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CASE REPORT
Heart failure

Takayasu arteritis manifesting as acute kidney injury and congestion due to renal artery stenosis and myocarditis: a case report

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Background Takayasu arteritis is a large-vessel vasculitis that affects the aorta and its primary branches. Myocarditis is a rare life-threatening complication and potential diagnostic pitfall in patients with Takayasu arteritis.

Case summary A previously healthy 18-year-old woman presenting with fever, back pain, and dyspnoea was admitted to another hospital for acute hypertension (blood pressure, 230/106 mmHg) and congestive heart failure. Intravenous methylprednisolone pulse with antihypertensive and diuretic medications slightly improved her congestion. However, she developed acute kidney injury and was transferred to our hospital. Transthoracic echocardiography indicated a left ventricular ejection fraction of 45% and diffuse left ventricular hypokinesis. Doppler ultrasound test and magnetic resonance angiography revealed severe bilateral renal artery stenosis. Her diagnosis was Takayasu arteritis, and she received high-dose glucocorticoids. She required temporary haemodialysis, but 2 months after admission, her serum creatinine improved to 1.1 mg/dL without surgical or cardiovascular interventions. Although the pre-discharge test with 1.5 T cardiac magnetic resonance initially failed to diagnose myocarditis, 3 T cardiac magnetic resonance imaging revealed increased native T_1 values on T_1 mapping (1283–1393 ms), moderate pericardial effusion, and systolic left ventricular wall motion abnormality, indicating active myocarditis. During 6-month subcutaneous tocilizumab treatment (162 mg/week), a left ventricular ejection fraction improved to 55–60% without a relapse.

Discussion This case report highlights the benefits of early multimodal imaging tests including cardiac magnetic resonance imaging for myocarditis and renal artery involvement in Takayasu arteritis. Tocilizumab might be an efficient therapeutic option for severe acute manifestations including myocarditis in young women of reproductive age.

Keywords Takayasu arteritis • Myocarditis • Secondary hypertension • Renal artery stenosis • Cardiac magnetic resonance • Case report

ESC curriculum 6.4 Acute heart failure • 2.3 Cardiac magnetic resonance • 2.1 Imaging modalities

Learning points

- Myocarditis is a rare life-threatening complication and potential diagnostic pitfall in patients with Takayasu arteritis.
- Multimodal imaging tests for renal artery involvement and myocarditis including 3 T cardiac magnetic resonance imaging are crucial in Takayasu arteritis.

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Introduction

Takayasu arteritis (TA) is a large-vessel vasculitis that affects the aorta and its primary branches.[1] The clinical features of TA depend on ethnic backgrounds, age, and sex.[2] Renal artery stenosis (RAS) affects 13.1% of Japanese TA patients who are at greater risk for hypertension, congestive heart failure, and kidney dysfunction than those without RAS.[2,3] Myocarditis is a rare life-threatening complication in TA patients, tends to occur early in the disease course, and appears to correlate with the disease's activity.[4] Cardiac magnetic resonance (CMR) imaging is recommended as a mandatory diagnostic test according to the current European Society of Cardiology (ESC) guidelines.[5] Here, we report a patient presenting with acute hypertension, congestive heart failure, and dialysis-requiring acute kidney injury (AKI). This case highlights the importance of early multimodal imaging tests for myocarditis and renal artery involvement in TA.

Summary figure

4 weeks before admission	Presentation with fever and back pain.
2 weeks before admission	Serum creatinine (SCr) and C-reactive protein levels were 0.68 and 6.56 mg/dL, respectively.
4 days before admission	Admission to another hospital for congestive heart failure and markedly elevated blood pressure (230/106 mmHg). Transthoracic echocardiography (TTE) indicated a left ventricular ejection fraction (LVEF) of 34% and diffuse left ventricular hypokinesis. Intravenous methylprednisolone (1 g/day) for 3 days and antihypertensive and diuretic medications were initiated.
Day 1	Transfer to our hospital. Her SCr level was 5.21 mg/dL. We diagnosed her with TA, and oral prednisolone (1 mg/kg/day) and aspirin were initiated.
Day 19	Temporary haemodialysis was required three times a week to manage congestive heart failure.
Day 33	Seven haemodialysis sessions could be terminated.
Month 2	Noncontrast 1.5 T CMR showed no myocardial oedema on T_2-weighted images. After discharge from hospital, tocilizumab was initiated.
Month 3	Three tesla CMR revealed increased native T_1 value mapping, indicating active myocarditis.
Month 9	No relapse of TA was observed, and LVEF improved to 55–60% on her TTE.

