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CASE REPORT
Cardiac Imaging

Role of imaging for diagnosis and management of aortic valve papillary fibroelastoma and cardiac amyloid light chain amyloidosis: a case report

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Background We report the case of a patient who presented with concomitant aortic valve papillary fibroelastoma (PFE) and cardiac amyloidosis. Although histologically benign, PFE confers an increased thromboembolic risk, and surgical excision is often indicated. However, outcomes of cardiac surgery are poor in patients with cardiac amyloidosis.

Case summary A 61-year-old man with complaints of dyspnoea and weight loss of 10 kg developing over the past 5 months was evaluated in the cardiology clinic. Echocardiography revealed sessile aortic valve PFE and was also highly suggestive of cardiac amyloidosis. The diagnosis of amyloid light chain amyloidosis secondary to indolent multiple myeloma was eventually confirmed. Therapy with daratumumab, bortezomib, cyclophosphamide, and dexamethasone allowed full remission over a 6-month period and resulted in marked improvement in symptoms and cardiac function as evaluated by global longitudinal strain. Further workup with cerebral magnetic resonance revealed multiple vascular sequelae. Surgical removal of the aortic fibroelastoma with bioprosthetic aortic valve replacement was performed successfully and the patient had an uneventful recovery.

Discussion Papillary fibroelastoma and cardiac amyloidosis are rare and most likely unrelated entities. Concomitant presentation of both conditions in the same patient presents a unique therapeutic challenge. By allowing cardiac function to be monitored during chemotherapy, speckle-tracking echocardiography can prove instrumental in determining the optimal timing of surgical intervention.

Keywords Case report • Papillary fibroelastoma • Cardiac amyloidosis • Heart surgery • Speckle-tracking echocardiography • Global longitudinal strain

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Learning points

- While papillary fibroelastoma commonly presents as an incidental finding in asymptomatic individuals, cerebral imaging may detect subclinical embolic events.
- Speckle-tracking echocardiography may provide useful information regarding improvement in cardiac function after amyloidosis therapy.

Introduction

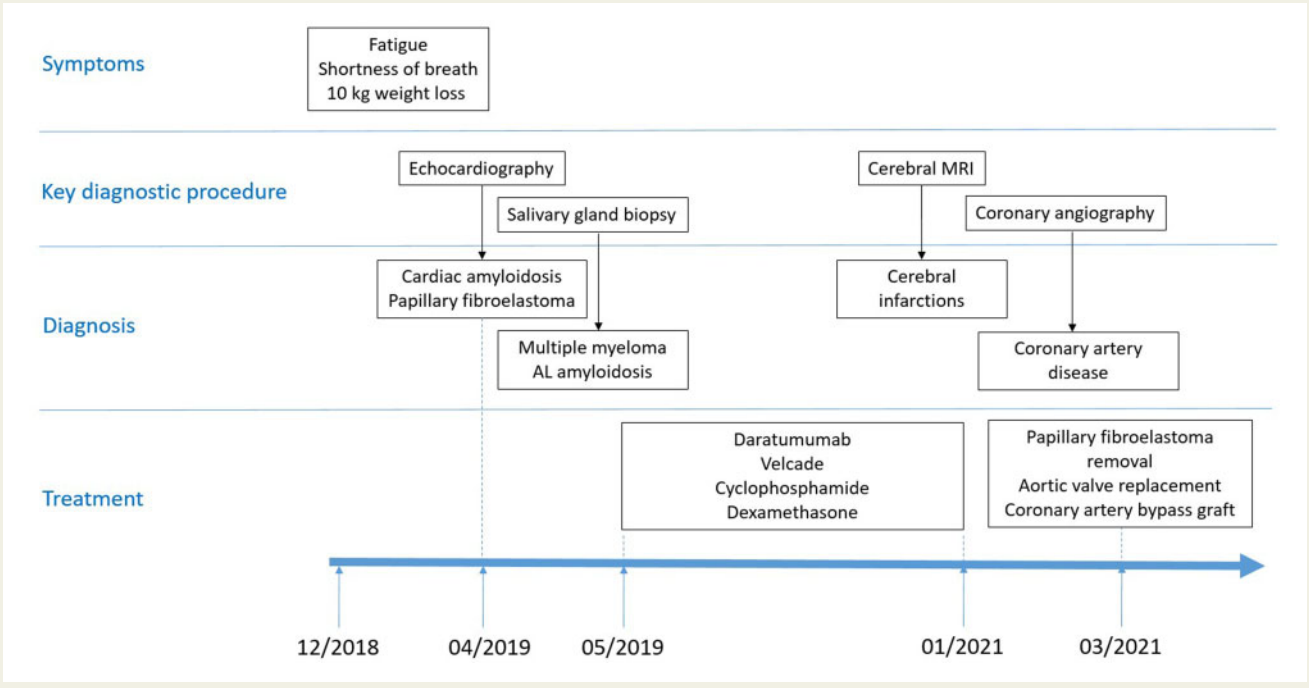
Historically, papillary fibroelastoma (PFE) has been considered as one of the less frequent primary cardiac tumours.[1] However, with technical improvements in echocardiography, PFE has become the most commonly detected benign cardiac tumour in adults, ahead of myxomas.[2] Although histologically benign, PFE confers an increased thromboembolic risk, and surgical excision is often warranted.[2–4]

