

Occult myocardial infarction due to an unusual cause: a case report of periarteritis involving the left coronary artery

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Background

Immunoglobulin G4-related disease (IgG4-RD) is an immune-mediated condition that affects multiple organs and systems.

Case summary

A 51-year-old man with a history of occult left apex myocardial infarction diagnosed based on electrocardiographic and echocardiographic findings underwent coronary computed tomography (CT) angiography for the evaluation of coronary artery disease; the findings revealed a soft-tissue mass that surrounded the aortic root and the distal portion of the left coronary artery. The mass was considered an inflammatory lesion; high glucose uptake on positron emission tomography/CT supported this assumption. Coronary angiography revealed 80% stenosis of the distal portion of the left anterior descending artery, which corresponded with the infarction. Intravascular ultrasound revealed hypoechoic regions outside the lumina of the stenotic segment. Based on these findings, IgG4-related periaortitis/periarteritis was suspected; the patient was accordingly treated with oral prednisone and methotrexate. At the 3-month follow-up, the periaortic mass had slightly reduced in size.

Discussion

Identification and diagnosis of IgG4-related cardiovascular disease are challenging; cases with localized coronary artery involvement may be misdiagnosed as atherosclerotic coronary artery disease. Although imaging techniques, including intracoronary imaging, may aid in differential diagnosis, their sensitivity and specificity still warrant further studies. Practical criteria that facilitate diagnosis and a better understanding of the disease are required.

Keywords

Immunoglobulin G4-related disease • Periaortitis/periarteritis • Coronary artery disease • Intravascular ultrasound • Case report

ESC curriculum

2.3 Cardiac magnetic resonance • 2.4 Cardiac computed tomography • 2.5 Nuclear techniques • 3.1 Coronary artery disease • 3.4 Coronary angiography

Learning points

- In rare cases, myocardial ischaemia and infarction with coronary artery involvement may be the initial manifestations of immunoglobulin G4-related disease.
- Vasculitis and other secondary conditions should be accorded equal importance in patients who typically are at high atherosclerotic risk.
- Because imaging, rather than pathology, could be more valuable in the diagnosis of immunoglobulin G4-related cardiovascular disease, its utility should be explored further.

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Introduction

Different types of vasculitis can cause myocardial ischaemia by involving the coronary arteries.¹ Immunoglobulin G4-related disease (IgG4-RD) is an immune-mediated chronic fibroinflammatory condition that affects nearly all organs and systems.^{2,3} Similar to atherosclerotic cardiovascular disease (ASCVD), IgG4-RD is more prevalent in the older and male populations.³ The IgG4-related peri-aortitis/periarteritis (IgG4-PAO/PA) is a subset of IgG4-RD that affects the cardiovascular system, with the abdominal aorta and iliac artery showing the highest susceptibility.⁴ The coronary arteries can be also involved in few cases, exhibiting radiological findings of diffuse wall thickening, stenosis, or aneurysm formation.⁵ Patients with IgG4-PAO/PA typically present with specific (e.g. back and abdominal pain) or systemic damage (e.g. swollen lymph nodes and enlarged saliva glands) symptoms.⁴ The recommended treatment strategies include corticosteroids with or without immunosuppressant agents, which are generally effective.⁶ Here we report a case of suspected IgG4-PAO/PA that affected the patient's aorta and left coronary artery.

Timeline

Time	Events
12-10-2020	The patient presented to a local hospital with palpitation. Electrocardiograph showed poor R-wave progression and T-wave inversion in the precordial leads, indicating myocardial ischaemia or infarction of the anterior wall of the left ventricle.
20-11-2020	The patient presented to our outpatient clinic. Echocardiogram revealed occult infarction with mural thrombus formation in the left apex. Coronary computed tomography angiography revealed soft-tissue masses wrapped around the aortic root and the left coronary artery.
12-12-2020	The patient was admitted for further investigation. A thorough examination and multidisciplinary consultation led to a possible diagnosis of immunoglobulin G4-related peri-aortitis/periarteritis.
21-1-2021	Treatment with oral prednisone and methotrexate was initiated.
12-3-2021	At follow-up, the patient was symptom free and the size of the periaortic mass had slightly reduced.