Case presentation

A previously healthy 18-year-old Japanese woman experienced fever and back pain 4 weeks before admission. Two weeks before admission, blood tests revealed that SCr and C-reactive protein levels were 0.68 mg/dL (normal range 0.46–0.79 mg/dL) and 6.56 mg/dL (normal range <0.14 mg/dL), respectively. She was admitted to another hospital for congestive heart failure and markedly elevated blood pressure (230/106 mmHg). Transthoracic echocardiography indicated a LVEF of 34% and diffuse left ventricular hypokinesis. Intravenous methylprednisolone (1 g/day for 3 days) was initiated with a suspicion of immune-mediated myocarditis and eosinophilic myocarditis, slightly improving her congestion. On the second day after admission, her blood pressure was successfully controlled to about 140/90 mmHg with intravenous nitroglycerine, carperitide, and diuretics. However, she developed AKI (SCr level, 5.21 mg/dL) and was transferred to our hospital. Based on her age and severe acute hypertension, secondary hypertension was suspected according to the current ESC/European Society of Hypertension guidelines.[6]

Upon admission, she was afebrile with a blood pressure of 146/95 mmHg and oxygen saturation of 98% while receiving oxygen at a rate of 1 L/min via a nasal cannula. Physical examinations revealed no murmurs and clear breath sounds. She had a bruit on her abdomen and pitting oedema in her lower legs. A funduscopic test did not show flame haemorrhages and papilloedema. Blood tests revealed the following: erythrocyte sedimentation rate, 58 mm/h (normal range 3–15 mm/h); C-reactive protein level, 0.38 mg/dL (normal range <0.14 mg/dL); haemoglobin level, 9.1 g/dL (normal range 11.6–14.8 g/dL); creatinine level, 5.21 mg/dL (normal range 0.46–0.79 mg/dL); and brain natriuretic peptide (BNP) level, 960 pg/mL (normal range <18.4 pg/mL) (*Table 1*). Plasma renin activity and aldosterone levels were 11 ng/mL/h (normal range 0.2–3.9 ng/mL/h) and 1410 pg/mL (normal range 4.0–82.1 pg/mL), respectively. Serological tests for autoimmune diseases were within normal limits. Urine tests showed no haematuria, mild proteinuria, and epithelial casts. Ischaemic-type electrocardiographic changes were not seen (*Figure 1*). Chest radiography revealed cardiac enlargement and bilateral pleural effusions. Transthoracic echocardiography indicated a LVEF of 45% and diffuse left ventricular hypokinesis (see Supplementary material online, *Videos S1* and *S2*). Doppler ultrasound test revealed severe bilateral RAS, and the diameters of the right and left renal arteries at the origin were 1.9 and 0.8 mm, respectively. The peak systolic velocity in the left renal artery was 561 cm/s. The right and left kidneys were 82.2 and 104.6 mm long, respectively. Magnetic resonance (MR) angiography revealed wall thickening and stenosis in the coeliac artery, superior mesenteric artery, and renal arteries. No blood flow was detected in the right renal artery, and the flow of the left renal artery was weak because of the strong stenosis at the origin (*Figure 2A* and *B*).

According to the 2022 American College of Rheumatology/EULAR classification criteria[7] and JCS 2017 Guideline,[1] her diagnosis was TA given clinical features and vascular imaging findings, which were supported by the presence of the HLA-B*52 allele. Initially, bilateral RAS causing hyperactivation of the renin–angiotensin–aldosterone system (RAAS) was the most likely diagnosis. Furthermore, myocarditis as well as hypertensive heart disease was suspected.

She received intravenous methylprednisolone (1 g/day for 3 days), and oral prednisolone (1 mg/kg/day)[8] and aspirin (100 mg/day) were subsequently initiated (*Figure 3*). Although her C-reactive protein levels decreased, congestion and marked RAAS hyperactivity (plasma renin activity, 133 ng/mL/h and aldosterone level, 1310 pg/mL) persisted, prompting temporary haemodialysis thrice weekly. After the gradual decrease of RAAS hyperactivation, seven haemodialysis sessions could be terminated. The use of olmesartan was temporal due to the worsening kidney function. Two months after admission, her SCr level improved to 1.1 mg/dL without surgical/cardiovascular interventions.

