original magnification x400). B, Many inflammatory cells are plasma cells (VS38, original magnification x400). C and D, Most plasma cells are IgG and IgG4-positive (immunostaining of IgG (C) and IgG4 (D), original magnification x400).

Table 1. Patient profiles of IgG4-related disease including coronary artery lesions in the previous reports and in this report. PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting.

FIGURE 1.

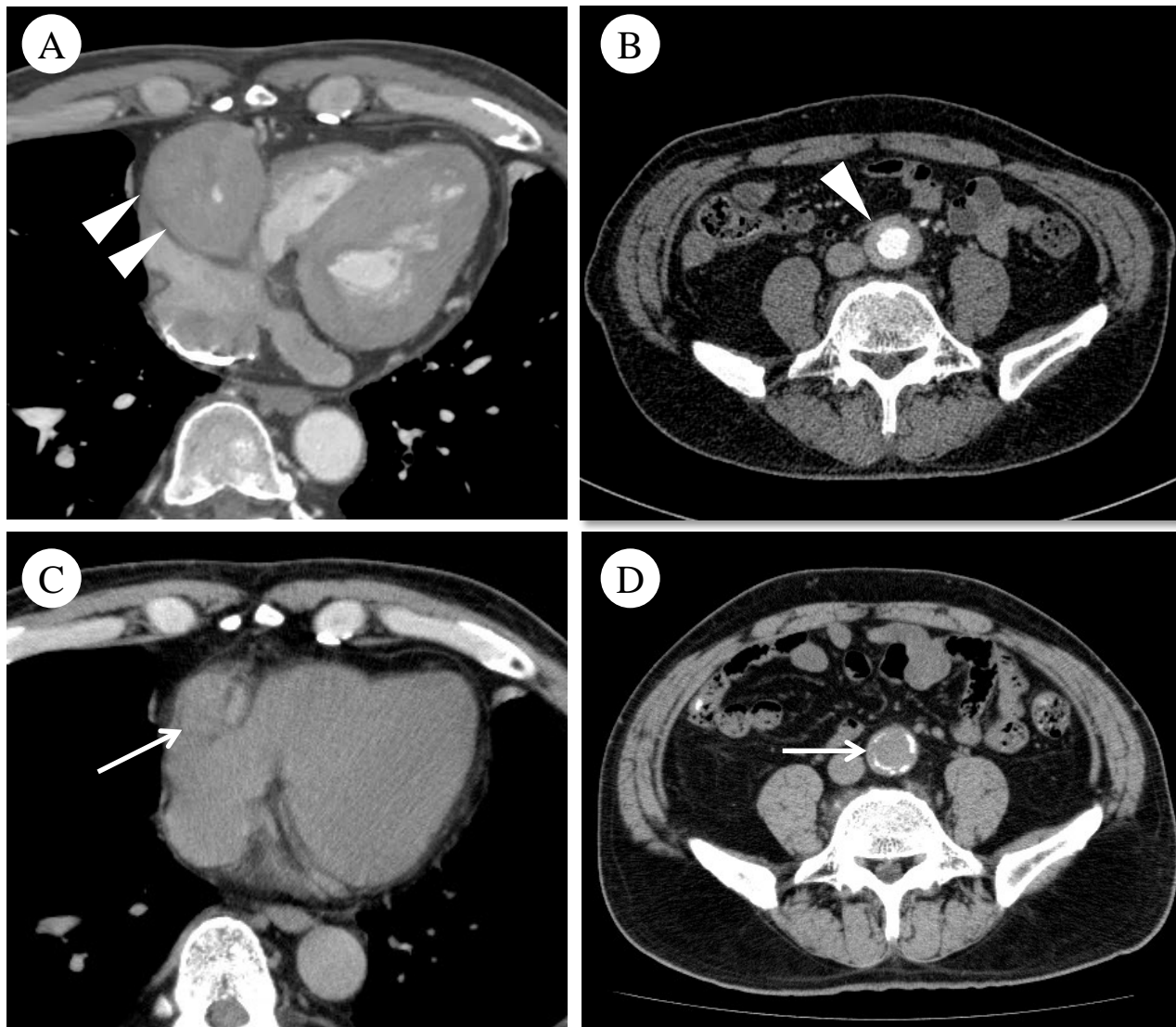


FIGURE 2.