Case presentation

A 51-year-old man initially presented to a local clinic with paroxysmal palpitation but no other accompanying symptoms. Electrocardiography revealed brief bursts of atrial tachycardia and abnormal R- and T-waves on precordial leads (see [Supplementary material online, Figure S1](#)). Antiarrhythmic drugs

(oral propafenone and metoprolol) were administered for 4 weeks, but the palpitation did not subside. The patient then visited our clinic. A thorough review of the patient's medical history revealed several risk factors for ASCVD, including a 10-year-old history of Stage 1 hypertension, a 7-year-old history of a transient ischaemic attack, heavy smoking, and alcohol consumption. Additionally, the patient had experienced polyneuritis and scleritis at the age of 8 and 50 years, respectively; both diseases were cured with corticosteroids.

At presentation, the patient's vital signs were stable and body mass index was 28.68 kg/m². Physical examination revealed no positive findings. Coronary artery disease was suspected initially. The outpatient physician suggested an immediate transthoracic echocardiography, which revealed a left ventricular (LV) ejection fraction of 58% in addition to hypokinesis and thrombus formation of the LV apex, indicating an old myocardial infarction (MI; [Figure 1A–D](#)). Then the coronary computed tomography (CT) angiography (CCTA) revealed soft-tissue masses wrapped around the aortic root, left main coronary artery (LM), and distal left anterior descending artery (LAD; [Figure 2A–D](#)). Based on the patient's medical history and above-mentioned findings, non-atherosclerotic disease, particularly an inflammatory condition, was considered a more possible diagnosis.

The patient was admitted to our inpatient ward for further investigation. Laboratory examinations showed that his complete blood count, troponin level, liver and kidney functions, coagulation function, inflammatory markers, and autoantibody level were all within the normal range. However, immunoglobulin (Ig) E level significantly increased to 273 (normal range <100) kU/L; levels for other Igs, including IgG and its subclass, were normal. Although CT angiography of the whole aorta revealed atherosclerotic lesions involving the aorta and peripheral arteries, no other periaortic mass was found ([Figure 2E,F](#)). Cardiac magnetic resonance imaging (MRI) further confirmed the abnormal mass surrounding the LAD; the mass was characterized by obscure boundaries and significant enhancement, indicating an inflammatory lesion ([Figure 3E–H](#)). We also confirmed transmural infarction and thrombus formation in the LV apex ([Figure 3A–D](#)). Positron emission tomography (PET)/CT findings were remarkable for an elevated maximum standard uptake value for the ascending aorta and ostium of the LM ([Figure 4](#)), indicating active inflammation; the pericoronary mass was also noted, but detailed evaluation was impossible because of its small size. Furthermore, coronary angiography (CAG) revealed 80% stenosis of the distal LAD, which corresponded with the location of the pericoronary mass detected on CCTA, cardiac MRI, and PET/CT ([Figure 5](#)). Intravascular ultrasound (IVUS) revealed a diffuse fibroatheroma along the LAD as well as echoic regions in the media/adventitia of the stenotic segment ([Figure 5D](#)). We attempted optical coherence tomography (OCT) but could not complete it because of a flow-restricted coronary spasm, which was successfully managed via dilation and massage with a small balloon. Thus, no stent implantation was required.

A multidisciplinary consultation was held with a vasculitis expert, a rheumatologist, and several radiologists. Takayasu arteritis, giant cell arteritis, and other systemic vasculitis were ruled out based on the atypical clinical manifestations and imaging characteristics observed