Table 1 Laboratory data at hospital admission

Laboratory test	Value	Normal range
Urine red blood cells, /HPF	1–4	<4
Urine protein to creatinine ratio, g/gCr	0.85	<0.15
White blood cell, /μL	10 700	3300–8600
Haemoglobin, g/dL	9.1	11.6–14.8
Platelets, $\times 10^4/\mu L$	265	158–348
Total protein, g/dL	5.7	6.6–8.1
Albumin, g/dL	2.8	4.1–5.1
Urea nitrogen, mg/dL	76	8–20
Creatinine, mg/dL	5.21	0.46–0.79
eGFR, mL/min/1.73 m^2	10.3	>60
Sodium, mEq/L	132	138–145
Potassium, mEq/L	4.4	3.6–4.8
Creatine kinase MB isoenzyme, ng/mL	0.6	0.0–3.3
Cardiac troponin I, pg/mL	39	0–24
C-reactive protein, mg/dL	0.38	<0.14
Erythrocyte sedimentation rate, mm/h	58	3–15
Brain natriuretic peptide, pg/mL	960	<18.4
Plasma renin activity, ng/mL/h	11	0.2–3.9
Aldosterone, pg/mL	1410	4.0–82.1

eGFR, estimated glomerular filtration rate; HPF, high-power field.

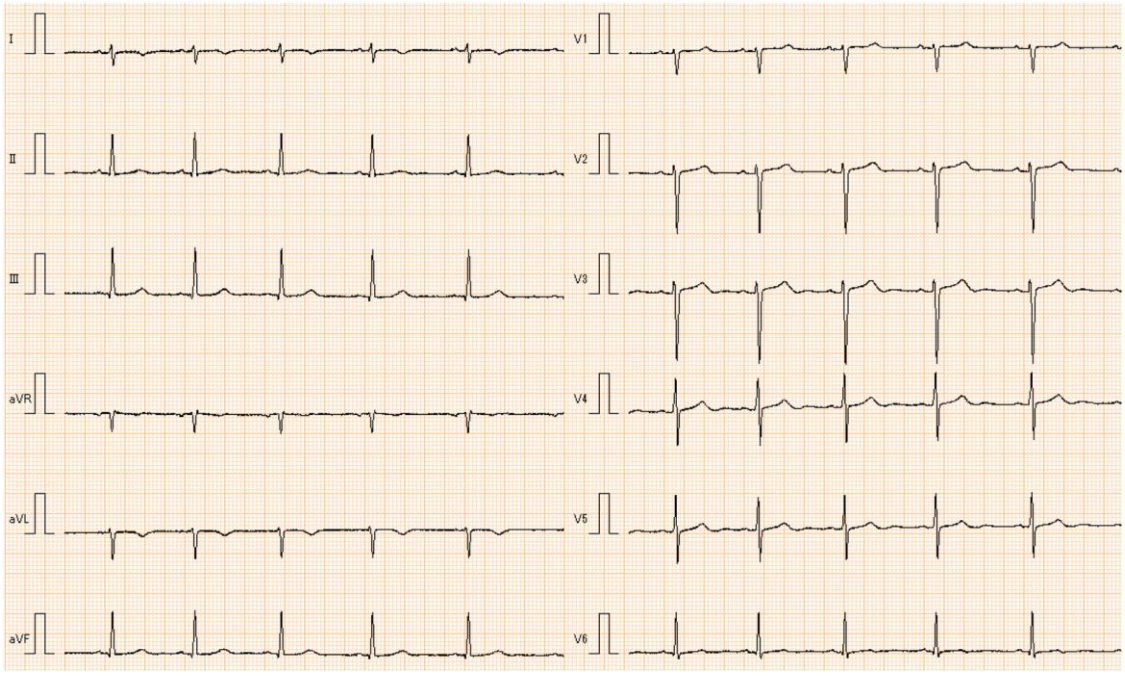

Figure 1 Electrocardiogram on admission. Ischaemic-type electrocardiographic changes were not seen.

