Case Report
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Giant Coronary Artery Aneurysm with Thrombosis Complicated in a Patient with Idiopathic Hypereosinophilic Syndrome

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Idiopathic hypereosinophilic syndrome (iHES) is a rare systemic disease that is characterized by persistent peripheral eosinophilia (absolute eosinophil count ≥1500/uL) for more than 6 months, with end-organ damage and absence of a primary cause for eosinophilia. Coronary artery aneurysm (CAA) is a rare but life-threatening complication. Here, we report a case of CAA with thrombosis in a patient with iHES in whom the disease activity was well-controlled (eosinophil count <500/uL) for several years. Despite modest control of the disease activity, giant CAA can be associated with iHES; and therefore, close surveillance and monitoring for the development of complications is warranted.

Key Words: Eosinophilia, hypereosinophilia, hypereosinophilic syndrome, coronary artery aneurysm

INTRODUCTION

Idiopathic hypereosinophilic syndrome (iHES) is a rare systemic disease entity of hypereosinophilia. It is characterized by persistent peripheral eosinophilia (blood eosinophil count ≥1500/uL for more than 6 months), with end-organ damage and absence of a primary cause for eosinophilia.[1] Although any organ can be involved, cardiovascular manifestations are the major source of morbidity and mortality in iHES.[2] Cardiovascular manifestations classically include endomyocardial fibrosis which leads to subsequent congestive cardiac failure, atrioventricular (AV) valvular dysfunction or increased thrombotic tendency.[2] Coronary artery aneurysm (CAA) is a rare but life-threatening complication.[2,3] Here, we present a case of a patient who developed CAA with thrombosis despite well-controlled iHES with immunosuppressant. Written informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

CASE REPORT

A 61-year-old male patient with iHES presented with chest discomfort that developed 3 days ago. In 2009, this patient was referred to our center for persistent hypereosinophilia with fingertip necrosis in both hands (right second and left third finger). He had no previous history of asthma or recurrent sinusitis. Upon evaluation for eosinophilia, there were no abnormal findings in lung parenchyma or airway in enhanced chest computed tomography (CT), and the patient had no peripheral neuropathy on nerve conduction study. The patient had no clinical signs of a systemic vasculitis, and autoantibody test results were all negative, including fluorescent anti-nuclear antibody (FANA) and serum anti-neutrophil cytoplasmic antibodies (ANCA). The patient underwent bone marrow biopsy,

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but no PDGFRB nor PDGFRA rearrangement was found. He was otherwise healthy, without any family history of genetic disorder. The patient was diagnosed with iHES, and fingertip necrosis was considered a thrombotic complication of uncontrolled hypereosinophilia.

The patient was treated with oral corticosteroid afterwards, and blood eosinophil counts gradually decreased in response to steroids but increased whenever steroid tapering was attempted; thus, oral azathioprine was added for steroid-salvaging purpose while the patient was continuously taking prednisolone 12.5 mg every other day (equivalent to 6.25 mg every day). The patient visited the outpatient clinic regularly every 3 to 6 months during the 12 years of follow-up and for recent 2 years, and had maintained a blood eosinophil count of less than 500/μL.