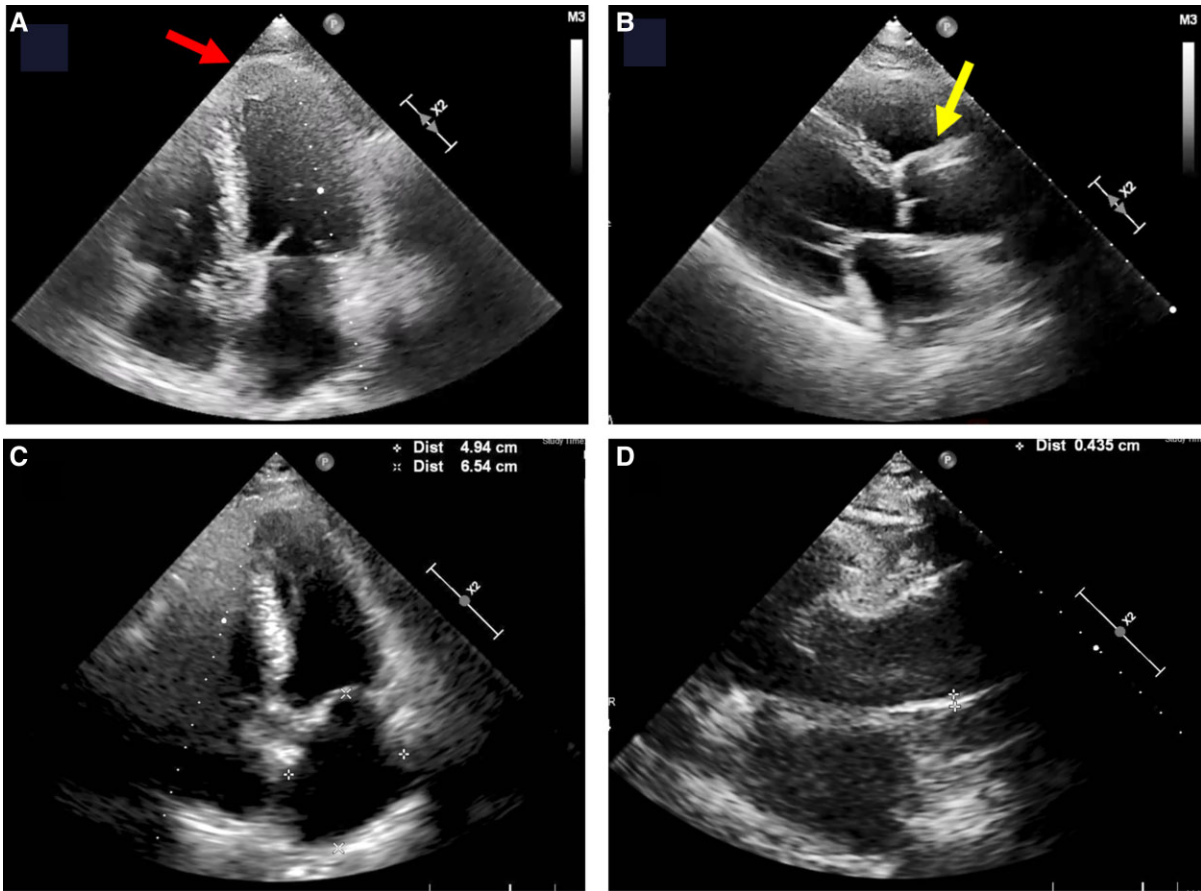


Figure 1 The transthoracic echocardiography showed (A) thrombus formation at the left ventricular apex (red arrow), and (B) a 10 mm hypoechoic mass surrounding the aortic root (yellow arrow). Echocardiography at 3 months follow-up showed (C) remained left ventricle thrombus and (D) shrunken periaortic mass.

on the above-mentioned examinations. The experts eventually highlighted IgG4-PAO/PA as a plausible explanation for the periaortic and pericoronary mass with subsequent MI. Ultrasound of the lymph nodes, salivary glands, and abdominal organs performed to screen for IgG4-RD-induced systemic damage showed unremarkable findings.

After we ruled out immunosuppressive therapy contraindications, the patient received oral prednisone (30 mg/day for 3 weeks and then tapered to 10 mg/day by 9 weeks) and methotrexate (15 mg/week). Rivaroxaban (20 mg/day) was prescribed to treat the LV thrombus because of its convenience as well as its non-inferiority over warfarin in dissolving thrombus and reducing embolic events.⁷ Clopidogrel (75 mg/day) was prescribed as an antiplatelet therapy following balloon massage because of coronary spasm; metoprolol (50 mg twice a day) was prescribed for hypertension and arrhythmia and atorvastatin (20 mg/day) for atherosclerosis.

At the 3-month follow-up, the patient was symptom-free with good exercise tolerance and free from immunosuppressive therapy-related side effects. The CCTA revealed slight thinning of the aortic root wall (Figures 1D and 2F-H). Clopidogrel was

discontinued, but rivaroxaban was continued because the LV thrombus sustained (Figure 1C). The patient was referred to a rheumatologist for additional treatment and monitoring.