However, she displayed persistent cardiac enlargement and high BNP levels ranging from 500 to 600 pg/mL. She was discharged 71 days after transfer to our hospital. After her discharge, she suffered from shingles and pneumonia as a side effect of immunosuppression. The prednisolone dose was reduced to 15 mg/day, and subcutaneous tocilizumab (162 mg/week) was initiated. Although the pre-discharge 1.5 T CMR without T_1/T_2 mapping and extracellular volume mapping failed to diagnose myocarditis, 3 T CMR revealed increased native T_1 values

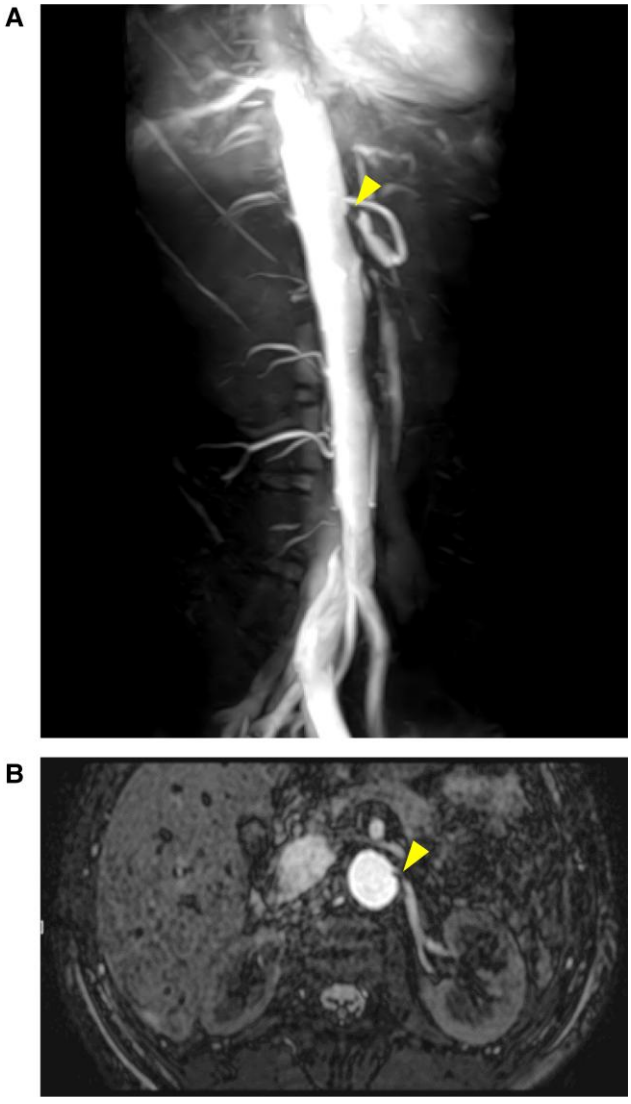

Figure 2 Magnetic resonance angiography of the renal arteries. (*A*) 3D magnetic resonance angiography revealed the stenosis of the left renal artery (arrowhead). (*B*) A horizontal magnetic resonance image showed severe left renal artery stenosis at the origin (arrowhead).

on T_1 mapping (1283–1393 ms), moderate pericardial effusion, and systolic left ventricular wall motion abnormality indicating active myocarditis (*Figure 4*).[5,9] During the 6-month tocilizumab treatment, the BNP level decreased to approximately 300 pg/mL, and the SCr level ranged from 0.7 to 0.9 mg/dL. The dosage of her antihypertensive and diuretic medications was reduced, and her LVEF improved to 55–60% (see Supplementary material online, *Video S3*).

Discussion

We reported the TA case of a young woman who presented with new-onset congestive heart failure and AKI requiring dialysis due to bilateral RAS and hidden myocarditis, which could be diagnosed using native T_1 mapping via 3 T CMR.

Although previous case series have estimated the prevalence of myocarditis to be 2.8%, cross-sectional studies using CMR in TA patients indicated that subclinical myocarditis is more prevalent.[10,11] An update of the Lake Louise Criteria using the 'two out of two' approach, with positive T_1-based and T_2-based criteria, increased the specificity of detecting acute myocardial inflammation. Single marker (T_1 based or T_2 based) may still support a diagnosis of acute myocardial inflammation, and particularly, native T_1 mapping provides high diagnostic accuracy.[5,9] The rise in native T_1 values on the cardiac magnetic resonance imaging usually indicates myocardial interstitial oedema, necrosis, and scarring. In this case, the persistent increase in native T_1 mapping under the well-controlled blood pressure was most likely to represent myocardial interstitial oedema suggestive of myocarditis, but not hypertensive heart disease. Myocardial oedema was absent on T_2-weighted imaging presumably because the test was performed after initiating steroid therapy and in the chronic phase.

