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CASE REPORT
Coronary heart disease

Immunoglobulin G4-related masses surrounding coronary arteries: a case report

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Background

Immunoglobulin G4 (IgG4)-related disease (IgG4-RD) is an immune-mediated fibroinflammatory condition with high serum IgG4 levels affecting various organs, such as the pancreas, lacrimal and salivary glands, thyroid, kidney, and lung. Typical cardiovascular manifestations of IgG4-RD include periaortitis, coronary arteritis, and pericarditis. However, reports of IgG4-RD associated with coronary arteritis are rare. Here, we report a case of IgG4-related masses surrounding the coronary arteries.

Case summary

A 59-year-old man was referred to our hospital because of mediastinal masses detected by computed tomography (CT). Coronary CT angiography revealed masses surrounding the right coronary artery and the left anterior descending coronary artery. An elevated serum level of IgG4 and histological findings led to the diagnosis of IgG4-related coronary arteritis with mass formation. Coronary angiography showed numerous feeding arteries to the masses, which were demonstrated as multiple microchannels in the intravascular ultrasound (IVUS) images.

Discussion

IgG4-RD involving the cardiovascular system has been reported. However, coronary artery disease associated with IgG4-RD is very rare, and the mechanism of mass formation in IgG4-related coronary arteritis is unclear. In our case, within the cardiovascular system, IgG4-RD was limited to the coronary arteries, suggesting that the affected coronary arteries may provide the necessary blood supply to the mass, thus, aiding its growth. These findings were supported by the images from coronary angiography and IVUS.

Keywords

Immunoglobulin G4-related disease • Coronary arteritis • Intravascular ultrasound • Coronary angiography • Mediastinal mass • Case report

Learning points

- In immunoglobulin G4-related disease (IgG4-RD), cardiovascular involvement is commonly expressed as periaortitis, and coronary arteritis is rare.
- In this case, although mediastinal lymphadenopathy existed, cardiac involvement in IgG4-RD was limited to the coronary arteries with mass formation. IgG4-RD should be considered in the case of coronary arteritis with mass formation.
- A multidisciplinary approach is important for the accurate diagnosis in the case of mediastinal lymphadenopathy with mass formation around the heart.

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Introduction

Immunoglobulin G4 (IgG4)-related disease (IgG4-RD) is a chronic fibroinflammatory disorder characterized by elevated serum IgG4 levels and the infiltration of IgG4-positive plasma cells into various tissues, such as the pancreas, salivary glands, retroperitoneal organs, and liver.¹ However, IgG4-RD of the cardiovascular system is very rare, and typical cases of IgG4-RD with cardiovascular involvement are characterized by periaortitis, coronary arteritis, and pericarditis.^{2,3}

Here, we report a case of IgG4-related masses surrounding the coronary arteries.

Timeline

Events	
4 months before admission	Chest radiography showed a shadow overlying the heart at the hilum of the left lung. Computed tomography (CT) of the chest revealed mediastinal lymphadenopathy and masses around the heart.
2 months before admission	¹⁸ F-fluorodeoxyglucose (¹⁸ F-FDG) positron emission tomography/CT revealed an increased uptake of ¹⁸ F-FDG in the mediastinal lymph nodes and masses.
1 month before admission	Thoracoscopic mediastinal lymph node biopsy was performed. An immunoglobulin G4 (IgG4)-related disease was diagnosed because of high serum IgG4 level (1310 mg/dL) and the infiltration of IgG4 positive plasma cells in the lymph node. Coronary CT angiography revealed that the masses were surrounding the coronary arteries.
Day 0	The patient was admitted to our hospital.
Day 2	Coronary angiography and intravascular ultrasound demonstrated multiple feeding arteries from coronary arteries to the masses without stenosis of coronary arteries.
Day 4	50 mg of prednisolone daily was started.
Day 25	Serum IgG and IgG4 levels decreased, and the follow-up thoracic CT showed markedly regressed masses.
Day 85	Patient was discharged with a prescription of 20 mg of prednisolone daily.
8 months after discharge	Prednisolone dosage was reduced to 10 mg/day, and there was no further enlargement of the masses.

