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CASE REPORT
Cardiac imaging

Concomitant myocardial injury and valvular disease in Sneddon syndrome: a case report

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Background Cardiac involvement in Sneddon syndrome (SS) is rare, the physiopathology is still unclear. We report a first case of SS without antiphospholipid antibodies who had coexisting ischaemia with no obstructive coronary arteries and aortic valve diseases.

Case summary A 34-year-old woman with SS without antiphospholipid antibodies, was admitted for aphasia, and paresthaesia with confirmed right opercular ischaemic lesions at brain magnetic resonance imaging. Transthoracic echocardiographic examination showed akinesis of apical segments, moderate aortic valve stenosis, and moderate aortic insufficiency. Coronary angiogram was normal. Cardiac magnetic resonance showed transmural necrosis in the territory of the left anterior descending artery. Seven years later, our patient had no change or progression of myocardial ischaemic lesions or valvular disease.

Conclusion We will discuss different hypothesis, diagnosis, treatment, and evolution of cardiac involvement in SS. Close follow-up should be regularly performed for early diagnosis, hence the importance of multimodality imaging, to guide treatment and prevent further complications.

Keywords Sneddon syndrome • Stroke • Livedo reticularis • Ischaemia with no obstructive coronary arteries • Aortic valve disease • Case report

Learning points

- First case of negative antiphospholipid antibodies, who had coexisting ischaemia with no obstructive coronary arteries and aortic valve diseases.
- Importance of multimodality imaging to early diagnose cardiac diseases in Sneddon syndrome, to guide treatment and prevent further complications.
- Stability of the lesions after 7 years of follow-up with proper treatment.

Introduction

Sneddon syndrome (SS) is a rare syndrome associated with stroke and livedo reticularis. Its annual incidence is four cases per million inhabitants with an estimated mortality rate of 9.5%.[1] It generally affects women between 20 and 42 years of age.[2]

The pathophysiology of this syndrome is not fully understood, but the presence of antiphospholipid antibodies in 50% of patients, as well as the skin and brain biopsy findings, suggest progressive disorder affecting small and medium-sized arteries of the skin and the brain.[3–5] Associated cardiac manifestations have been previously described

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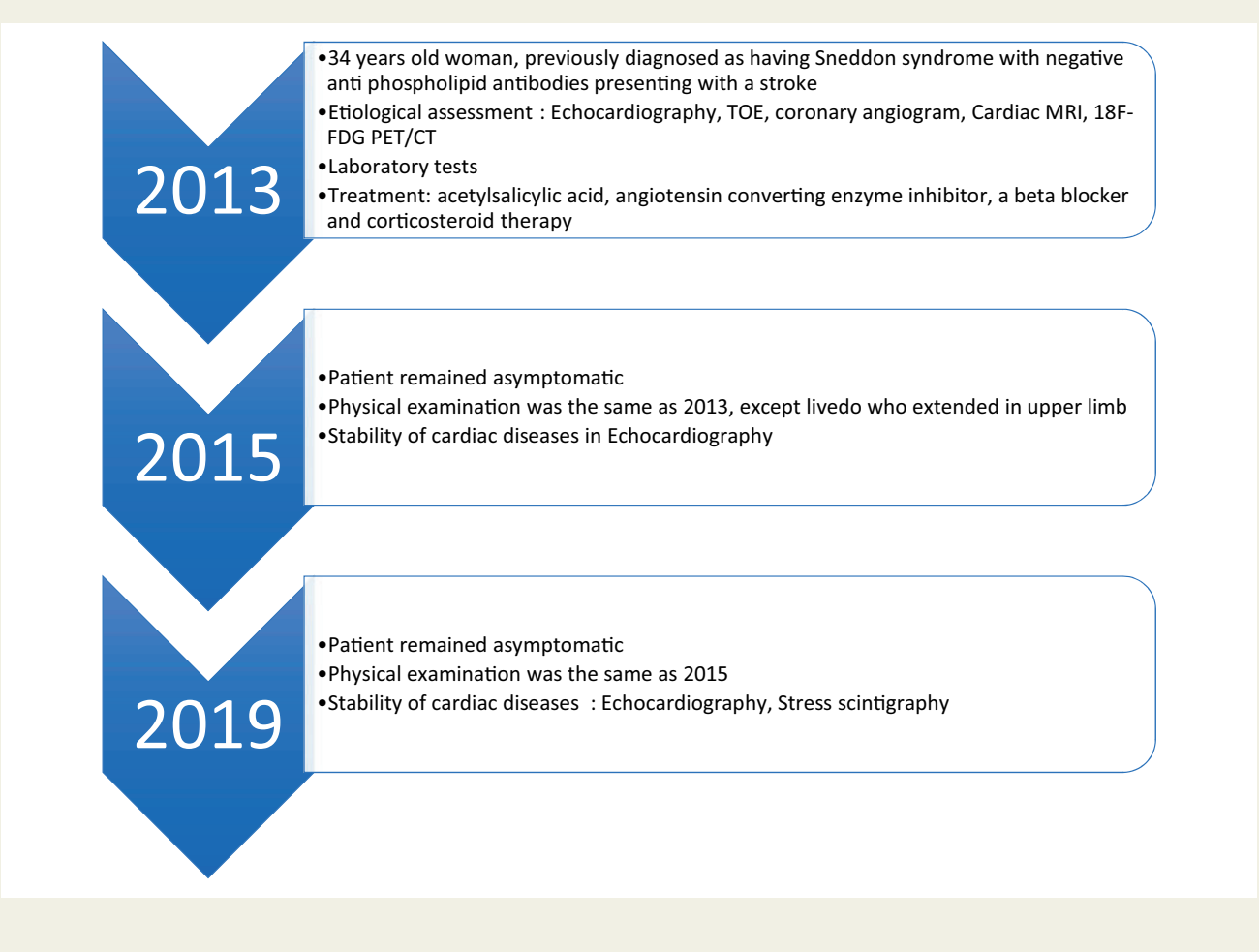
including mitral valve thickening and coronary artery disease (CAD).[6–9]