The 2018 EULAR guidelines for the pharmacologic treatment of TA recommend a two-phase strategy involving the combination of glucocorticoids and conventional synthetic disease-modifying anti-rheumatic drugs (DMARDs) in phase I and a biologic DMARD in phase II, if relapse occurs.[8] The 2021 American College of Rheumatology guidelines recommend a

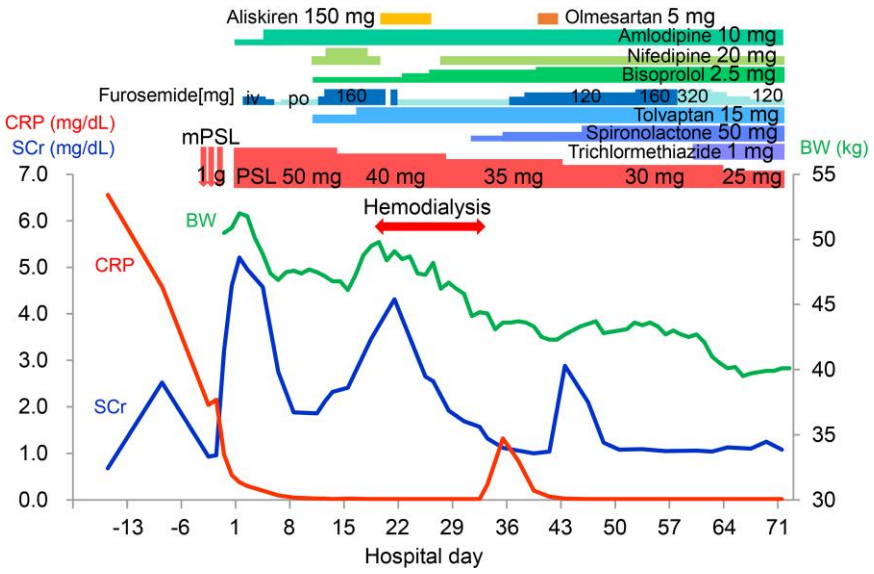

Figure 3 Clinical course of the patient. Multiple immunosuppressants, antihypertensive medications, and diuretics were used to control her congestion and disease activity in Takayasu arteritis. Aliskiren for her hyperreninaemia was ceased because of her skin rash. The use of olmesartan was also temporal due to the worsening kidney function. BW, body weight; CRP, C-reactive protein; PSL, prednisolone; mPSL, methylprednisolone; SCr, serum creatinine.

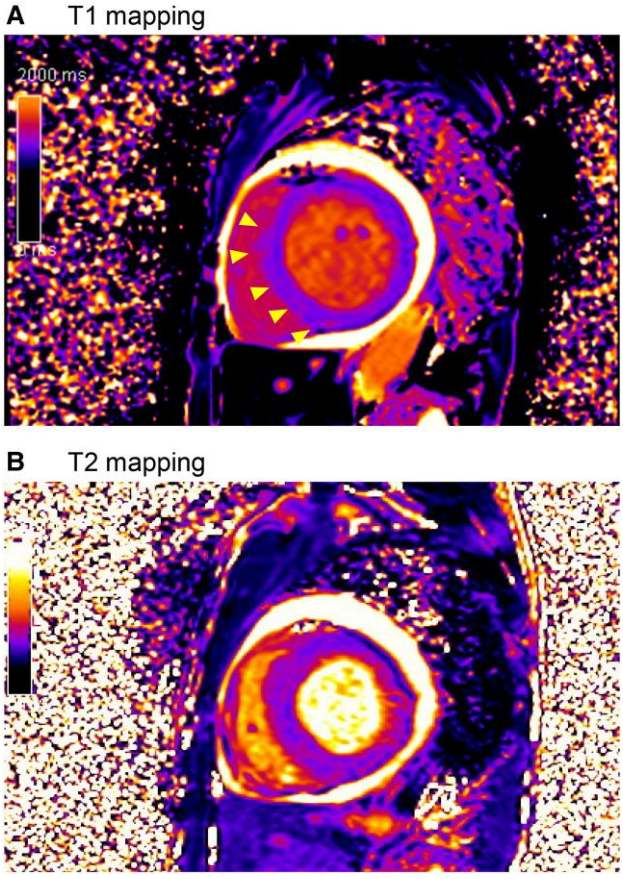

Figure 4 Three tesla cardiac magnetic resonance imaging. (*A*) Cardiac magnetic resonance imaging revealed increased native T_1 values on T_1 mapping (1283–1393 ms; arrowheads), moderate pericardial effusion, and systolic left ventricular wall motion abnormality. (*B*) T_2 mapping cardiac magnetic resonance imaging.