Case presentation

A 59-year-old man with a history of diabetes mellitus and myocardial infarction at 35 years of age was asymptomatic but was found to have a shadow overlying the heart at the hilum of the left lung on chest radiography (Figure 1A) performed during an annual medical examination. Computed tomography (CT) of the chest performed at another hospital revealed mediastinal lymphadenopathy (Figure 1B and C) and masses (Figure 1D–I). He was then referred to the Department of Respiratory Medicine at our hospital. Because malignant lymphoma was suspected, ¹⁸F-fluorodeoxyglucose (¹⁸F-FDG) positron emission tomography/CT (PET/CT) was performed, which revealed an increased uptake of ¹⁸F-FDG in the paratracheal and parathoracic aortic lymph nodes and in the masses on the right side of the origin of the ascending aorta and the hilum of the left lung (Figure 2A–E). Laboratory findings were as follows: total protein 9.5 g/dL (normal value: 6.6–8.1 g/dL), amylase 83 U/L (normal value: 44–132 U/L), and soluble interleukin-2 receptor: 490 U/ml (normal value: 122–496 U/ml). The immunoglobulin profile was then examined because of the elevation of serum total protein, which showed the following values: IgG 3864 mg/dL (normal value: 861–1747 mg/dL), IgG2 1260 mg/dL (normal value: 239–838 mg/dL), IgG4 1310 mg/dL (normal value: 4.5–117 mg/dL), IgA 204 mg/dL (normal value: 93–393 mg/dL), IgM 215 mg/dL (normal value: 33–183 mg/dL), free light chain κ 93.9 mg/dL (normal value: 3.3–19.4 mg/dL), and free light chain λ 62.0 mg/dL (normal value: 5.7–26.3 mg/dL). Thoracoscopic mediastinal lymph node biopsy was performed, and histological examination revealed chronic inflammatory infiltration of IgG4 positive plasma cells (Figure 2F). Therefore, the patient was diagnosed with IgG4-RD and was referred to our department because he was considered to have IgG4-related cardiovascular disease. Electrocardiography showed a QS pattern in lead V1. Coronary CT angiography (Figure 3) revealed a stent in the left anterior descending coronary artery (LAD) along with masses surrounding the right coronary artery (RCA) and LAD. There seemed to be no obvious stenosis, but the characteristics of the site of the stent were unclear. He was then admitted to our hospital. At that time, he was taking 1 mg of trandolapril, 2.5 mg of bisoprolol fumarate, 3 mg of glimepiride once daily, and 25 mg of omarigliptin once a week orally. A physical examination documented blood pressure of 132/84 mmHg, heart rate of 76 b.p.m., and body temperature of 36.3°C. Heart sounds were normal on auscultation, with no audible murmur.

Coronary angiography on hospital Day 2 showed no stenosis of any of the coronary arteries, and numerous microvessels from the RCA and LAD (Figure 4A and B, Supplementary material online, Videos S1 and S2). Intravascular ultrasound (IVUS) demonstrated the thickening of the adventitia at the site of masses surrounding the RCA and LAD with multiple microchannels (Figure 4C and D, Supplementary material online, Videos S3 and S4). Subsequently, treatment with 50 mg of oral prednisolone was initiated, and its dosage was gradually tapered. The serum IgG and IgG4 levels dramatically decreased and normalized on the 20th day, and both masses had markedly regressed on the follow-up thoracic CT 1 month after the initiation of prednisolone (Figure 5A and B). Eight months later, the dosage of prednisolone was reduced to 10 mg/day, no enlargement of the masses was noted (Figure 5C and D), and there were no symptoms suggestive of myocardial ischaemia.