We describe the case of a patient presenting with aortic valve PFE in the setting of amyloid light chain (AL) cardiac amyloidosis. While surgical resection of PFE was indicated, operative risk was increased by the presence of amyloidosis. Speckle-tracking echocardiography-derived left ventricular global longitudinal strain (GLS) was used to monitor improvement in cardiac function during amyloidosis treatment, enabling optimal timing of surgical intervention.

Case presentation

A 61-year-old man with a history of type 2 diabetes and tobacco smoking who complained of dyspnoea and weight loss of 10 kg developing over the past 5 months was evaluated in the cardiology clinic. Physical examination was unremarkable; blood pressure was 135/90 mmHg, and heart rate was 72 b.p.m. The electrocardiogram showed low QRS voltage in the limb leads and a pseudo-infarct pattern with anteroseptal Q waves (*Figure 1*). Echocardiography revealed moderate symmetric left ventricular hypertrophy with a speckled appearance of the myocardium and thickened mitral and tricuspid valves (*Figure 2A* and *Video 1*). Left ventricular ejection fraction was within normal limits (57%) but GLS was markedly decreased (-9.4%) with an apical sparing pattern (*Figure 3A*). There was a restrictive left ventricular filling pattern (E/A ratio 4.20; E/e′ 24.5). The constellation of these findings strongly suggested cardiac amyloidosis. In addition, there was an echo dense sessile and irregular mobile mass (10 mm × 6 mm) consistent with PFE on the ventricular side of the right aortic coronary cusp (*Figure 2B and C* and *Video 2*) without valvular obstruction or regurgitation. N-terminal prohormone of brain natriuretic peptide (NT-proBNP) level was 2230 ng/L (normal

