Scientific Research Publishing

Case Reports in Clinical Medicine, 2024, 13, 345-352
https://www.scirp.org/journal/crcm
ISSN Online: 2325-7083
ISSN Print: 2325-7075

IgG4 Coronary Arteritis Presenting as a Cardiac Pseudo-Tumour

Elaine Mo-Chee Chau[1], Catherine Yuet-Hung Wong[2], Raymond Hin-Suen Liang[3]

[1]Cardiology Centre, Hong Kong Sanatorium & Hospital, Hong Kong SAR, China
[2]Nuclear Medicine Department, Hong Kong Sanatorium & Hospital, Hong Kong SAR, China
[3]Comprehensive Oncology Centre, Hong Kong Sanatorium & Hospital, Hong Kong SAR, China
Email: echau@hksh.com

How to cite this paper: Chau, E.M.-C., Wong, C.Y.-H. and Liang, R.H.-S. (2024) IgG4 Coronary Arteritis Presenting as a Cardiac Pseudo-Tumour. *Case Reports in Clinical Medicine*, **13**, 345-352.
https://doi.org/10.4236/crcm.2024.139042

Received: July 27, 2024
Accepted: September 1, 2024
Published: September 4, 2024

Abstract

We report on an unusual case presenting with a cardiac pseudo-tumour on echocardiogram, which corresponded to a large soft tissue mural thickening around the mid-right coronary artery. There were similar but not as thick mural lesions around other parts of the coronary arteries. The so-called "pigs-in-a-blanket" sign on computed tomography (CT) scan was pathognomonic of IgG4 coronary arteritis. The IgG4 level was grossly elevated at more than 10 times the upper limit of normal. Positron emission tomography (PET)-CT scans with ^{18}F-fluoro-deoxy-glucose (FDG) and ^{68}Ga-Fibroblast Activation Protein Inhibitor (FAPI) were performed to assess the extent of organ involvement of the IgG4-related disease. The patient was treated with 8 injections of rituximab with good serological response. However, the coronary arteritis findings on CT scan remained unchanged.

Keywords

IgG4-Related Disease, Coronary Arteritis, Cardiac Pseudo-Tumour, "Pigs-in-a-Blanket" Sign

1. Introduction

Immunoglobulin G4 (IgG4)-related disease (IgG4-RD) is a systemic immune-related condition that was first recognized in 2003 and is characterized by infiltration of IgG4-positive plasma cells and fibrosis in systemic organs and elevation of serum IgG4 levels. Approximately 1/5 of IgG4-RD patients have large vessel involvement in the form of aortitis or periaortitis [1] [2]. IgG4-related coronary arteritis cases are rare and limited to case reports and small case series [3]-[8]. Coronary arteritis may cause coronary artery stenosis or coronary aneurysms and

present clinically as congestive heart failure, acute myocardial infarction, pericarditis or sudden cardiac death. We report on an unusual case with incidental finding of a cardiac pseudo-tumour, which turned out to be isolated IgG4-related coronary arteritis and discuss the different modalities used for diagnosis and treatment.