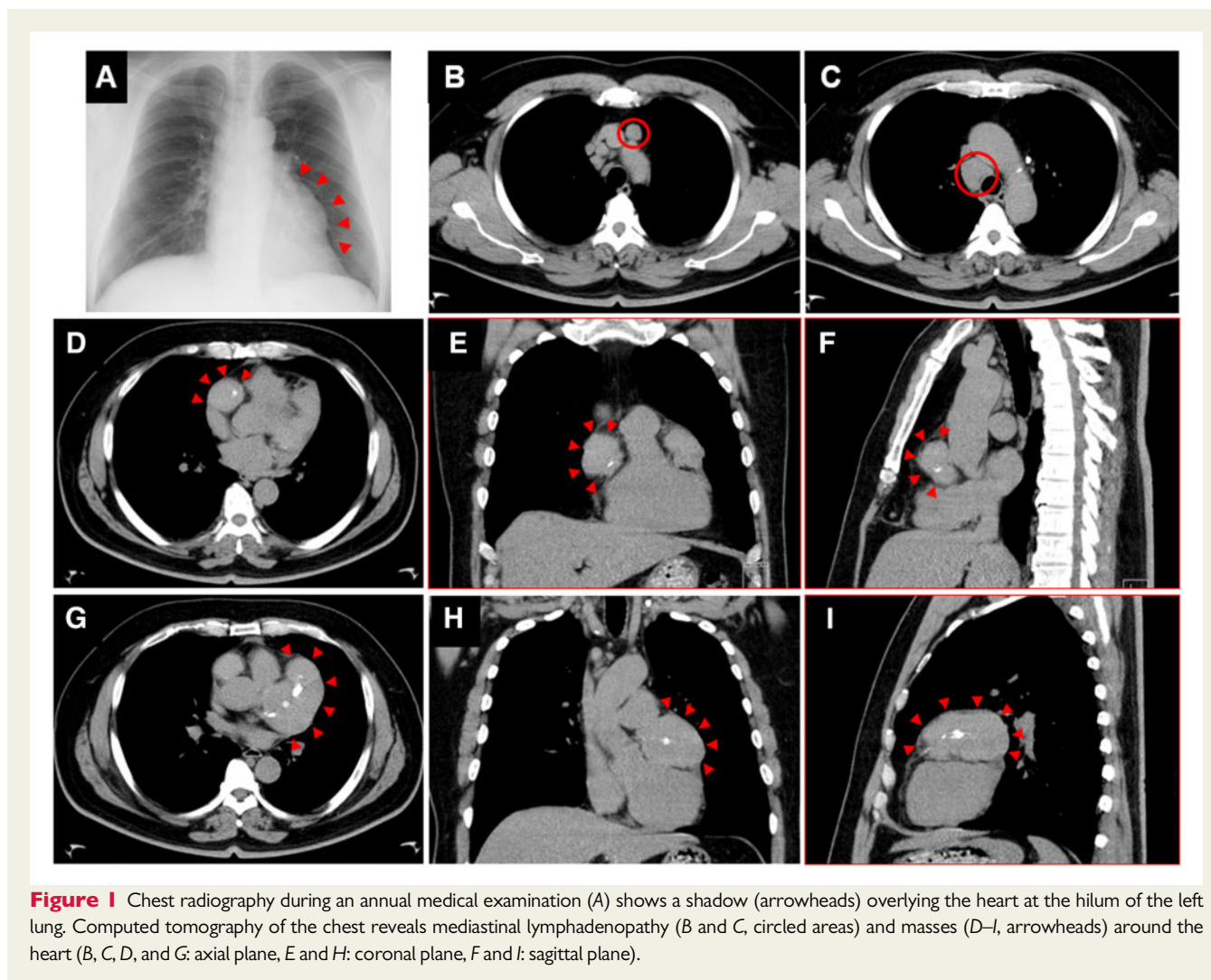


Figure 1 Chest radiography during an annual medical examination (A) shows a shadow (arrowheads) overlying the heart at the hilum of the left lung. Computed tomography of the chest reveals mediastinal lymphadenopathy (B and C, circled areas) and masses (D–I, arrowheads) around the heart (B, C, D, and G: axial plane, E and H: coronal plane, F and I: sagittal plane).

Discussion

IgG4-RD is a systemic immune-mediated inflammatory disease characterized by elevated serum IgG4 concentration and the infiltration of IgG4 positive plasma cells into various organs, such as the pancreas, salivary glands, retroperitoneal organs, and liver.¹ The cardiovascular system is also a target of IgG4-RD, and arterial involvement is usually observed in the medium to large arteries, such as the abdominal aorta.⁴ Histopathologically, IgG4-related arterial lesions usually exhibit thickening of the adventitia due to inflammation and fibrosis.⁵ On the other hand, the involvement of the coronary arteries in IgG4-RD is very rare.^{6,7} Coronary artery lesions are classified into 3 types (stenosis, aneurysm, and diffuse wall thickening), and rare cases shows wall thickening alone.⁸ Additionally, IgG4-related mass formation surrounding the coronary artery has also been reported.^{9–11} In our case, cardiac involvement of IgG4-RD was limited to the coronary arteries with mass formation, showing the thickening of the adventitia without stenosis nor aneurysm.

