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Case Report

Pulmonary and coronary arterial abnormalities in patients with IgG4-related disease ☆,☆☆

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ABSTRACT

IgG4-related disease (IgG4-RD) is an immune-mediated multiorgan fibroinflammatory disorder with variable clinical presentations. IgG4-RD cardiovascular involvement is considered rare, with pulmonary arterial involvement reported in a small subset of cases. Known pulmonary artery manifestations include pulmonary arteritis, pulmonary artery stenoses and central pulmonary artery aneurysms. Here we report 2 different patients with multifocal dilatation of the segmental and subsegmental pulmonary arteries with differing degrees of severity. Both patients also had coronary arterial abnormalities.

Introduction

IgG4-related disease (IgG4-RD) is a fibroinflammatory disorder characterized by lymphoplasmacytic infiltrates and storiform fibrosis with heterogeneous presentation [1]. Originally described in patients with sclerosing pancreatitis for whom elevated serum IgG4 concentrations were detected [2], the disease is now known to represent a complex multiorgan condition. Pulmonary manifestations of IgG4-RD are variable and include masses, nodules, consolidation, ground glass opacities, interstitial abnormalities, bronchiectasis, or bronchial wall thickening [3]. Cardiovascular involvement is less common and often first revealed as an incidental finding in the extensive diagnostic imaging that is usually performed in patients with suspected IgG4-RD [4,5]. Most reports of coronary artery involvement have described perivascular soft tissue encasement with or without aneurysm. Recognition of coronary artery involvement is very important, as nearly half of patients experience complications of myocardial ischemia [6]. There

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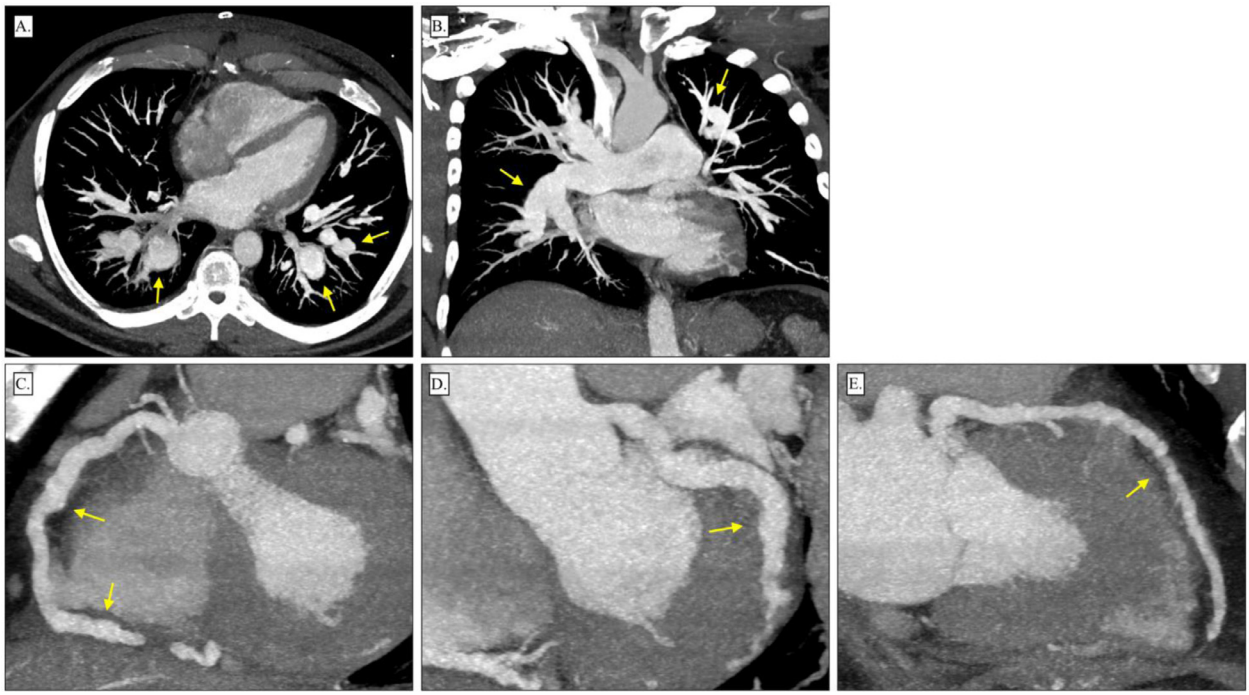

Fig. 1. (– A and B) Axial and coronal maximum intensity projection images from a contrast-enhanced chest computed tomography for patient 1 demonstrating multiple fusiform and saccular segmental and subsegmental pulmonary artery aneurysms (arrows). (C-E) 3D reformatted images from a contrast-enhanced prospectively gated cardiac CT images of patient 1 demonstrating the (C) right coronary, (D) left circumflex, and (E) left anterior descending arteries. There is diffuse ectasia of the coronary arteries with multifocal narrowing and dilatation, resulting in an extensive beaded appearance. Segmental regions of mild perivascular soft tissue thickening are also present (arrows).

are several distinct pulmonary vascular IgG4-RD associations including pulmonary arterial hypertension [7,8], pulmonary artery aneurysms and pulmonary arterial stenosis [9]. However, few publications describe IgG4-RD cases with pulmonary arterial involvement, with descriptions limited to central pulmonary arterial enlargement. Here we report 2 IgG4-RD patients with coronary artery abnormalities and multifocal ectasia and aneurysmal dilatation involving the segmental and subsegmental pulmonary arteries.