Discussion

In addition to atherosclerosis, systemic vasculitis can occasionally involve the coronary arteries; in rare cases, the patients can initially present with ischaemia and infarction of the downstream myocardium. We reported the case of an occult MI in a middle-aged man with high ASCVD risk who presented with an unusual underlying aetiology.

The IgG4-RD has been identified only recently.³ Evidence suggesting systemic damage, elevated serum IgG4 levels, and typical pathological features are required for establishing the diagnosis of IgG4-RD.⁸ Diagnosing IgG4-PAO/PA is challenging because not only is coronary artery involvement not included in the current diagnostic criteria,⁸ but also systemic damage that confirms the diagnosis may not be present as the underlying disease might not have

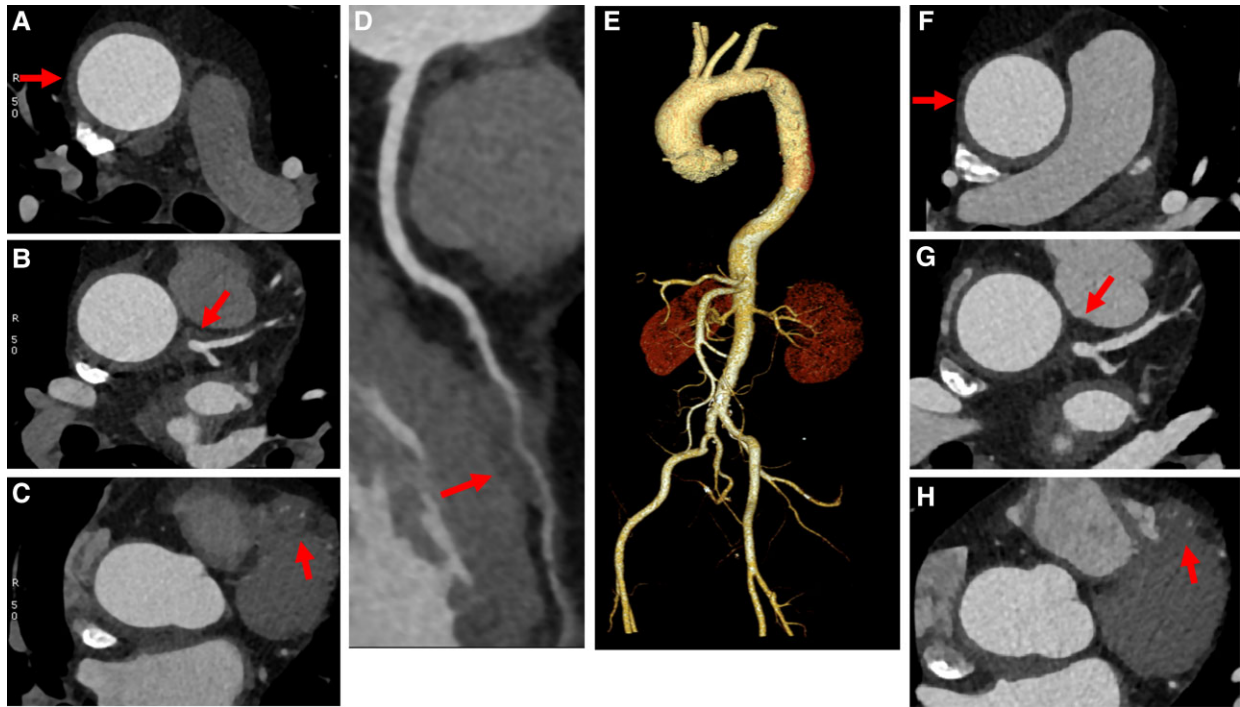


Figure 2 Coronary computed tomography angiography revealed soft-tissue density masses wrapping (A) aortic root, (B) left-main coronary artery, and (C, D) distal segment of the left anterior descending artery. Throughout atherosclerotic lesions can be seen on peripheral arteries and other segments of the aorta (E). Coronary computed tomography angiography at 3 months follow-up showed the aortic wall was a little thinner (F, G), while the pericoronary mass remained (H).