Timeline



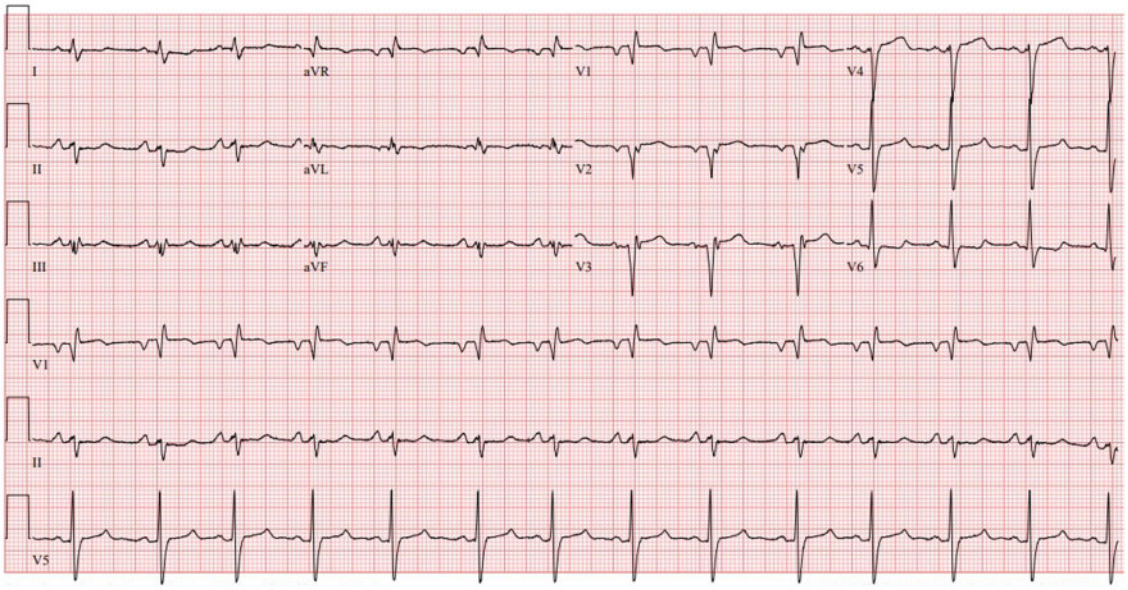


Figure 1 Electrocardiogram showing low QRS voltage in limb leads, and pseudo-infarct pattern with anteroseptal Q waves.

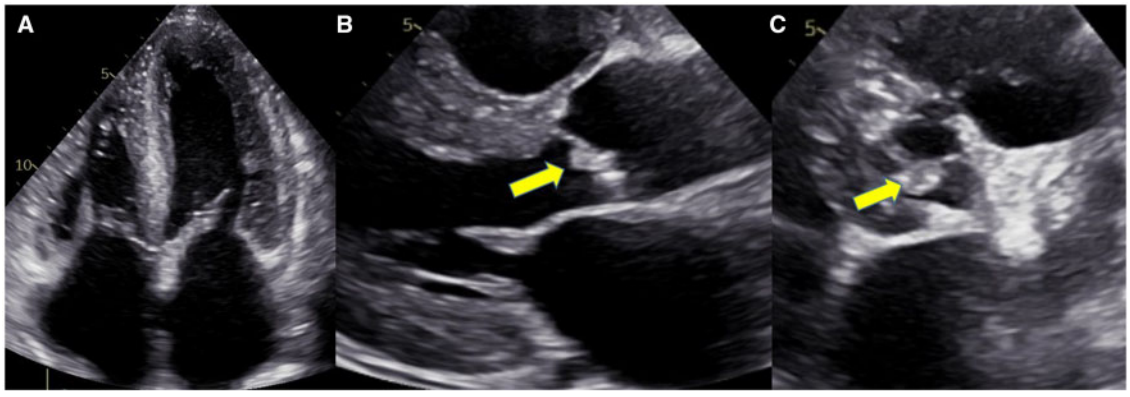
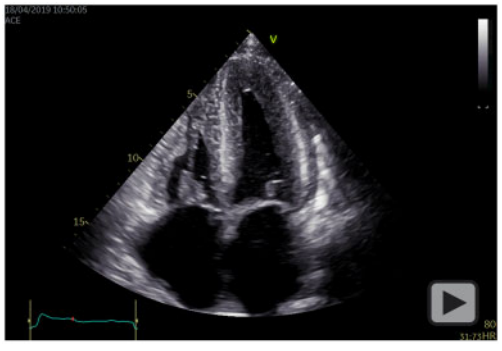
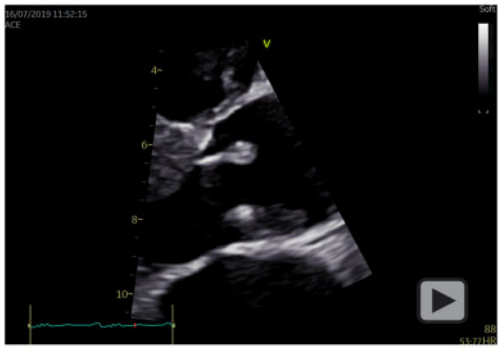


Figure 2 Apical four-chamber view showing severe concentric left ventricular hypertrophy with granular and sparkling appearance of the ventricular myocardium (*A*). Mobile mass consistent with papillary fibroelastoma observed on the ventricular aspect of the right aortic coronary cusp [parasternal long-axis and short-axis views (*B and C*), respectively].