We report a case of a 34-year-old woman presenting with SS and double cardiac involvement, associating aortic valve involvement and myocardial ischaemic lesion.

Timeline



Case presentation

A 34-year-old woman was admitted on November 2013 because of an acute episode of aphasia. She has been previously diagnosed as an SS without antiphospholipid antibodies, because of livedo reticularis, transient ischaemic stroke, and confirmed obstruction of arterioles by an intimate proliferation in the skin biopsy. The physical examination at admission revealed livedo reticularis limited to the lower limbs, a systolic aortic murmur, disabling rotary vertigo, weakness of the left upper limb with paresthaesia.

A brain magnetic resonance imaging confirmed the stroke, showing a semi-recent right opercular ischaemic lesion of the middle cerebral artery.

The electrocardiogram (ECG) showed a regular sinus rhythm, with sequelae of necrosis in the apicolateral territory (*Figure 1*). The 24-h ECG was normal. Transthoracic echocardiography showed akinesis of apical segments, preserved ejection fraction, significant thickening of the aortic valve leaflets resulting in a moderate aortic valve stenosis (valve area 1.58 cm^2 and 0.89 cm^2/m^2, Vmax 2.94 m/s, mean gradient 22 mmHg) and a moderate-to-severe aortic insufficiency (vena contracta 8 mm, diastolic flow reversal in the descending aorta 0.19 m/s, EROA 0.22 cm^2, regurgitant volume 58 mL), no mitral valve involvement (*Figure 2A*). Transoesophageal echocardiogram was performed and ruled out embolic causes of stroke, such as patent foramen ovale (PFO), intracardiac thrombus, or vegetation.

Coronary angiogram was normal (*Figure 3A*). Cardiac magnetic resonance (CMR) with late gadolinium enhancement showed transmural necrosis in the territory of the left anterior descending artery [segments 14–15–16–17: 15% of the left ventricular (LV)], and an intermediate sequelae in mid-inferior lateral and apical (segment 11). T2-weighted CMR showed an inferolateral apical hypersignal witnessing a recent ischaemic lesion (*Figure 3B and C*). Furthermore, aortic insufficiency was confirmed with a regurgitant fraction at 30%. So, all these examinations were in favour of the diagnosis of ischaemia with no obstructive coronary arteries.