2. Case Report

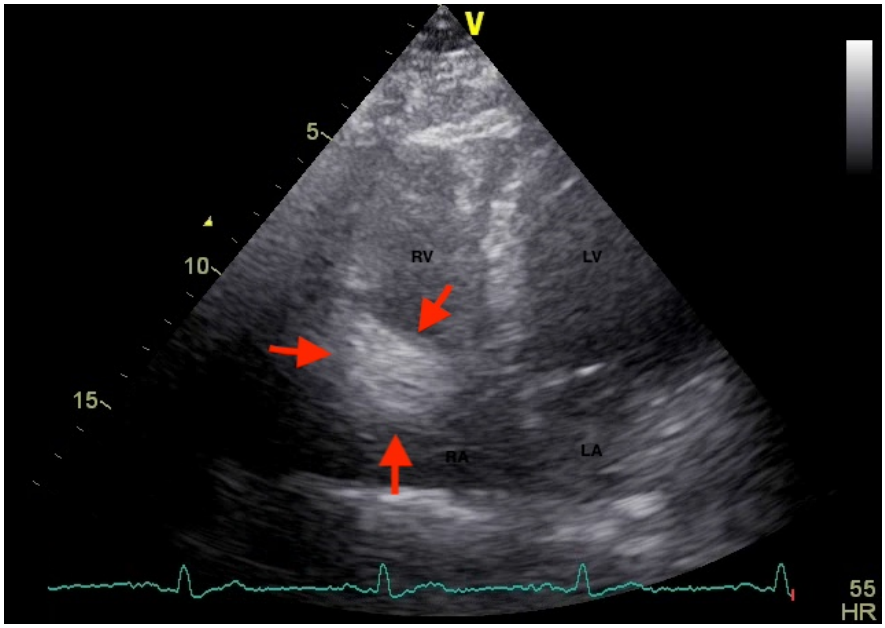

Figure 1. Four-chamber view on trans-thoracic echocardiogram showed a large cardiac pseudo-tumour (red arrows) at the right atrioventricular groove. RV = right ventricle, RA = right atrium, LV = left ventricle, LA = left atrium.

The patient was a 74-year-old Chinese male who presented with left hemiparesis due to intra-cranial haemorrhage in the right thalamus. He had history of hepatitis B carrier status, bronchiectasis and hyperlipidaemia. He was referred for echocardiogram, which showed a large solid-looking "tumour" mass (2.2 × 2.3 cm) in the right atrioventricular groove with mass effect (**Figure 1**). Magnetic Resonance Imaging scan of the heart showed a concentric mural lesion (measuring 3.2 × 2 × 2.3 cm) encasing the mid-to-distal right coronary artery (RCA) and a similar but smaller concentric mural lesion encasing the mid-left anterior descending artery (LAD). Computed tomography (CT) coronary angiogram showed non-obstructive coronary artery disease with multiple segments of concentric mural thickening around the RCA, LAD, diagonal artery and left circumflex artery (LCx), compatible with coronary arteritis. The largest lesion at mid-distal RCA had the appearance of a "pig-in-a-blanket" (**Figure 2**). Serum IgG4 level was grossly elevated at 9.85 g/L (normal range 0.04 - 0.86 g/L). The diagnosis of IgG4 coronary arteritis was made. Further assessment of the extent of the disease was performed by PET/CT scan with ^{18}F-fluoro-deoxy-glucose (FDG) and ^{68}Ga-Fibroblast Activation

Protein Inhibitor (FAPI) tracers. PET/CT demonstrated mild ^{18}F-FDG and ^{68}Ga-FAPI activity at the soft tissue densities along the LAD, RCA and LCx, suggestive of inflammation along the coronary arteries (Figure 3). A small ^{68}Ga-FAPI-avid focus at pancreatic head, suggestive of same disease involvement, was not detectable by ^{18}F-FDG scan. While the ^{18}F-FDG scan showed mild grade activity along the ascending and descending thoracic aorta and lymph nodes (non-specific findings), activity was not detectable on the ^{68}Ga-FAPI scan. Bone marrow aspirate was normal and did not show any increase in plasma cells. Despite the lack of symptoms, treatment was indicated to prevent the progression of IgG4-RD in the heart and other major organs. In view of his hepatitis B carrier status, it was decided not to give him glucocorticoid therapy. He was given 8 doses of intravenous rituximab (an anti-CD20 antibody) at 375 mg/m^2 weekly for 4 doses followed by 375 mg/m^2 once every 2 months for 4 more doses with good serological response (Figure 4). He had good recovery from his stroke and remained free from any cardiac symptoms. Repeat CT coronary angiogram after the rituximab therapy showed similar mural thickening around the coronary arteries with no change in the size of the largest pseudo-tumour around the RCA.