The mechanism by which the coronary arteries are affected in IgG4-RD is unclear. In the heart, lymphatic vessels exist along coronary arteries, and their dysfunction induces the adventitial inflammation of coronary arteries.¹² This mechanism may be involved in the development of coronary arteritis in IgG4-RD.

Our patient was diagnosed with IgG4-RD based on his elevated serum IgG4 level and the histological findings. Malignant lymphoma was initially suspected due to the findings of the ¹⁸F-FDG PET/CT. However, the images of ¹⁸F-FDG PET/CT were also consistent with IgG4-RD,¹³ and laboratory data suggested the possibility of IgG4-RD. Therefore, thoracoscopic mediastinal lymph node biopsy was performed to confirm the diagnosis. Additionally, histological findings are one of the essential diagnostic criteria for IgG4-RD.¹⁴ Endobronchial ultrasound (EBUS) and EBUS-guided transbronchial needle aspiration are both well-established methods in terms of safety and diagnostic accuracy for the evaluation of mediastinal lymphadenopathy. Although EBUS was not used in our case due to a lack of availability of trained

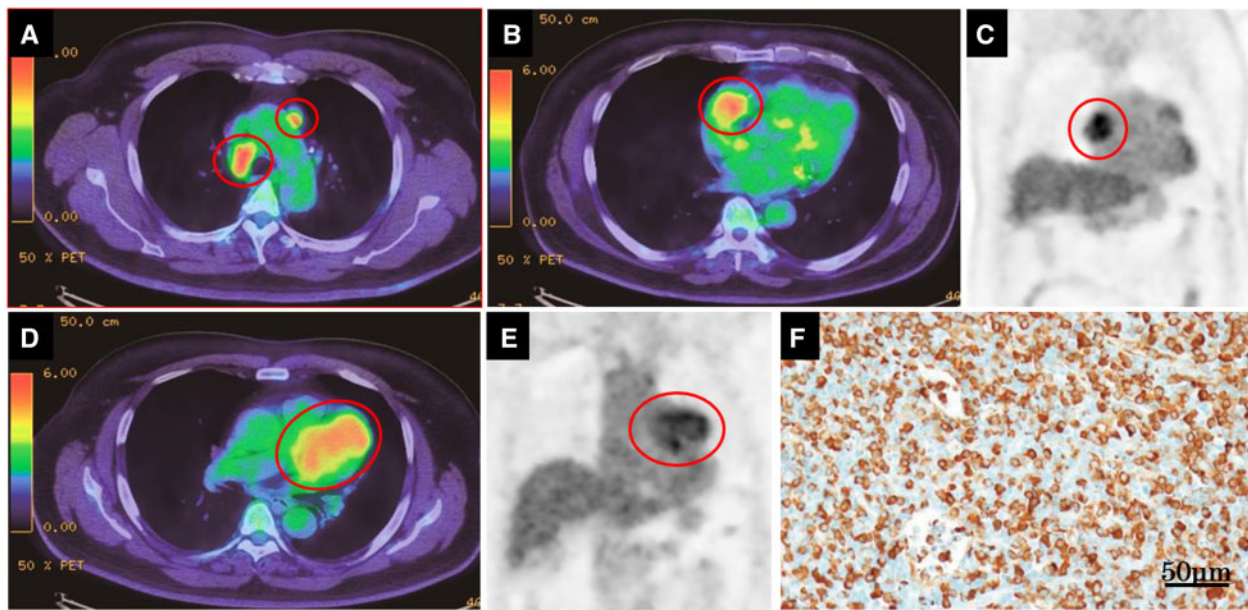


Figure 2 ^{18}F -fluorodeoxyglucose positron emission tomography/computed tomography shows increased uptake of ^{18}F -fluorodeoxyglucose (circled areas) in the paratracheal and parathoracic aortic lymph nodes (A), and in the masses on the right side of the origin of ascending aorta (B: axial plane and C: coronal plane) and the hilum of the left lung (D: axial plane and E: coronal plane) (max standardized uptake value values were 6.00, 5.12, 6.66, and 5.95, respectively). Immunostaining for immunoglobulin G4 of mediastinal lymph node performed according to ABC method shows chronic inflammatory infiltration of immunoglobulin G4 positive plasma cells (F).