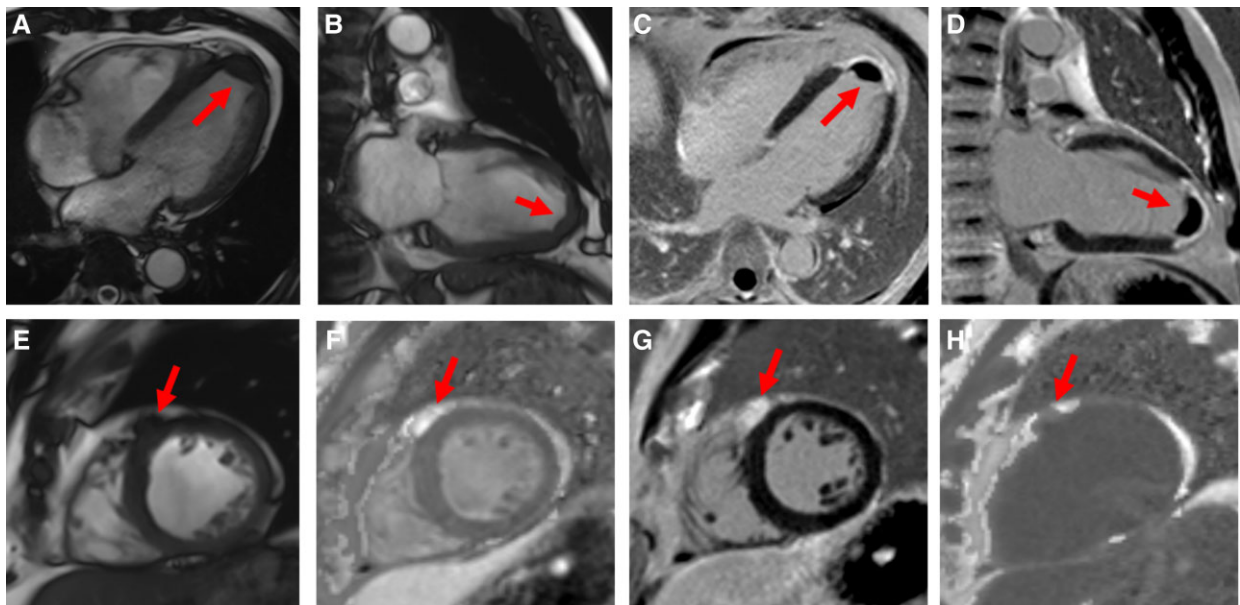


Figure 3 Cardiac magnetic resonance imaging. (A, B) Cine sequence and (C, D) late gadolinium enhancement sequence showed perfusion defect inside the left ventricle and transmurular enhancement at the left apex, indicating transmural infarction and thrombus formation. An abnormal mass surrounding the left anterior descending artery was identified. The mass had obscure boundaries on (E) cine sequence, significant enhancement on (F) late gadolinium enhanced sequence, high signal on (G) water-only mDixon sequence, and low signal on (H) fat-only mDixon sequence. These indicated an inflammatory lesion.