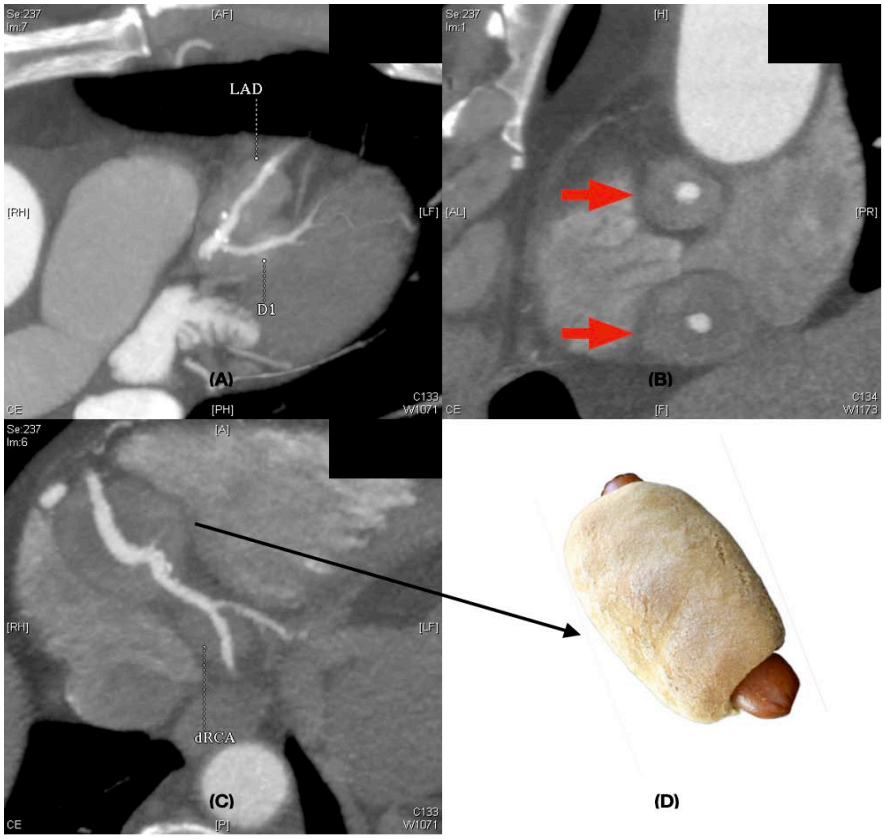

Figure 2. (A) CT coronary angiogram showing soft tissue density around the left descending artery (LAD) and first diagonal artery (D1) (B) CT coronary angiogram showing the concentric mural thickening around the proximal and distal right coronary artery, giving the appearance of pseudo-tumours (red arrows). (C) CT finding of large soft tissue density around the mid-right coronary artery looked similar to a "pig-in-a-blanket" (D).