Video 1 Four-chamber view showing severe concentric left ventricular hypertrophy with granular and sparkling appearance of the ventricular myocardium.



Video 2 Parasternal long-axis view (zoom) showing a mobile mass on the ventricular aspect of the right coronary cusp of the aortic valve.

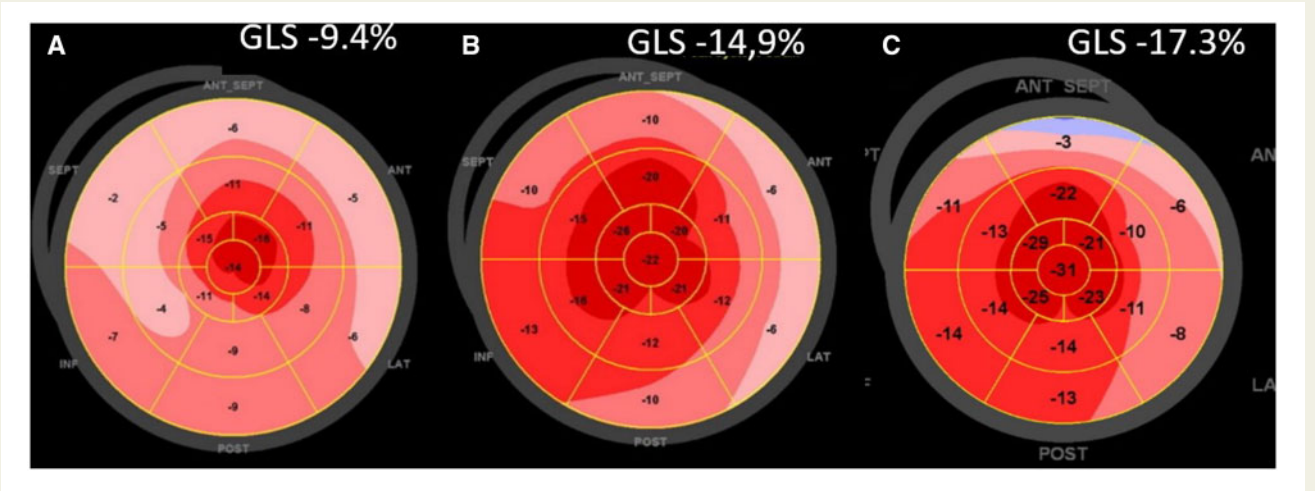


Figure 3 Longitudinal strain at baseline (*A*), after 6 months (*B*), and after 12 months of chemotherapy (*C*). GLS, global longitudinal strain.

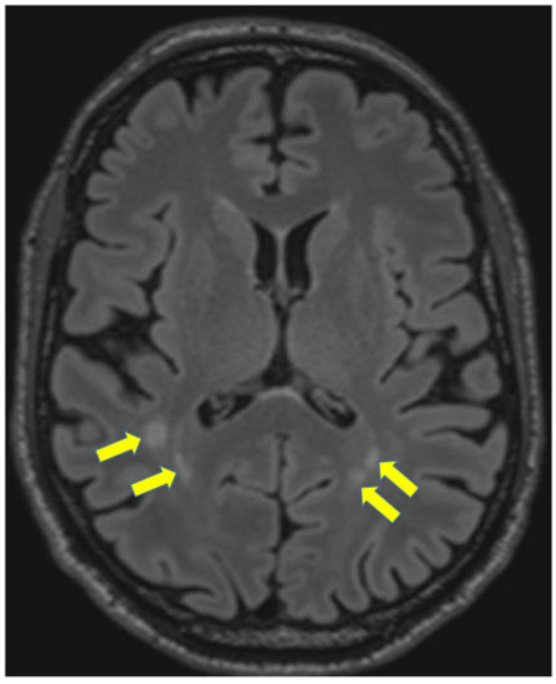


Figure 4 Cerebral magnetic resonance imaging with FLAIR sequence showing bilateral hyperintense lesions (arrows) consistent with vascular sequelae.