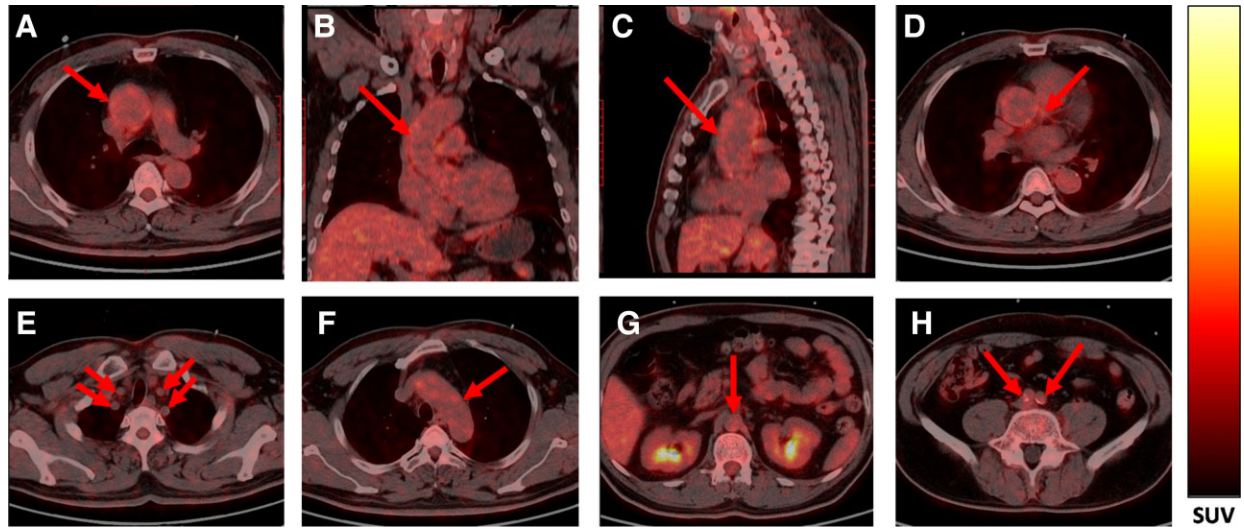


Figure 4 Positron emission tomography/computed tomography showed a higher maximum standard uptake value of (A–C) ascending aorta (3.1) and (D) ostium of the left main artery (3.3) vs. average standard uptake value of the liver (2.7). Maximum standard uptake value of (E) carotid arteries and subclavian arteries (1.8–2.0), (F) aortic arch (2.1), (G) abdominal aorta (1.6–2.7), and (H) common iliac arteries (1.9–2.1) were all lower than the average standard uptake value of the liver.