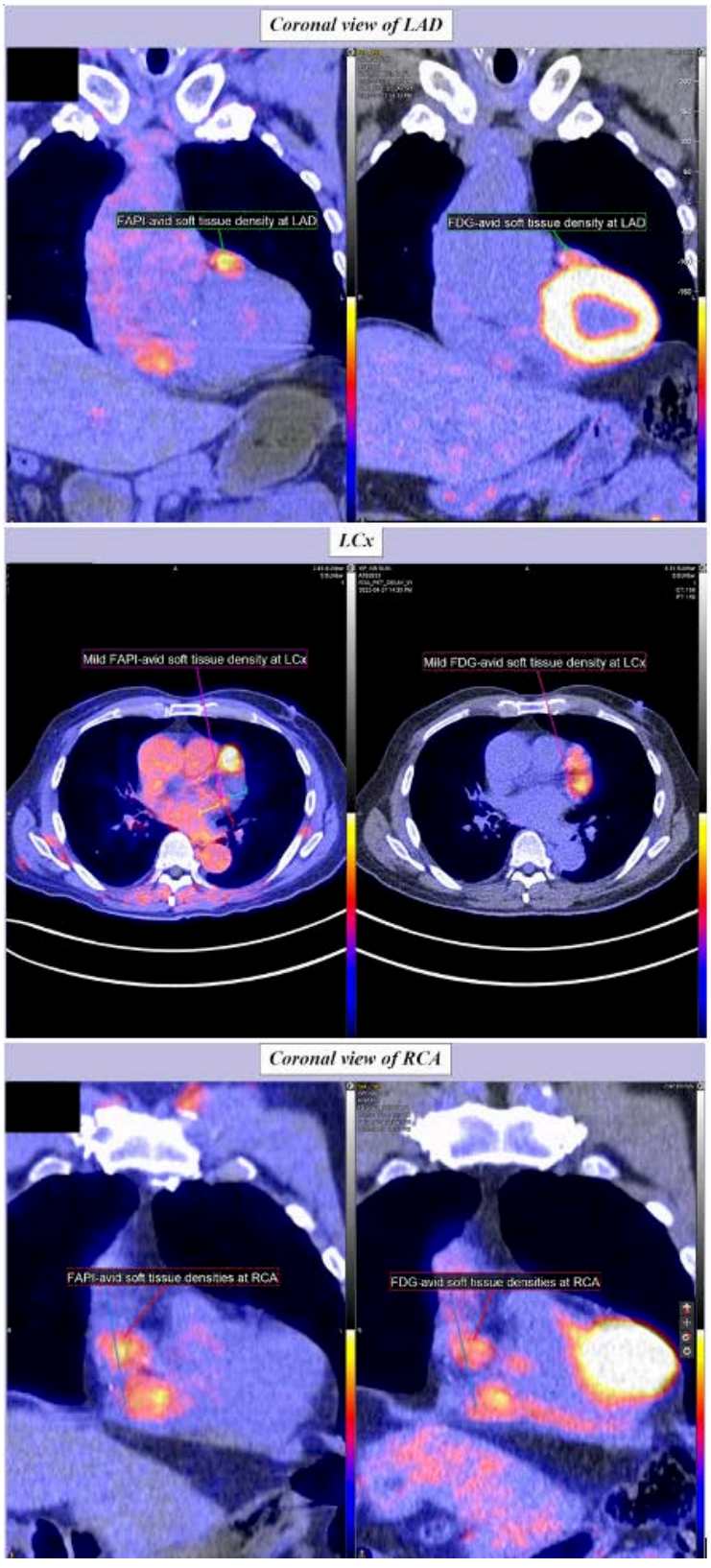

Figure 3. Corresponding ^{68}Ga-FAPI PET/CT scan images (left hand side) and ^{18}F-FDG PET/CT scan images (right hand side) of the three coronary arteries: left anterior descending artery (LAD), left circumflex (LCx) and right coronary artery (RCA).