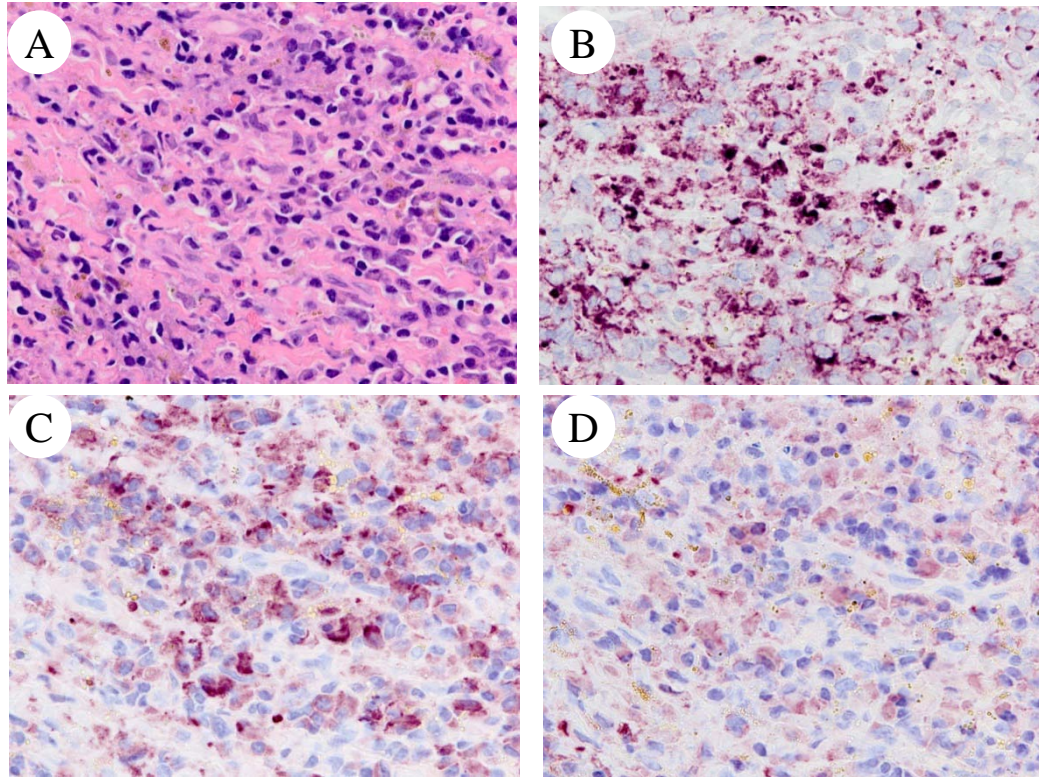


Table 1.

No	age sex	Site of IgG4 related disease	Diagnostic procedure	treatment	outcome	reference
1	63 F	Mass lesion surrounding RCA RCA aneurysm with mural thrombus Abdominal aorta	Open biopsy	CABG +resection of the aneurysm around coronary artery and abdominal aorta	survival	[6]
2	83 M	Mass lesions surrounding RCA and LCA LCA aneurysm with thrombus Celiac artery Abdominal aorta Kidney ,spleen, salivary gland	Needle biopsy (Kidney)	PCI Corticosteroid	Death from Aneurysm Rupture	[7]
3	69 M	Mass lesions surrounding RCA and LCA Post operation for abdominal aortic aneurysm	Open biopsy	corticosteroid	survival	[8]
4	83 M	Mass lesion surrounding LCA LCA aneurysm with mural thrombus	Open biopsy	CABG + resection of the aneurysm surrounding coronary artery	survival	[9]
5	75 M	Mass lesions surrounding RCA and LCA RCA aneurysm Abdominal aorta and aortic arch Pancreas, Parotid gland	Open biopsy	Corticosteroid PCI CABG + resection of the aneurysm surrounding coronary artery	survival	[10]
6	62 M	Mass lesions surrounding RCA and LCA Abdominal aorta	Needle biopsy	corticosteroid	survival	The present case