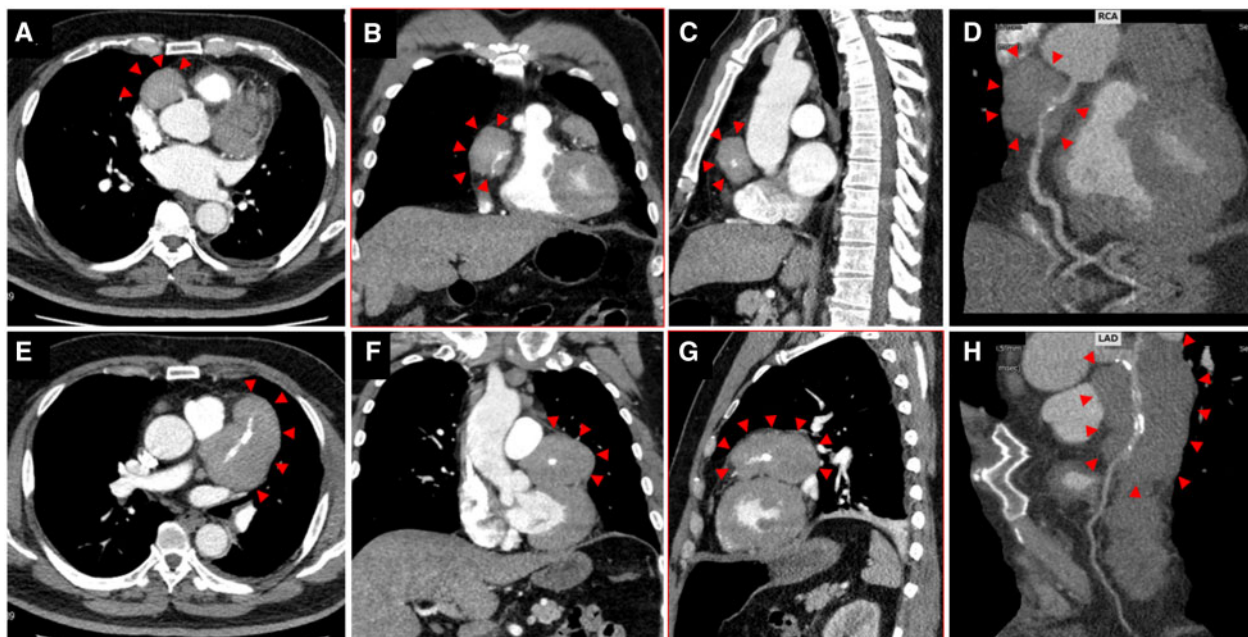
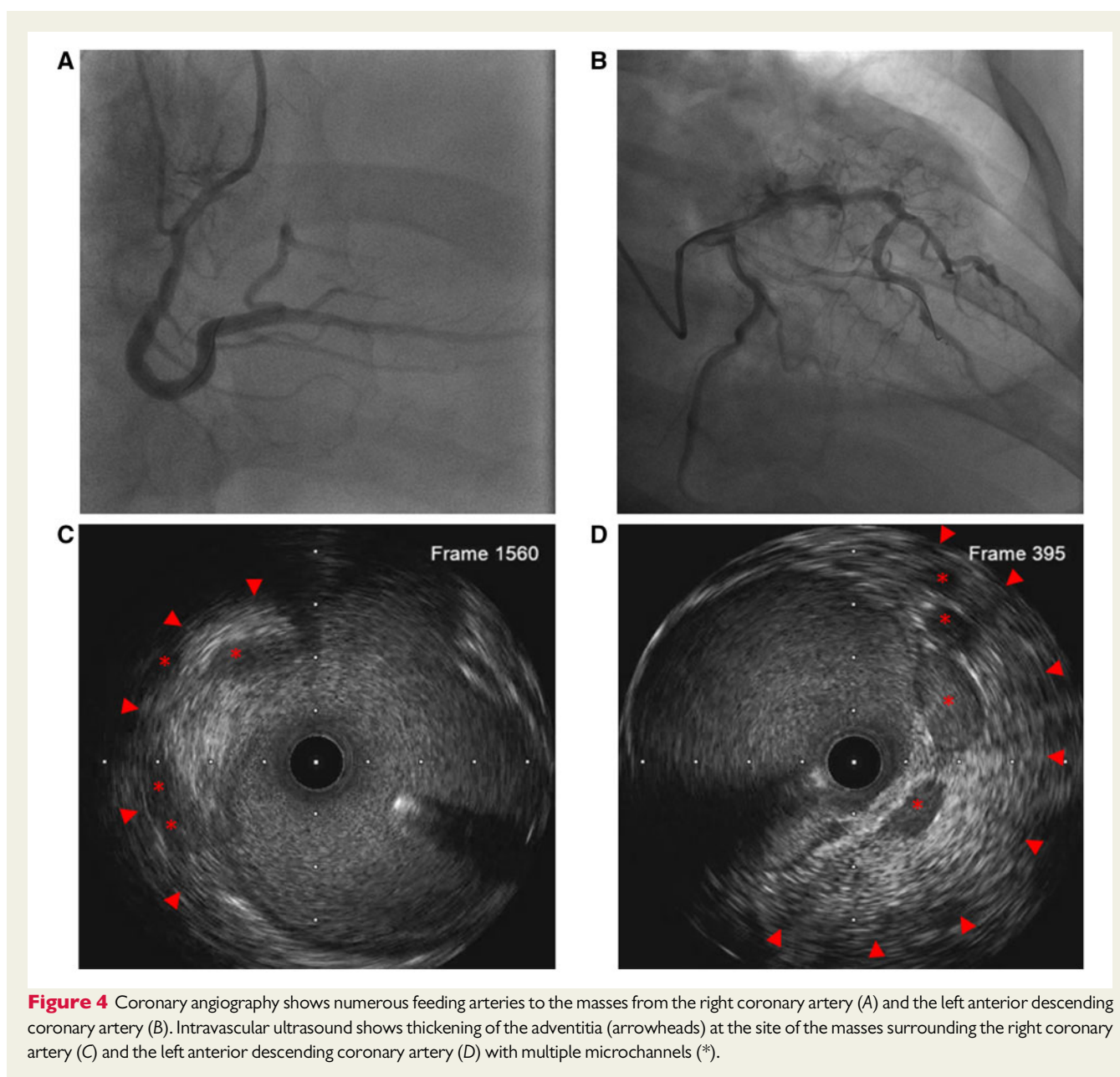