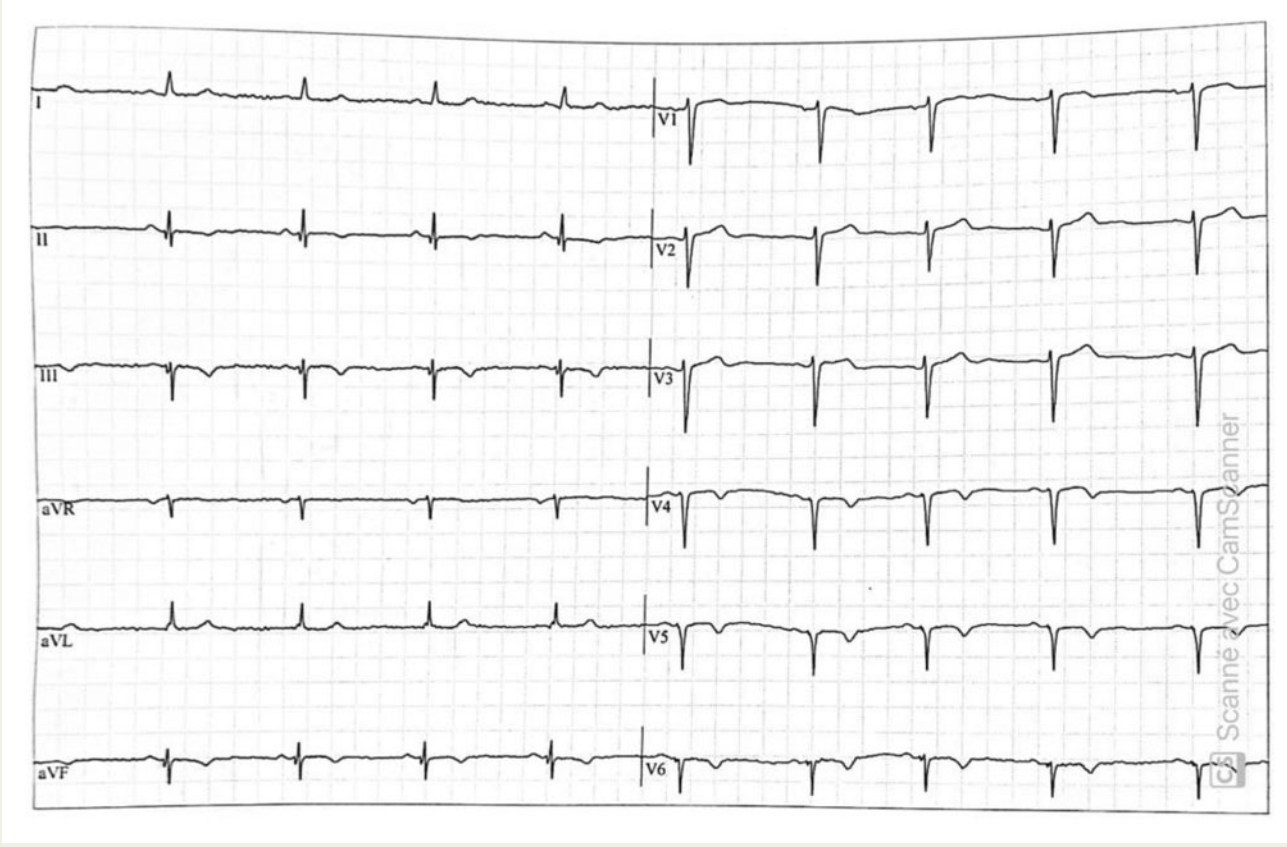


Figure 1 Twelve-lead electrocardiogram showing a normal sinus and regular rhythm, with sequelae of necrosis in the apicolateral territory.