combination therapy with glucocorticoids and DMARDs, and anti-IL-6 receptor antibody tocilizumab for refractory disease.[12] Intravenous cyclophosphamide is usually required for treating life-threatening diseases including myocarditis and is switched to DMARDs while gradually reducing the dosage of prednisolone. Tocilizumab is considered when cyclophosphamide is ineffective or patients desire fertility preservation, similar to the current case.[10] Regarding RAS treatment, a current report recommends the avoidance of invasive therapy during active disease because of its frequent complications.[13]

A test using contrast media was avoided in this case due to renal dysfunction, and native T_1 mapping helped diagnose myocarditis. Despite severe dialysis-dependent AKI and congestion, the patient was successfully managed with immunosuppressive therapy, antihypertensive drugs, and diuretics. Cyclophosphamide was not used due to fertility concerns, and DMARD use was limited due to renal dysfunction. Tocilizumab might be an efficient therapeutic option in young women of reproductive age.

Lead author biography

Dr Misato Hara earned her MD from Tokyo Medical and Dental University in 2016 and is currently a physician at the Department of Nephrology of Tokyo Metropolitan Ohtsuka Hospital. Her research interests include kidney diseases associated with connective tissue diseases and Takayasu arteritis to improve their long-term kidney outcomes.

Supplementary material

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

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Data availability

Anonymized data underlying this article will be shared upon reasonable request to the corresponding author.

References

1. Isobe M, Amano K, Arimura Y, Ishizu A, Ito S, Kaname S, et al. JCS 2017 guideline on management of vasculitis syndrome—digest version. *Circ J* 2020;**84**:299–359.
2. Watanabe Y, Miyata T, Tanemoto K. Current clinical features of new patients with Takayasu arteritis observed from cross-country research in Japan: age and sex specificity. *Circulation* 2015;**132**:1701–1709.
3. Chen Z, Li J, Yang Y, Li H, Zhao J, Sun F, et al. The renal artery is involved in Chinese Takayasu's arteritis patients. *Kidney Int* 2018;**93**:245–251.
4. Mason JC. Takayasu arteritis—advances in diagnosis and management. *Nat Rev Rheumatol* 2010;**6**:406–415.
5. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J* 2021;**42**:3599–3726.
6. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 ESC/ESH guidelines for the management of arterial hypertension. *Eur Heart J* 2018;**39**:3021–3104.
7. Grayson PC, Ponte C, Suppiah R, Robson JC, Gribbons KB, Judge A, et al. 2022 American College of Rheumatology/EULAR classification criteria for Takayasu arteritis. *Ann Rheum Dis* 2022;**81**:1654–1660.
8. Hellmich B, Agueda A, Monti S, Buttgereit F, de Boysson H, Brouwer E, et al. 2018 update of the EULAR recommendations for the management of large vessel vasculitis. *Ann Rheum Dis* 2020;**79**:19–30.
9. Ferreira VM, Schulz-Menger J, Holmvang G, Kramer CM, Carbone I, Sechtem U, et al. Cardiovascular magnetic resonance in nonischemic myocardial inflammation: expert recommendations. *J Am Coll Cardiol* 2018;**72**:3158–3176.
10. Bechman K, Gopalan D, Nihoyannopoulos P, Mason JC. A cohort study reveals myocarditis to be a rare and life-threatening presentation of large vessel vasculitis. *Semin Arthritis Rheum* 2017;**47**:241–246.
11. Porter A, Youngstein T, Babar S, Mason JC. A rare life-threatening presentation of Takayasu arteritis. *Rheumatology (Oxford)* 2021;**60**:iii6–iii8.
12. Maz M, Chung SA, Abril A, Langford CA, Gorelik M, Guyatt G, et al. 2021 American College of Rheumatology/Vasculitis Foundation guideline for the management of giant cell arteritis and Takayasu arteritis. *Arthritis Rheumatol* 2021;**73**:1349–1365.
13. Joseph G, Goel R, Thomason VS, Joseph E, Danda D. Takayasu arteritis: JACC Focus Seminar 3/4. *J Am Coll Cardiol* 2023;**81**:172–186.