When this patient visited the emergency room in 2021, he had chest discomfort that had developed 3 days ago. His vital signs were stable without fever, and he still had no clinical signs or features or laboratory results suggestive of vasculitis or other immunological disorder. The patient's lab results were as follows: total leucocyte count of 9.41×10^3/μL (reference range 3.8×10^3/μL to 10.58×10^3/μL) with 0.7% eosinophils (absolute eosinophil count 50/μL, reference range 0 to 500/μL), erythrocyte sedimentation rate 21 mm/hr (reference range 0 to 27 mm/hr), C-reactive protein 4.18 mL/dL (reference range 0 to 0.5 mL/dL), CK-MB 107 ng/mL (reference range 0 to 4.87 ng/mL), Troponin T 3.620 ng/mL (reference range 0 to 0.014 ng/mL), and NT-proBNP 706 pg/mL (reference range 0 to 222 pg/mL). An electrocardiogram had ST-segment elevation in leads II, III, and aVF with second-degree AV block (Mobitz type I). Under suspicion of acute infero-posterior wall infarction, emergent coronary angiography was performed. The proximal right coronary artery (RCA) was totally occluded, and the wire could not proceed into the artery during the coronary intervention. On echocardiogram, there was a round 4.6×9.4-cm-sized mass adjacent to the right atrium and right ventricular junction that was compressing the right atrium. Coronary CT angiography (Fig. 1) and cardiac magnetic resonance imaging (MRI) (Fig. 2) revealed a thrombosed aneurysm of 5.0×8.2 cm in the mid-RCA. Due to the large size, and as the thrombosed coronary aneurysm was suspected to cause bradycardia by compressing the conduction system, RCA aneurysmectomy and coronary artery bypass were performed. A muddy thrombus was found inside the aneurysm. Histopathologic examination