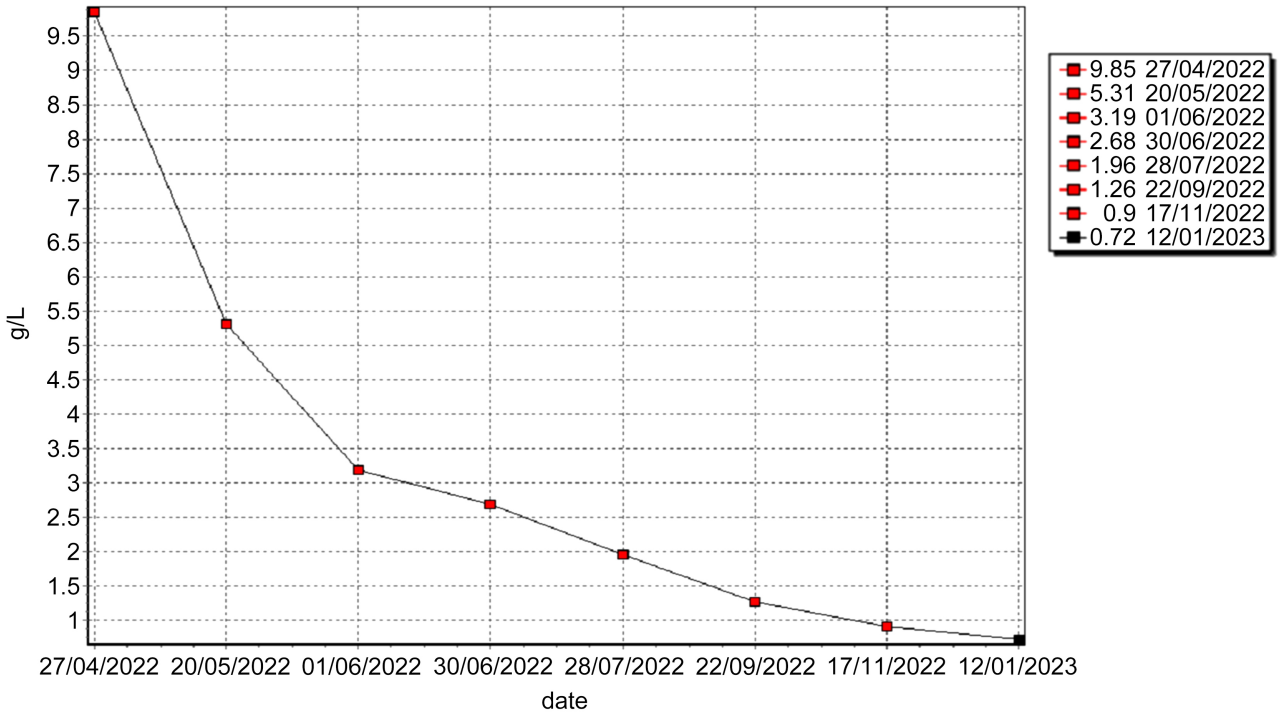

Figure 4. The serum IgG4 level fell from the initial level of 9.85 g/L (normal range 0.04 - 0.86 g/L) to 0.72 g/L after 8 doses of intravenous rituximab.

3. Discussion

3.1. Diagnosis of IgG4-Related Coronary Arteritis

IgG4-related coronary arteritis may be suspected in patients presenting with cardiac symptoms and with history of biopsy proven IgG4-related disease in other major organs, such as the pancreas, lacrimal and parotid glands [3], kidneys, orbits [4], skin, lymph nodes, etc. Biopsy of small-to-medium sized vessels to look for lymphoplasmacytic infiltration and IgG4 deposits is impossible unless the patient happens to undergo coronary artery bypass grafting [5]. Although conventional coronary angiography can detect luminal stenosis and aneurysm formation, CT angiography has the advantage in allowing direct visualization of vessel walls and mural thickening [6].

3.2. Cardiac Pseudo-Tumour

Our case was unusual in having no preceding cardiac symptoms and the IgG4-related disease seemed to be limited to the coronary arteries only. The incidental finding of the cardiac pseudotumour on echocardiogram prompted us to evaluate his cardiac condition further with MRI and CT coronary angiogram. The finding of the "pigs-in-a blanket" sign on CT scan was pathognomonic of IgG4-related coronary arteritis [7]. Unfortunately, histopathological confirmation was not available because the disease was limited to coronary arteries, which were not amenable to biopsy. However, according to the 2019 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) classification

criteria for IgG4-RD, biopsy for histopathologic confirmation is not required when the diagnosis is straightforward on the basis of clinical, serologic and radiologic findings [9].