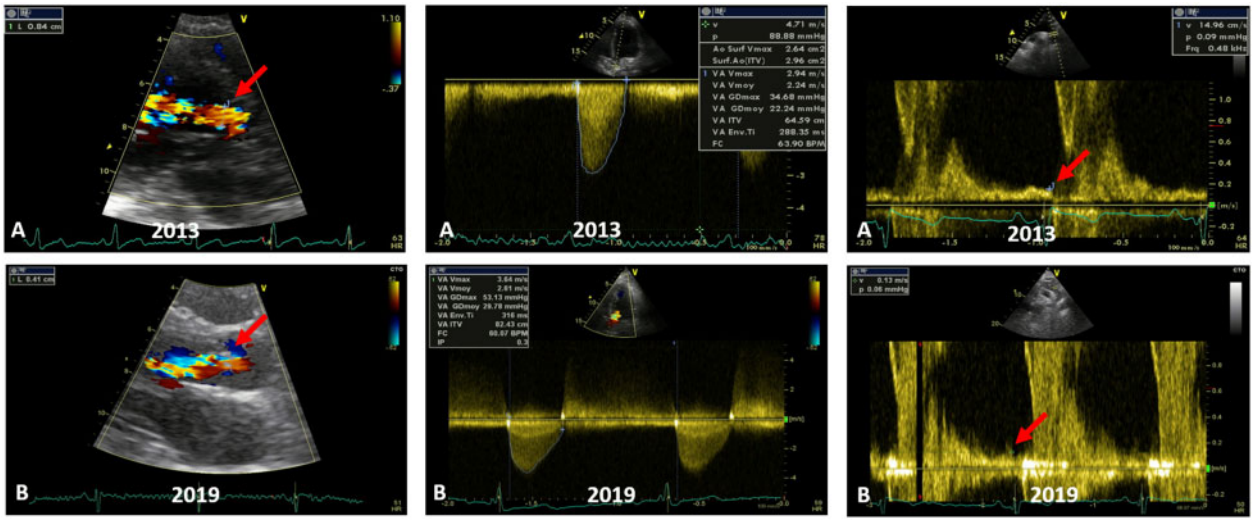


Figure 2 (*A*) Transthoracic echocardiography showing combined moderate aortic valve stenosis (valve area 1.58 cm^2 and 0.89 cm^2/m^2, mean gradient 22 mmHg, Vmax 2.94 m/s) and a moderate-to-severe aortic insufficiency (vena contracta 8 mm, diastolic flow reversal in the descending aorta 0.19 m/s). (*B*) Transthoracic echocardiography showing an improvement at 7 years of follow-up: aortic insufficiency was less important than on the initial echocardiography (vena contracta from 8 to 4 mm and diastolic flow reversal in the descending aorta from 0.19 to 0.13 m/s), the aortic stenosis is still moderate (valve area 1.35 cm^2 and 0.77 cm^2/m^2, mean gradient 29 mmHg, Vmax 2.61 m/s).

