

Peer Review File

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Reviewer A

I would like to thank the authors for this good work.

The authors reported a case of coronary and pulmonary artery involvement in a patient suspected of having IgG4-RD. This case report was interesting in concomitant involvements of coronary and pulmonary arteries, which were rare. A literature review of domestic cases would also be useful to domestic physicians.

However, I found several issues that should be clarified before further consideration for the publication. Particularly, the process of diagnosis was confusing and was not convincing. I explained this in the comments below.

[Major comments]

[Case report]

I personally would agree that this patient might be IgG4-RD. Authors should be asked to explain a more detailed process of diagnosis because this was a rare and atypical case of a rare disease.

#1. While I understood the main manifestations of this patient were cardiopulmonary symptoms, IgG4RD was a systemic inflammatory disease that required systemic evaluation. Did the patient have other organ involvement? What did the authors perform for the systemic evaluation? And, please mention the existence or absence of at least typical organ involvements in the 2019 ACR/EULAR criteria. In addition, please briefly clarify whether the patient had a fever and other features included in the exclusion criteria of 2019 ACR/EULAR or not in the manuscript.

Reply 1:

The patient had no other organ involvement, no fever during the course of the disease, and no other features included in the 2019 ACR/EULAR exclusion criteria.

Changes in the text: we added some data :

The patient had no fever during the course of the disease. The blood routine test showed WBC $7.51 \times 10^9/L$, Hb $91g/L$, PLT $390 \times 10^9/L$, EO $0.01 \times 10^9/L$. ANA was positive with the titer of 1:100, while anti-dsDNA、anti-SSA、anti-SSB, anti-Sm、anti-U1RNP and ANCA antibodies were negative. Ultrasound of salivary glands, including parotid and submandibular glands showed no obvious abnormalities. Ultrasound of superficial lymph nodes showed no clear abnormal enlarged lymph nodes. The test of Chest CT showed widening of pulmonary artery, thickening of pulmonary trunk, left and right pulmonary artery and ascending aorta wall, which indicated further clinical and aortic CTA examinations were recommended. There was no abnormality on abdominal CT. (see Page 3, line 48-62)

#1-1. If the patients had other organ involvement, please clarify why a biopsy could not be done.

#2 The authors mentioned they used the 2019 ACR/EULAR criteria. Based on the information in this report, the patient would not be classified as IgG4-RD. Please note that lesions in ascending aorta were not typical and should not be scored. Please mention which inclusion criteria (scores) the patient fulfilled except for IgG4 titers. I guess the patient had other organ involvement.

Reply 1 and 2:

No other organs were found to be involved.

#3 If the patient was not classified as IgG4RD by ACR/EULAR criteria, authors might use the diagnostic criteria for peri-arteritis (Mizushima, et al. Clinical and pathological characteristics of IgG4-related periaortitis/periarteritis and retroperitoneal fibrosis diagnosed based on experts' diagnosis. Annals of Vascular Diseases Vol. 12, No. 4 (2019))

Reply 1: According to the diagnostic criteria of IgG4-related periarteritis, this patient was diagnosed as possible IgG4-related periarteritis.

Changes in the text: (see Page 4, line 85)

#4 If your patient had other organ involvement and fit a definite diagnosis, please skip this comment. But if your case was diagnosed as possible IgG4-RD, I recommend that authors should use less definite words on the diagnosis of IgG4RD in your manuscript. It would be better to use possible IgG4-RD through your manuscript.

Reply 2:

I agree that this patient was diagnosed as a possible IgG4-RD, and make revisions in the paper.

Changes in the text: Change the diagnose of IgG4-RD to possible IgG4-RD(see Page 4, line 85, Page8, line150-152)"

[Discussion]

#1 Line 106-

IgG4 periarterial diseases were usually classified into wall-thickening, stenosis, and aneurysm based on the previous literature (e.g., please check reference No 16 Takanori I, et al). I recommend that authors follow this classification and discuss whether coronary artery findings in the patients were compatible with the typical imaging features of IgG4-related periarteritis.

Reply 1: Agree with the above classification, which has been changed in the article.