Figure 3 Coronary computed tomography angiography before the treatment shows masses (arrow heads) surrounding the right coronary artery (A–D) and the left anterior descending coronary artery (E–H) (A–C and E–G: early arterial phase, A and E: axial plane, B and F: coronal plane, C and G: sagittal plane, D and H: curved multiplanar reconstruction).



operators, its use should be considered in cases of mediastinal lymphadenopathy in the absence of contraindications.

Cardiac magnetic resonance imaging (CMR) characterizes cardiac masses with various pulse sequences and is superior to cardiac CT in the evaluation of cardiac masses in IgG4-RD.¹³ However, coronary CT angiography offers high spatial resolution and is superior to CMR in the evaluation of characteristics of coronary arteries. Thus, we performed coronary CT angiography because our patient had a history of myocardial infarction and coronary stent implantation. However, because of the unclear images of the stent implantation site, we performed coronary angiography for further evaluation.

IVUS was performed in several previous reports on IgG4-related coronary arteritis and demonstrated only thickening of the adventitia.^{10,11,15} In contrast, IVUS images of coronary arteries in our case showed the thickening of the adventitia and multiple microchannels, which were thought to be the feeding arteries to the masses, originally detected by coronary angiography, originating from the affected coronary arteries. The images of coronary angiography and IVUS in our case suggested that the feeding arteries from the affected coronary arteries may contribute to the mass formation in IgG4-related coronary arteritis.