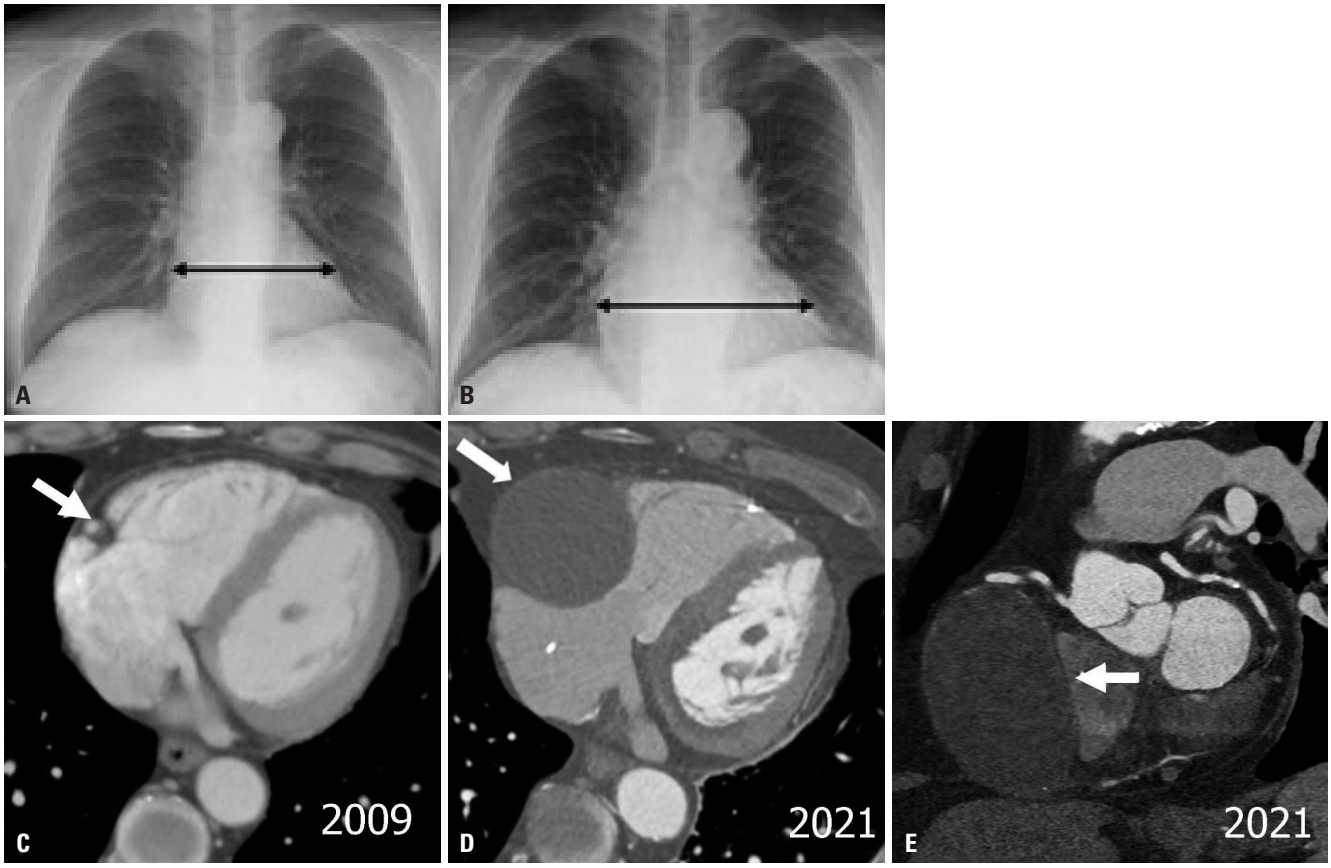

Fig. 1. Development of CAA with thrombosis in a patient who was treated for iHES for 12 years. Chest X-rays (A) at the time of iHES diagnosis in 2009 and (B) during follow-up in 2017 with increased cardiac width in black arrows. (C) Enhanced axial CT angiographic images of RCA (white arrow) at the time of iHES diagnosis and (D) when CAA with thrombosis in RCA (white arrow) was detected in 2021. (C) Initial chest CT image showed enhanced wall thickening of RCA and (D), (E) coronary CT angiography which performed after 12 years demonstrated huge thrombosed aneurysm of RCA (white arrows). CAA, coronary artery aneurysm; CT, computed tomography; iHES, idiopathic hypereosinophilic syndrome; RCA, right coronary artery.

did not show any signs of active vasculitis or eosinophilic infiltration. Follow-up autoantibody test results, such as FANA or ANCA, were still negative as initially tested 12 years ago. The patient successfully recovered without developing any immediate complications, and was discharged after 1 week of postoperative manage.

DISCUSSION

CAAs is a very uncommon condition that is defined as dilatation of the coronary artery exceeding 50% of the reference vessel diameter. CAA may occur due to several rare diseases, including infections (septic emboli, syphilis, and mycotic aneurysms), vasculitis (Takayasu arteritis, giant cell arteritis, polyarteritis nodosa, granulomatosis with polyangiitis, and eosinophilic granulomatosis with polyangiitis), genetic diseases (Loeys-Dietz syndrome, Marfan syndrome, and Ehlers-Danlos syndrome), or other immunological diseases (Kawasaki disease, IgG4-related disease, and hyper-IgE syndrome).[4] CAA associated with HES has also been previously reported,[3,5] either being presented with CAA before being diagnosed with iHES,[5] or has been recently diagnosed with iHES.[3] Eosinophilic infiltrations have been implicated in the development of de novo coronary aneurysms.[5] It has been proposed that cytotoxic substances are released from perivascular eosinophils and result in direct medial destruction, predisposing the body to aneurysm formation.[6-8]

Our patient is a rather peculiar case in that he was already diagnosed with iHES more than 10 years ago and CAA occurred while the disease activity of iHES was relatively well-maintained, without eosinophilic infiltration. Despite that the disease activity of iHES was considered to be well-controlled in our patient, as his blood eosinophil count maintained less than 500/μL for the most of the follow-up period, his eosinophil counts had been relatively higher (500 to 1500/μL) than usual for about 8 months in 2017 (Fig. 3). Serial review of the chest X-ray images showed right hilar enlargement since this spike of eosinophil count (Fig. 1). Although the pathophysiological mechanism is unclear, it can be assumed that the hypercoagulability of eosinophils may have contributed to the development of de novo CAA and thrombosis when the blood eosinophil levels were temporarily increased, and then progressed into a giant thrombosed CAA. This suggests that close monitoring and controlling the blood eosinophil level may be required even when a patient is stable without symptom.