3.3. Evaluation of the Extent of IgG4-RD

Traditionally ^{18}F-FDG positron emission tomography/computed tomography (PET/CT) is used to assess the extent of inflammation in IgG4-RD and to monitor disease activity after treatment. ^{18}F-FDG PET/CT had a sensitivity of 85.7% and specificity of 66.1% for diagnosing IgG4-RD. However, false-negative finding of ^{18}F-FDG PET was also noted in some studies [10] [11]. In IgG4-RD, fibrosis produced by the large number of fibroblasts is a major histopathologic feature. Therefore, a recently introduced PET agent targeting fibroblast activation protein, ^{68}Ga-fibroblast activation protein inhibitor (^{68}Ga-FAPI), has been used to assess IgG4-RD. Unlike ^{18}F-FDG which accumulates in cancer cells and active inflammatory lesions, ^{68}Ga-FAPI uptake is associated with the degree of fibrosis and is more specific for IgG4-RD. There is evidence that ^{68}Ga-FAPI PET/CT had a higher positive rate than ^{18}F-FDG PET/CT in the detection of IgG4-RD in the pancreas, bile duct/liver, and salivary gland [12]. In our patient, although both ^{18}F-FDG and ^{68}Ga-FAPI PET/CT showed involvement of the coronary arteritis, there were differences in tracer uptake in other organs. There was non-specific FDG uptake in the aorta and lymph nodes which were not ^{68}Ga-FAPI avid while a small ^{68}Ga-FAPI-avid focus at pancreatic head was not detectable on the ^{18}F-FDG scan. Even though pancreas is a common organ to be involved in IgG4-RD, the clinical significance of this small ^{68}Ga-FAPI-avid focus remained unclear.

3.4. Treatment of IgG4-RD

Glucocorticoid therapy is an effective treatment for IgG4-related disease but many IgG4-RD patients relapse during or after glucocorticoid taper and the long-term use of glucocorticoids may lead to undesirable side-effects such as obesity, hypertension, diabetes, osteoporosis and hyperlipidaemia, especially in elderly patients. In addition, in patients who are hepatits B carriers, like our patient, glucocorticoids may cause reactivation of fulminant hepatitis. Traditional disease-modifying anti-rheumatic drugs (DMARDs) had been used for IgG4-RD but are generally ineffective [13]. In IgG4-RD, excessive production of plasmablasts from activated CD20+ B lymphocytes together with CD4 cytotoxic T-lymphocytes is believed to be responsible for the lymphoplasmacytic infiltration, tissue damage and storiform fibrosis at sites of inflammation. B-lymphocyte depletion therapy with anti-CD20 monoclonal antibodies (Rituximab) has been shown to be effective for induction therapy and treatment of relapses in IgG4-RD [14] [15]. Rituximab is well tolerated despite potential side effects such as infections, hypersensitivity and hypogammaglobulinaemia. Clinical response defined by improvement or resolution of symptomatic organ involvement is high [14]. However, despite good clinical improvement, radiological normalization is seen in less than one-third of

patients by conventional radiologic imaging (CT or MRI) and in less than half of patients by ^{18}F-FDG PET/CT imaging [14]. Persistent mural thickening of the coronary arteries in the repeat CT scan of our patient probably represented irreversible scar-fibrotic lesions due to long-standing chronic inflammation.

4. Conclusion

This was an unusual case of isolated IgG4-related coronary arteritis, which presented as an incidental finding of a cardiac pseudo-tumour on echocardiogram. The diagnosis was made on the basis of typical CT "pigs-in-the-blanket" sign, elevated serum IgG4 level and ^{18}F-FDG and ^{68}Ga-FAPI-avid soft tissue densities around the coronary arteries. Serological normalization of IgG4 level was achieved with 8 doses of intravenous rituximab.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Perugino, C.A., Wallace, Z.S., Meyersohn, N., Oliveira, G., Stone, J.R. and Stone, J.H. (2016) Large Vessel Involvement by IgG4-Related Disease. *Medicine*, **95**, e3344. https://doi.org/10.1097/md.0000000000003344

[2] Oyama-Manabe, N., Yabusaki, S., Manabe, O., Kato, F., Kanno-Okada, H. and Kudo, K. (2018) IgG4-Related Cardiovascular Disease from the Aorta to the Coronary Arteries: Multidetector CT and PET/CT. *RadioGraphics*, **38**, 1934-1948. https://doi.org/10.1148/rg.2018180049

[3] de la Fuente, J. and Bird, J. (2019) Coronary Arteritis in IgG4-Related Disease. *New England Journal of Medicine*, **380**, 2156-2156. https://doi.org/10.1056/nejmicm1809588