Changes in the text: (see Page 7, line 129-132)

#Line 120-

I agree that biopsies were often difficult in patients with isolated aortitis or coronary periarteritis. Which differential diagnoses should be carefully considered in patients with ascending aortitis with or without coronary or pulmonary artery involvement, particularly when biopsies are difficult? Please discuss the differential diagnosis in the case report or in the discussion.

Reply 1:

This patient is involved in coronary arteries, and the identification with coronary atherosclerosis is necessary : both of them may show coronary stenosis and elevated inflammatory indicators, but coronary atherosclerosis does not form aneurysms, and IgG4

levels and biopsy results can be used as the main basis for identification. In addition, it needs differential diagnosis of IgG4-RD with giant cell arteritis and Takayasu arteritis: the latter two mainly affect the thoracic aorta and primary branches of the aorta, especially the subclavian artery. Pathologically, IgG4-associated vasculitis is less likely to involve the outer membrane, whereas giant cell arteritis usually involves severe thickening of the outer membrane due to the role of inflammatory mediators.

Changes in the text: we added differential diagnosis. (see Page 8, line 152-161)

[Minor comment]

#1 There were several typos and inappropriate spacing in the manuscript. Please check and revise.

Reply 1: Typos and inappropriate spacing in the manuscript have been modified in the manuscript.

Reviewer B

This case is a rare case of IgG4-related arterial disease in which the coronary and pulmonary arteries are simultaneously affected, and the use of multiple imaging modalities allowed for appropriate diagnosis and therapeutic intervention.

Below are some comments on the paper.

Comment 1. It would be helpful to see echocardiographic images of the mass around the aorta and pulmonary artery and the coronary artery compression and stenosis, etc., which were supposedly confirmed by the echocardiogram.

Reply 1: In this case, cardiac ultrasound abnormalities were also first detected.

Changes in the text: see Page1, line12-14; Page3, line62-71;

Comment 2. How about the status of the disease in other organs, including lacrimal gland, salivary gland, pancreas, retroperitoneum, etc. are the most common target organs of IgG4-related diseases.

Reply 1: No other organs were found to be involved. Ultrasound of salivary glands, including parotid and submandibular glands showed no obvious abnormalities. Ultrasound of superficial lymph nodes showed no clear abnormal enlarged lymph nodes. The Chest CT showed widening of pulmonary artery, thickening of pulmonary trunk, left and right pulmonary artery and ascending aorta wall, which indicated further clinical and aortic CTA examinations were recommended. There was no abnormality on abdominal CT.

Changes in the text: we added some data: see Page3, line56-62;

Comment 3. The gold standard for the treatment of IgG4-related diseases is oral glucocorticoid. Yet, lacking is clear evidence for the treatment of coronary artery lesions.

Reply 1: The treatment of IgG4-related diseases is firstly oral glucocorticoid. And the patient got good effect after the oral glucocorticoid therapy.

Comment 4. Although glucocorticoid may be effective in controlling inflammation in perivasculitis (Yamaura H, et al. EHJ Case Reports 2022. ytac027), did the authors expect

to having stenosis in coronary artery stenotic lesions regressed? According to the report, glucocorticoid can suppress intimal thickening, which may lead to enlargement of the arterial system and thinning of the wall, resulting in an increase in the size of the aneurysm. In other reports, surgery has been used in some cases instead of drug therapy, but why was steroid therapy chosen in this case instead of surgery?

Reply 1:

Corticosteroids remain the preferred treatment for IgG4-RD patients, which can effectively control chronic inflammation around blood vessels. It has been reported that glucocorticoids can cause an increase in the size of aneurysms, but this claim remains controversial. The patient refused the suggestion of surgery and requested medical treatment. Therefore, surgery was not performed.

Comment 5. What are your plans for future follow-up after? What are the testing methods and follow-up intervals?

Reply 1: After initiation of drug treatment, longer follow-up is planned, including clinical symptoms, serum IgG4, cardiac ultrasonography and artery CT. Follow-up intervals were determined according to follow-up contents, for example, cardiac ultrasound every 3-6 months and coronary and pulmonary CTA after 1 year of treatment.

Changes in the text: see Page 5, line 89-90