Cardiovascular complications of HES has the worst prognosis and is responsible for a high rate of fatal outcome.[9] Thromboembolic disease associated with HES is also particularly difficult to control.[2] High-dose corticosteroid is used to control eosinophilia, and revascularization options including percutaneous coronary intervention and coronary artery bypass should be considered in symptomatic patients. Surgery is especially

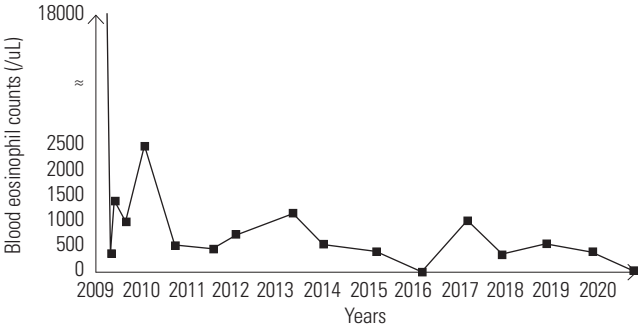

Fig. 3. Change in blood eosinophil counts since the diagnosis of iHES to the detection of RCA aneurysm with thrombosis. iHES, idiopathic hypereosinophilic syndrome; RCA, right coronary artery.

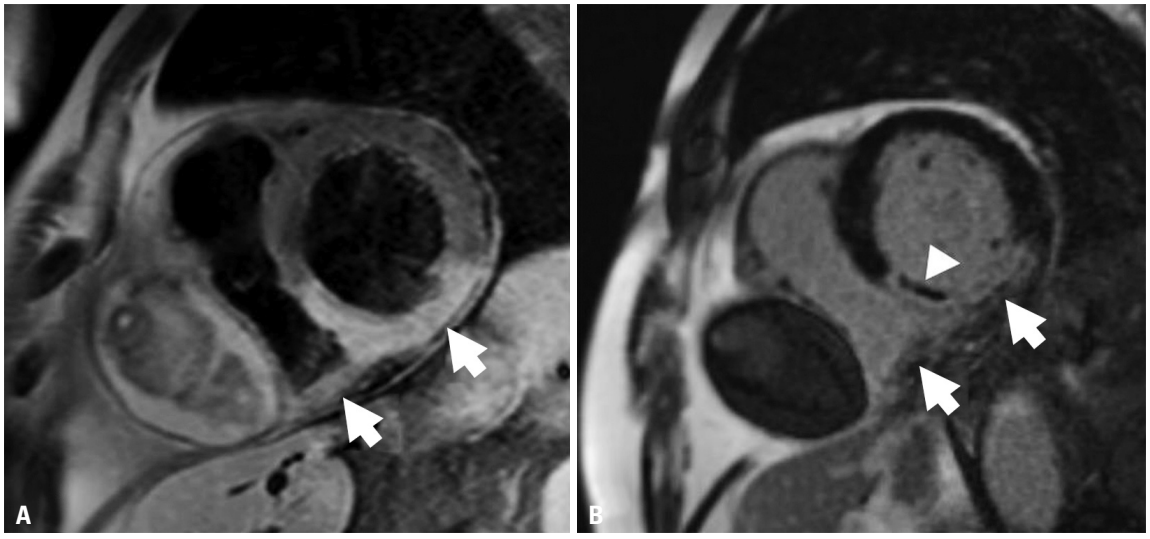

Fig. 2. Cardiac magnetic resonance images of RCA aneurysm with thrombosis. (A) T2-weighted black-blood image showed edema in the inferior wall of both ventricles (white arrows). (B) Late gadolinium enhancement image demonstrated myocardial infarction of RCA territory (white arrows) with microvascular obstruction (white arrowhead). RCA, right coronary artery.

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appropriate in patients with obstructive coronary artery disease or evidence of embolization leading to myocardial ischemia, as well as in patients with coronary aneurysm at risk of rupture.

In summary, despite modest control of the disease activity, giant CAA can be associated with iHES; and therefore, close monitoring is warranted for the surveillance of complications.

AUTHOR CONTRIBUTIONS

Conceptualization: Dong-Chull Choi Data curation: Noeul Kang. Investigation: all authors. Methodology: Duk-Kyung Kim, Kiick Sung, and Dong-Chull Choi. Visualization: all authors. Writing—original draft: Noeul Kang. Writing—review & editing: all authors. Approval of final manuscript: all authors.

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