Case report

Patient 1

A 55-year-old male with a history of essential hypertension, hypercholesterolemia, chronic kidney disease, submandibular gland enlargement, and undulating eosinophilia was referred to rheumatology for further workup of suspected IgG4-RD after initial studies demonstrated elevated IgG4 levels and a renal biopsy revealed chronic active interstitial nephritis with severe predominantly storiform fibrosis. Initial laboratory studies revealed elevated IgG4 level (207.3 mg/dL; normal 3.9-86.4) and upper limit of normal serum IgG level (1288 g/dL; normal 614-1295). At presentation his eosinophil level was within normal limits. A contemporaneous multi-detector computed tomography (CT) of the thorax revealed aneurysmal dilatation of the main pulmonary artery and bilateral, multifocal segmental pulmonary artery aneurysms. Non-vascular pulmonary findings included scattered solid nodules and hilar and mediastinal lymphadenopathy. The patient experienced periods of dyspnea with exertion that appeared to improve with glucocorticoids. Neither pulmonary function testing nor estimates of the pulmonary artery pressures were performed. Transthoracic echocardiogram demonstrated a normal left ventricular ejection fraction. Vascular findings from a recent cardiac gated CT revealed a main pulmonary artery measuring up to 4.4 cm, multifocal dilatation of the segmental and subsegmental pulmonary arteries (Figs. 1A and B), and diffuse irregularity of the coronary arteries with a “beaded” appearance (Figs. 1C-E).

Patient 2

A 68-year-old male with a history of hypertension, eczema, dacryoadenitis, asymptomatic paroxysmal atrial fibrillation, non-invasive imaging demonstrating severe multivessel cardiovascular disease with a remote myocardial infarction, and a long-standing diagnosis of IgG4-RD. He was treated with rituximab soon after diagnosis, but discontinued the medication due to serum sickness. Glucocorticoids were administered on a chronic basis, supplemented by high-dose glucocorticoid pulses during disease flares. The patient was treated briefly with a novel tyrosine kinase inhibitor as part of a clinical trial before resuming glucocorticoids due to further wors-