<125 ng/L). Cardiac magnetic resonance imaging (MRI) confirmed left ventricular hypertrophy (left ventricular mass 196 g) and showed areas of extensive late gadolinium enhancement in both ventricles (Supplementary material online, *Figure S1*). Monoclonal protein assessment detected a monoclonal lambda light chain on serum protein immunofixation. Kappa serum free light chain (FLC) was 17.2 mg/L (normal range 3.3–19.4 mg/L) and lambda serum FLC was 249.6 mg/L (normal range 0.7–26 mg/L) with kappa/lambda ratio at 0.07 (normal range 0.26-1.65). There was no significant proteinuria on the 24-h urine collection. Subcutaneous fat biopsy was negative, but labial salivary gland biopsy was positive for Congo red stain (Supplementary material online, *Figure S2*) with characteristic apple-green birefringence in the amyloid deposits. Immunofluorescent histology demonstrated Lambda light chain restriction establishing the diagnosis of AL amyloidosis. We concluded to the diagnosis of lambda AL amyloidosis at Stage IV of the revised Mayo Clinic staging system. Therapy consisted of six 28 days cycles of daratumumab (weekly in cycle 1–2, every 2 weeks in cycles 3–6) and weekly bortezomib (1.3 mg/m^2), cyclophosphamide (300 mg/m^2), and dexamethasone (20 mg) followed by daratumumab every 4 weeks for a further six cycles. The treatment allowed a complete haematological response. Global longitudinal strain improved after 6 months (*Figure 3B*) and was near normal (-17.3%, *Figure 3C*) after 12 months. At that moment, despite the persistence of left ventricular hypertrophy with a restrictive pattern of mitral inflow by Doppler echocardiography (E/A and E/e′ ratio of 2.9 and 18.1, respectively), patient's symptoms improved (New York Heart Association IIA) and NT-proBNP level dropped to 757 ng/L. Although there was no neurological deficit, the high incidence of neurological events reported with PFE[2–4] led us to perform cerebral MRI, which showed bilateral lesions consistent with ischaemic sequelae (*Figure 4*). No other cardiac or vascular source of emboli were detected, reinforcing the indication for surgical resection. Routine preoperative coronary angiography showed a significant stenosis of the middle portion of the left anterior descending artery (LAD). Surgery was performed and perioperative inspection revealed a sessile tumour on the ventricular side of right coronary cusp of the aortic valve (*Figure 5A*). Complete resection of the tumour with valve preservation was not feasible, leading to bioprosthetic valve replacement in addition to left internal mammary artery bypass graft on the LAD. Histopathology of the native valve confirmed the diagnosis of cardiac PFE (*Figure 5B*). In addition, staining with Congo red dye allowed identifying apple-green birefringent valvular deposits under polarized light, consistent with amyloid deposits. Postoperative follow-up, currently 4 months, is unremarkable.