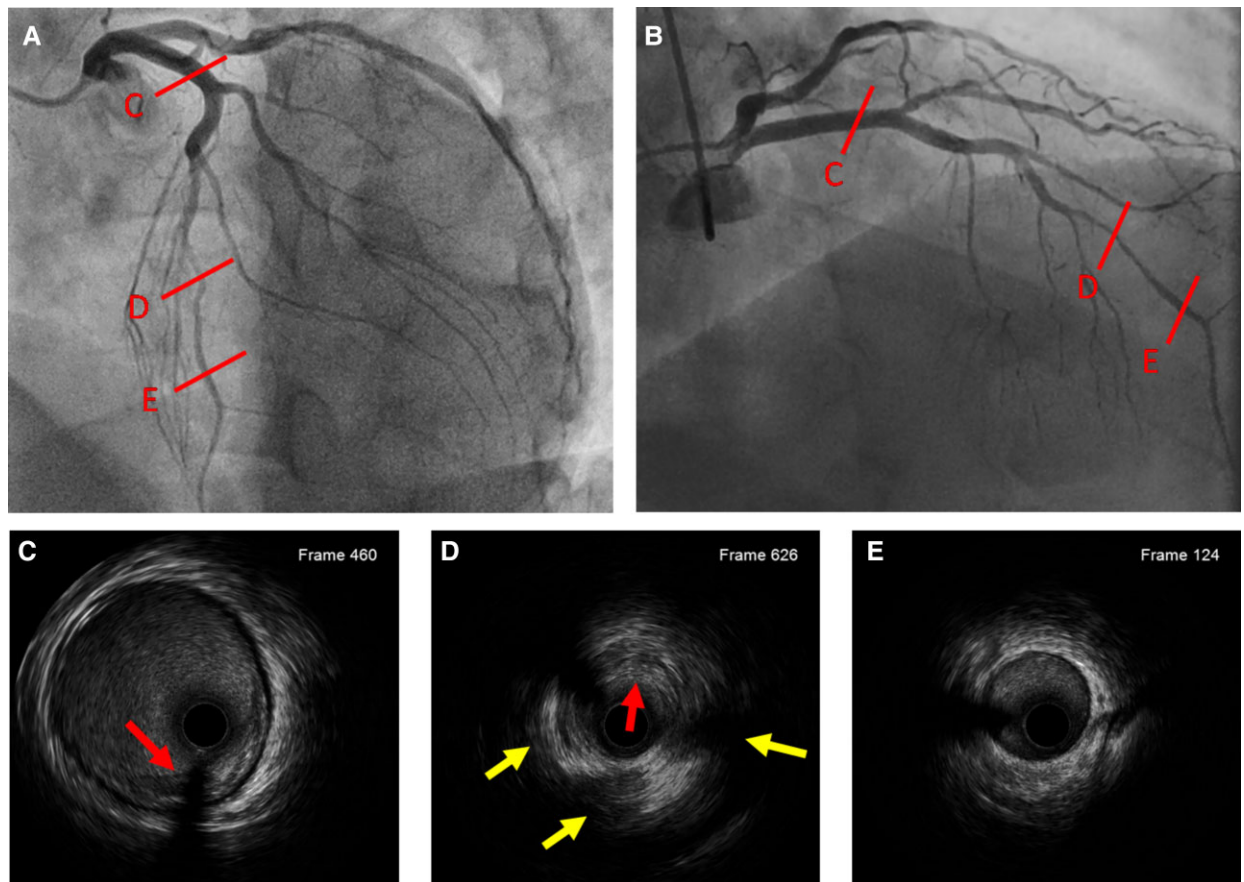


Figure 5 (A, B) Coronary angiography showed 80% stenosis at the distal segment of the left anterior descending artery. (C–E) Intravascular ultrasound showed diffuse fibroatheroma (red arrow, inside the lumen) along left anterior descending and low echoic regions (yellow arrow, outside the lumen) in the media/adventitia of the distal segment.

developed adequately. Furthermore, the serum levels of IgG4 may be normal in 3–45% of patients³; although higher serum IgE levels can be observed in 30–40% of patients and correlate with disease activity, this observation lacks diagnostic specificity.⁹ More importantly, obtaining a coronary artery biopsy sample is nearly impossible, particularly when surgical intervention is not indicated.

Although we could not establish a confirmed diagnosis because of the above-mentioned challenges, IgG4-RD was the preferred diagnosis based on several characteristic imaging findings. For instance, characteristic CT findings include substantially and circumferentially thickened aortic/artery wall and homogeneous enhancement in the later phase and PET/CT scan provide information on inflammatory processes that aid in distinguishing the lesion from other lesions formed due to ASCVD.¹⁰ Although, to our best knowledge, the MRI features of coronary lesions have not yet been reviewed systematically, summary MRI manifestations of IgG4-related retroperitoneal fibrosis, namely, that the mass is hypo/isointense on T1-weighted axial imaging and hyperintense on T2-weighted axial imaging, with intense contrast enhancement and high diffusion-weighted imaging signal, can be used as reference.¹¹ Several studies have reported the OCT findings of IgG4-related coronary lesions to be a layered signal pattern with microchannels, and IVUS findings of hypoechoic or isoechoic regions in the media of the involved vessel.^{12–14} However, these features of intracoronary images should be investigated further before they are used in the diagnosis of IgG4-PA.

Although the efficacy of corticosteroid therapy has been demonstrated in several registries of IgG4-RD and IgG4-PAO/PA,^{2,4,6} similar studies including patients with coronary involvement are rare. A review of 27 cases of IgG4-related coronary arteritis revealed that 33% of the patients had unfavourable outcomes such as disease progression and relapse.⁵ Pre-treatment stenosis and/or aneurysms are associated with disease progression.⁵ These findings support our patient's poor response to corticosteroids.

Previously studies^{12,15} have recognized coronary artery involvement mostly in patients who had already been diagnosed with IgG4-RD; however, performing CAG was reasonable in our case because of sufficient evidence for a previous MI and no indications of a systemic disease; this would have led to a diagnosis of ASCVD. Thus, CCTA and PET/CT provided valuable information that helped us establish an alternative diagnosis and avoid consequent sequelae such as irreversible stent implantation.

Early stage localized vasculitis may be frequently misdiagnosed; this 'rare disease' may not be as rare as expected. Thus, new organ-specific diagnostic criteria are urgently required to facilitate diagnosis and improve our understanding of this disease.

Conclusion

We reported a case of possible IgG4-PAO/PA with involvement of the aortic root and left coronary artery, wherein the patient presented with an occult MI. We could not confirm the diagnosis because of gaps in the current diagnostic criteria, lack of systemic damage, negative laboratory tests, and challenges associated with tissue biopsy. Nevertheless, we reported characteristic imaging findings that indicated an inflammatory disease rather than atherosclerosis.

Localized vasculitis should be considered even in patients presenting with classic ASCVD.

Lead author biography



Dr Xiaoyan Liu is a cardiologist and interested in complicated cases. She graduated from Peking University Health Science Center & Peking University First Hospital, China and got her bachelor's degree and doctorate. Now she is a third year trainee for cardiology specialist at Fuwai Hospital, Chinese Academy of Medical Sciences.

Supplementary material

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

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Slide set: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary material.

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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