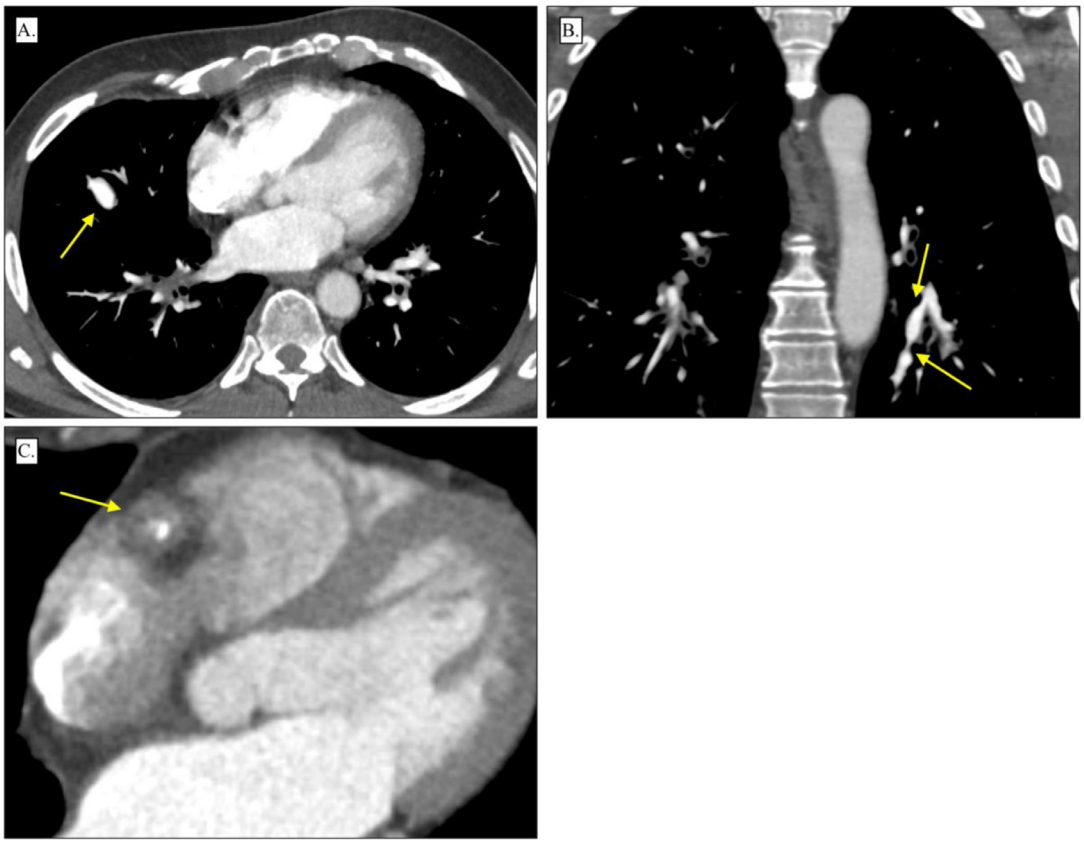

Fig. 2 – Contrast-enhanced chest computed tomography images for patient 2. Axial and coronal images demonstrate subsegmental pulmonary arterial dilatation (arrows) within the right middle (A and B) and lower lobes. Other less conspicuous foci of dilatation not shown. (C) Contrast-enhanced chest computed tomography images for patient 2 show soft thickening around the right coronary artery (arrows).

ening of disease burden as evidenced by imaging findings and increased serum immunoglobulin levels, including IgG (2765 mg/dl; normal 614-1295), IgG4 (1770.8 mg/dl; normal 3.9-86,4), and IgE (1695 IU/ml; normal 0-100).

Transthoracic echocardiography demonstrated apical left ventricular dysfunction and an ejection fraction of 49%. Contrast-enhanced CT of the thorax demonstrated increased multifocal segmental pulmonary artery dilatation and wall thickening with surrounding soft tissue (Figs. 2A and B) and soft tissue surrounding the right coronary artery with wall thickening and dilatation (Fig. 2C). Aside from mild dyspnea on exertion, the patient reported no symptoms of respiratory disease or underwent pulmonary function testing. Non-vascular signs of pulmonary disease on CT included scattered solid nodules, bronchial wall thickening and hilar and mediastinal lymphadenopathy.

Discussion

IgG4-related disease is an immune-mediated systemic disease with varying clinical presentations resulting from fibroinflammatory inflammation of numerous organs. IgG4-RD is more commonly found in males older than 60 years of age, in contrast to many other autoimmune disorders that have a predilection for younger females. Vascular involvement is less common, but typically results in inflammatory aortitis and periaortitis; imaging often shows perivascular soft tissue thickening, and histopathologic analysis typically demonstrates inflammatory changes in the adventitia [10]. Involvement of both the thoracic and abdominal aorta has been described in IgG4-RD [11,12]. In one report, IgG4-RD vasculitis was associated with 50% of inflammatory abdominal aortic aneurysms treated surgically [13]. Cases of medium vessel arteritis have described involvement of the mesenteric arteries, vertebral, carotid and coronaries. Coronary artery involvement manifests as perivascular soft tissue thickening and, in a subset of cases, aneurysmal dilatation [6]. Coronary artery fistulas are exceedingly rare, described in one report of an IgG4-RD patient with a coronary-pulmonary artery fistula [14]. It is critical for diagnostic radiologists to recognize coronary artery involvement in confirmed or suspected IgG4-RD patients as nearly half (48%) of reported cases demonstrate complications associated with myocardial ischemia/infarction [6].

Pulmonary arterial involvement is rarely described, and reported cases describe pulmonary artery stenosis and pulmonary arterial hypertension [7,8]. The 2 cases presented here had varying degrees of main, segmental, and subsegmental pulmonary artery dilatation and perivascular soft tis-

sue thickening. The multifocality of pulmonary arterial involvement in these patients appears to be a novel manifestation of IgG4-RD. Non-vascular thoracic manifestations are varied, ranging from mediastinal and hilar lymphadenopathy to solid parenchymal nodules, ground glass opacities, bronchial wall thickening and interlobular septal thickening [3,15]. In 2 cohort studies of IgG4-RD patients, lung disease has been described in up to 23% of patients [16,17]. Both patients presented reported dyspnea on exertion, but no formal pulmonary function testing was available. They also manifested similar non-vascular thoracic findings including scattered solid nodules and lymphadenopathy.

In summary, imaging evaluation will continue to be an important part of the diagnostic workup for patients with IgG4-RD [5,10,18], given the inherent risk of vascular biopsy. Further work is needed to determine the prevalence and clinical significance pulmonary and coronary arterial involvement in IgG4-RD.

Patient consent

Written informed consent for publication of the described cases was obtained from both patients.

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