In conclusion, our case suggests that coronary arteritis with mass formation can be associated with IgG4-RD. Therefore, IgG4-RD

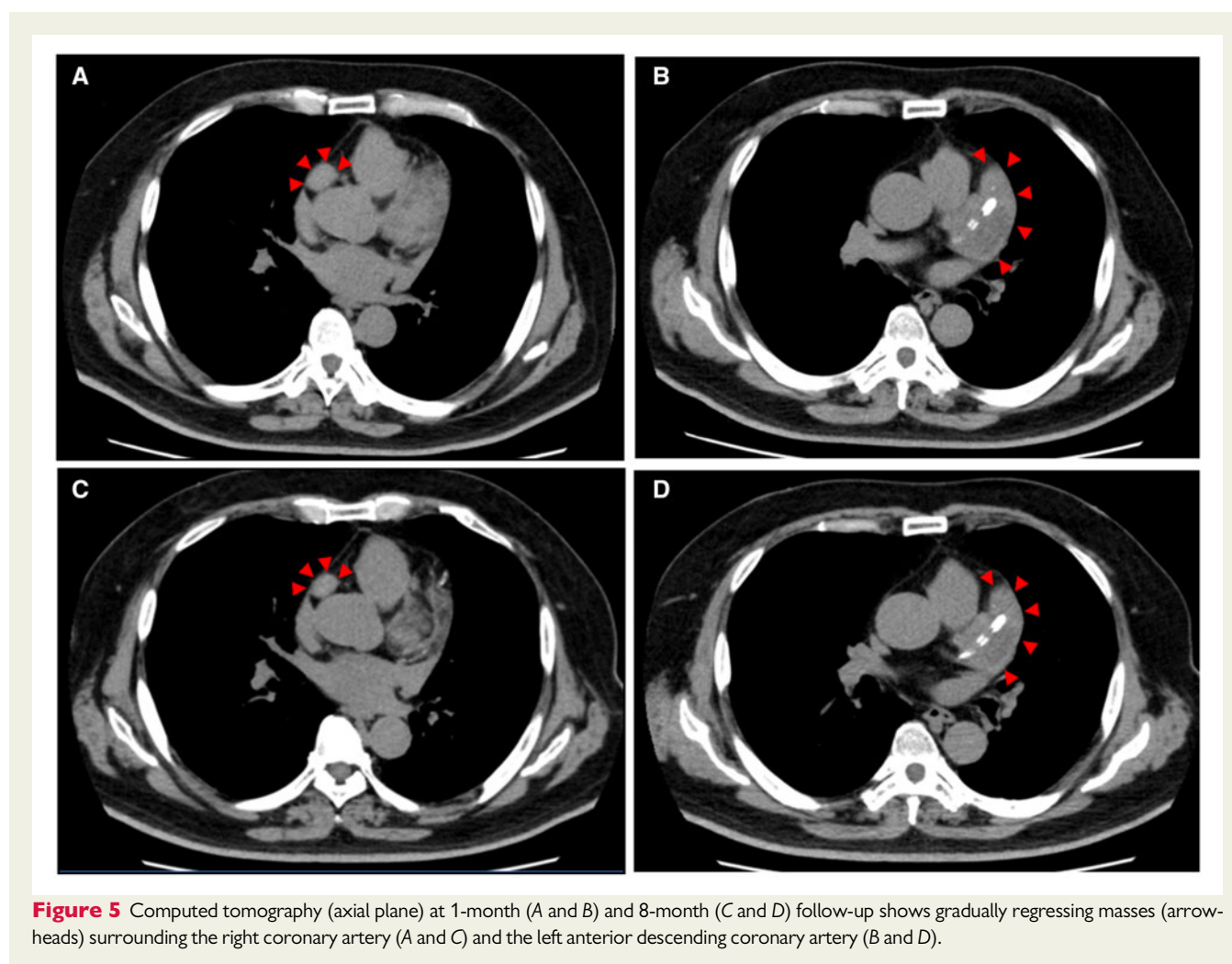


Figure 5 Computed tomography (axial plane) at 1-month (A and B) and 8-month (C and D) follow-up shows gradually regressing masses (arrowheads) surrounding the right coronary artery (A and C) and the left anterior descending coronary artery (B and D).

should be considered as a differential diagnosis in cases of cardiac mass.

Lead author biography



Takuya Nakamura was born in Shiga, Japan, in 1987. He received the MD degree from Nara Medical University, Kashihara, Japan in 2013. He completed 2 years of Japanese resident program at Nara Prefecture Seiwa Medical Center (2013–2015). Currently, he is working as an interventional cardiologist in the Department of Cardiovascular Medicine of Nara

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Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

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Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as [Supplementary data](#).

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

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