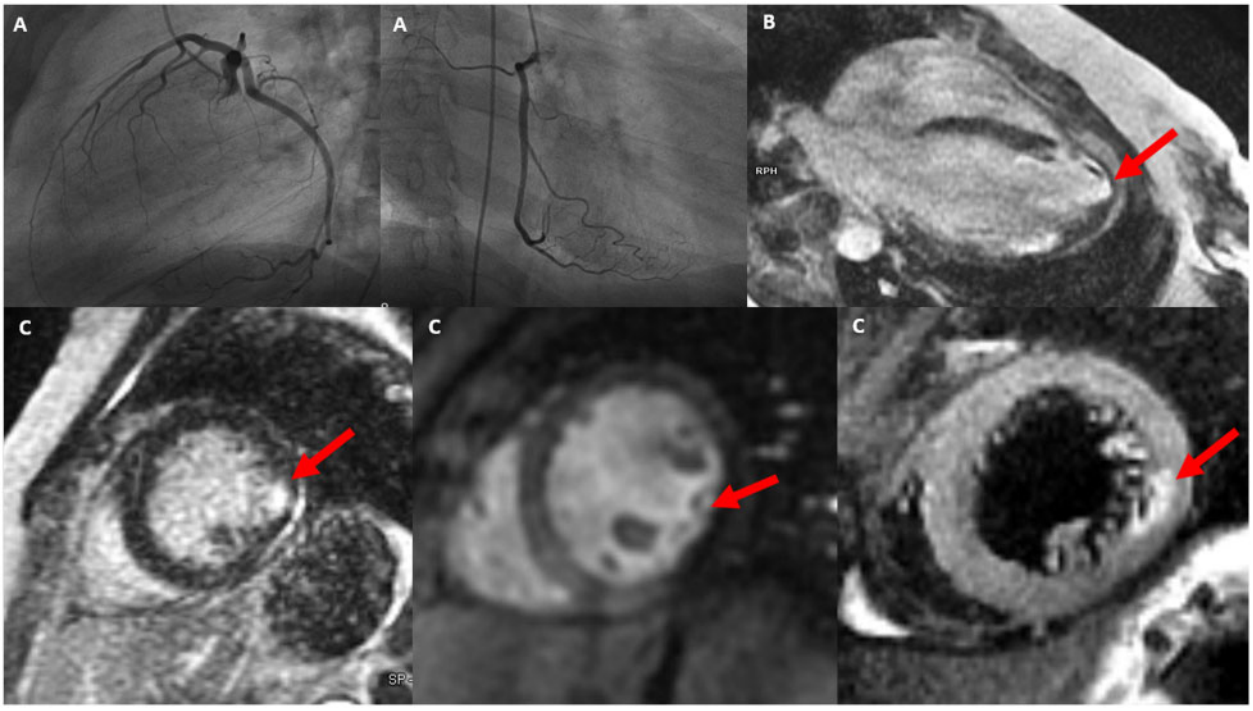


Figure 3 (*A*) Coronary angiography demonstrating a thin left anterior descending artery with no occlusion. (*B* and *C*) Cardiovascular magnetic resonance imaging: delayed gadolinium enhancement sequences showing an apical transmural necrosis in hypersignal (*B*: long-axis view, *C*: midventricle short-axis slice).

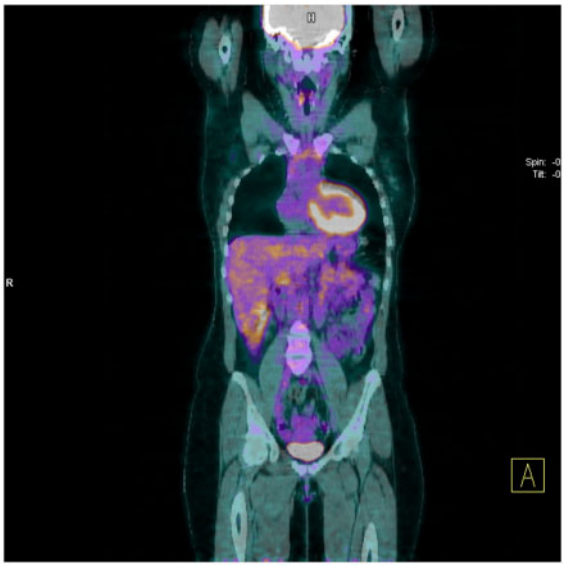


Figure 4 A positron emission tomographic scan performed during the acute phase revealing no argument in favour of vasculitis or infective endocarditis.

F-fluorodeoxyglucose positron emission tomography/computed tomography revealed no vasculitis or infective endocarditis (*Figure 4*).

Laboratory tests yielded negative results for lupus and antiphospholipid antibody syndrome (normal anti-cardiolipin antibodies, anti-beta2 glycoprotein1, antinuclear antibodies, anti-ENA, anti-dsDNA antibodies, anti-Sm antibodies, and complement).

Treatment included aspirin 160 mg, angiotensin-converting enzyme inhibitor 10 mg, beta blocker 5 mg, and corticosteroid therapy 8 mg.

The patient had regular follow-up. At 7 years follow-up visit, she remained asymptomatic, livedo reticularis extended to the upper limb. Echocardiography showed no change in LV morphology and function. Morphology of aortic valve was unchanged with thickened cusps, and aortic insufficiency was less important than initially (vena contracta from 8 to 4 mm and diastolic flow reversal in the descending aorta from 0.19 to 0.13 m/s, pressure half-time from 500 to 600 ms, SOR from 0.22 to 0.14 cm^2, regurgitant volume from 58 to 35 mL), the aortic stenosis was still moderate (valve area 1.35 cm^2 and 0.77 cm^2/m^2, Vmax 2.61 m/s, mean gradient 29 mmHg) (*Figure 2B*). Myocardial perfusion scintigraphy showed preserved LV function with a necrosis in apical segments (10% of the LV).