[4] Mohammadzadeh, A., Houshmand, G., Pouraliakbar, H., Soltani, Z., Salehabadi, G., Azimi, A., *et al.* (2023) Coronary Artery Involvement in a Patient with Igg4-Related Disease. *Radiology Case Reports*, **18**, 3699-3703. https://doi.org/10.1016/j.radcr.2023.07.062

[5] Keraliya, A.R., Murphy, D.J., Aghayev, A. and Steigner, M.L. (2016) IgG4-Related Disease with Coronary Arteritis. *Circulation*: *Cardiovascular Imaging*, **9**, e004583. https://doi.org/10.1161/circimaging.116.004583

[6] Zhang, B. and Li, X. (2024) Coronary Arteritis in Immunoglobulin G4-Related Disease. *Radiology*, **312**, e240180. https://doi.org/10.1148/radiol.240180

[7] Urabe, Y., Fujii, T., Kurushima, S., Tsujiyama, S. and Kihara, Y. (2012) Pigs-in-a-Blanket Coronary Arteries. *Circulation*: *Cardiovascular Imaging*, **5**, 685-687. https://doi.org/10.1161/circimaging.112.975946

[8] Ratwatte, S., Day, M., Ridley, L.J., Fung, C., Naoum, C. and Yiannikas, J. (2022) Cardiac Manifestations of IgG4-Related Disease: A Case Series. *European Heart Journal—Case Reports*, **6**, ytac153. https://doi.org/10.1093/ehjcr/ytac153

[9] Wallace, Z.S., Naden, R.P., Chari, S., Choi, H., Della-Torre, E., Dicaire, J., *et al.* (2019) The 2019 American College of Rheumatology/European League against Rheumatism Classification Criteria for IgG4-Related Disease. *Arthritis & Rheumatology*, **72**, 7-19. https://doi.org/10.1002/art.41120

[10] Lee, J., Hyun, S.H., Kim, S., Kim, D., Lee, J.K., Moon, S.H., *et al.* (2016) Utility of FDG PET/CT for Differential Diagnosis of Patients Clinically Suspected of IgG4-Related Disease. *Clinical Nuclear Medicine*, **41**, e237-e243. https://doi.org/10.1097/rlu.0000000000001153

[11] Ebbo, M., Grados, A., Guedj, E., Gobert, D., Colavolpe, C., Zaidan, M., *et al.* (2013) Usefulness of 2-[^{18}F]-fluoro-2-deoxy-D-glucose-Positron Emission Tomography/Computed Tomography for Staging and Evaluation of Treatment Response in IgG4-Related Disease: A Retrospective Multicenter Study. *Arthritis Care & Research*, **66**, 86-96. https://doi.org/10.1002/acr.22058

[12] Luo, Y., Pan, Q., Yang, H., Peng, L., Zhang, W. and Li, F. (2020) Fibroblast Activation Protein-Targeted PET/CT with ^{68}Ga-FAPI for Imaging IgG$_4$-Related Disease: Comparison to ^{18}F-FDG PET/CT. *Journal of Nuclear Medicine*, **62**, 266-271. https://doi.org/10.2967/jnumed.120.244723

[13] Perugino, C.A. and Stone, J.H. (2016) Treatment of IgG4-Related Disease. *Zeitschrift für Rheumatologie*, **75**, 681-686. https://doi.org/10.1007/s00393-016-0142-y

[14] Ebbo, M., Grados, A., Samson, M., Groh, M., Loundou, A., Rigolet, A., *et al.* (2017) Long-Term Efficacy and Safety of Rituximab in IgG4-Related Disease: Data from a French Nationwide Study of Thirty-Three Patients. *PLOS ONE*, **12**, e0183844. https://doi.org/10.1371/journal.pone.0183844

[15] Khosroshahi, A., Carruthers, M.N., Deshpande, V., Unizony, S., Bloch, D.B. and Stone, J.H. (2012) Rituximab for the Treatment of IgG4-Related Disease. *Medicine*, **91**, 57-66. https://doi.org/10.1097/md.0b013e3182431ef6