Discussion

This case is the first reported in the literature associating aortic valve disease without mitral valve disease and myocardial ischaemic lesions in a patient with SS without antiphospholipid antibodies.

SS is characterized by multi-systemic involvement due to autoimmune systemic disease. It is more common in women.[2,3] Most cases of SS are sporadic, but a few familial cases with autosomal dominant transmission have been reported. Genetic counselling may therefore be discussed.

The clinical symptoms of this syndrome are the result of the various pathological modifications in the small and medium-sized arteries, especially of the brain and skin. Clinical manifestations associate strokes, livedo reticularis, and heart valve disease. Systemic hypertension is present in approximately half of the patients.[3] Furthermore, several other organs may also be involved in this pathology.[10]

Cardiac involvement may increase morbidity and mortality.[11,12] Mitral valve thickening and myocardial ischaemic lesions are the main cardiac manifestations.[8,9,13] According to our review of the literature, cases of SS with ischaemic heart disease are described.[6] It is important to exclude other causes or risk factors of valvular disease and CAD. In our patient, SS was the only cause for the cardiac involvement.

Our patient presented with ischaemia with no obstructive coronary arteries. CMR was useful for tissue characterization and diagnosis of myocardial fibrosis, especially because it could detect scars potentially related to microvascular coronary disease despite a normal coronary angiography. Cardiac involvement detected by CMR usually shows focal area of apical myocardial oedema on T2-weighted images. T1-weighted inversion recovery images reveal multiple spots of delayed enhancement in the LV myocardium.[14]

Different hypothesis may explain these findings, such as thrombosis or inflammation. The presence of positive aPL antibodies suggests that symptoms may be secondary to thrombotic process. However, it is still unclear how it occurs in aPL-negative cases. Skin biopsy of aPL-negative patients are in favour of an inflammatory process leading to vascular smooth muscle cells proliferation and vessel lumen narrowing.[3,4]

In the SS without antiphospholipid syndrome (APL) antibodies, the valvular disease can be both aortic or mitral, while in antiphospholipid syndrome, mitral involvement is predominant.[3,4] Morphologically, lesions consist of valve thickening, annular calcifications, or sessile nodular changes corresponding to an abacterial endocarditis of Libman–Sacks.[4] The mechanism remains unknown, it may result from a contact effect with fibrino-platelet thrombi on the surface of the valvular tissue or from arteriolar endothelial damage.

This raises the possibility that an embolic mechanism may play a role in the occurrence of neurologic and skin manifestations of SS.

Cardiac manifestations are usually asymptomatic and unspecific in SS explaining why the diagnosis is usually made at an advanced stage.

We report an unusual case of a woman presenting with SS and important valve dysfunction, predicting a long-term poor outcome, especially because of the young age. However, after 7 years of follow-up, our patient remained asymptomatic with no change or progression of myocardial ischaemic lesion or valvular disease.

Therapy for SS is controversially discussed in the literature.[1,15] An immunosuppressive strategy is usually excluded, but antithrombotic therapy with acetylsalicylic acid is suggested.[3] Anticoagulation with warfarin is reasonable in cases of thrombotic disorders.[16] In our case, an anticoagulant treatment was not initiated at the time of diagnosis because of the negative antiphospholipid antibodies.

Conclusion

Pathogenesis of SS is still unclear. The optimal management of these patients is still under discussion. Close follow-up including clinical examination and non-invasive imaging techniques should be regularly performed, to early diagnose valvular heart disease and CAD, and allow proper treatment on time, in order to avoid potentially harmful complications.

Lead author biography

Soukaina Scadi was born on 1 February 1991 in Khouribga, Morocco. She had a doctorate degree in medicine in September 2017 with very honourable mention and congratulations from the jury in University Hassan II of Medicine in Casablanca. She started her residency in cardiology in International University Hospital Cheikh Khalifa in Casablanca, Morocco for 2 years. She is a fourth year resident in Regional University Hospital of Nancy, since November 2019, doing a specialized medical training diploma in cardiac echocardiography and cardiac MRI.

Supplementary material

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

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

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