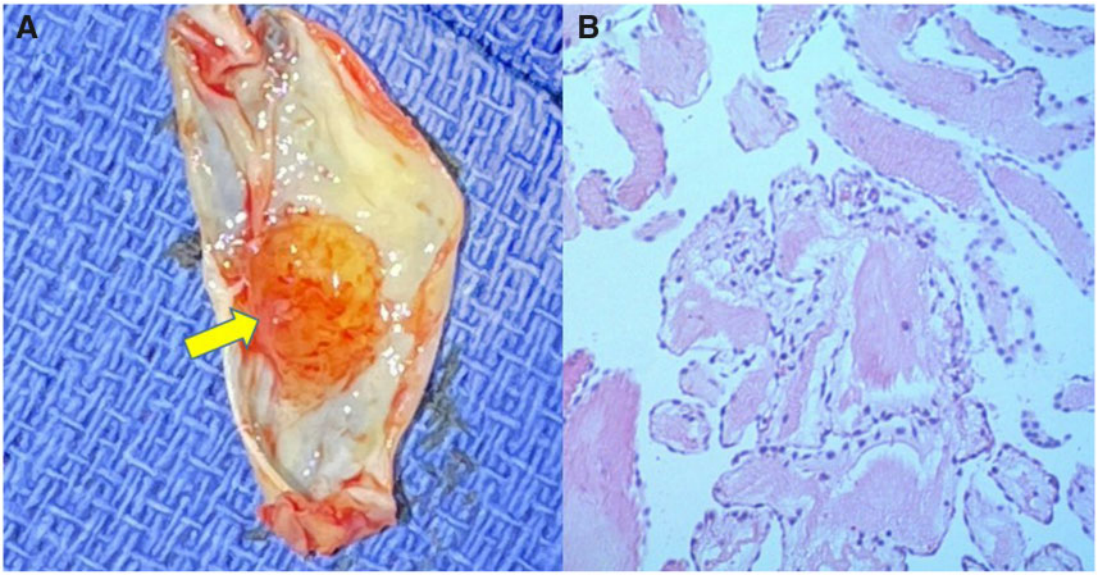


Figure 5 (*A*) Gross appearance of the papillary fibroelastoma, located on the ventricular aspect of the right coronary cusp. (*B*) On pathological examination, a core of collagen and elastic fibres with endothelial lining is observed using haematoxylin–eosin stain (magnification ×100).

Discussion

We herein report the case of a patient in whom echocardiography led to the diagnosis of two different, and as far as we know, unrelated conditions, namely an aortic valve PFE and cardiac AL amyloidosis secondary to indolent multiple myeloma.

Papillary fibroelastoma is a histologically benign cardiac tumour, but it may affect prognosis due to its thromboembolic potential. Indeed, neurological events, including transient ischaemic attack and stroke are the most common presenting symptoms of PFE, observed in 30% of patients, whereas it may be an incidental finding in up to one-third of patients.[5]

Cardiac amyloidosis frequently occurs in the setting of systemic amyloidosis with multi-organ involvement and results from extracellular deposition of misfolded and aggregated proteins forming amyloid fibrils. The three main types of amyloidosis associated with cardiac involvement are AL amyloidosis, hereditary transthyretin amyloidosis, and wild-type transthyretin amyloidosis.[6] The diagnosis is often suspected by echocardiography typically showing symmetric left ventricular hypertrophy with a speckled and granular appearance of the myocardium. The relative apical sparing of longitudinal deformation is particularly useful to distinguish amyloidosis from other causes of left ventricular hypertrophy.[7] Electrocardiographic low voltage in the limb leads and pseudo-infarct pattern further suggest the diagnosis. Amyloid deposits may induce valvular thickening; however, in the present case, the appearance of the mass argued against this hypothesis. It should be noted that amyloidosis in itself may cause arterial thromboembolic events, even in patients in sinus rhythm.[8]

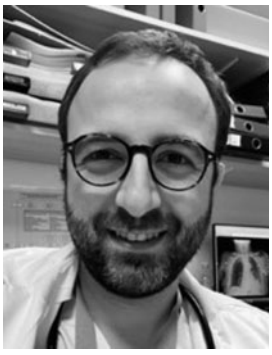
The management of the PFE was complicated because of the concomitant presence of cardiac amyloidosis. It has been proposed that patients with left-sided PFE should be offered surgical excision regardless of size, mobility, and location if they are good surgical candidates.[2] In the current case, the presence of vascular sequelae on cerebral imaging was an incentive to perform surgery, but we were concerned by an increased operative risk in this setting. Indeed, the surgical management of patients with cardiac amyloidosis can be challenging. Diastolic dysfunction is not included in current preoperative risk stratification tools such as EuroSCORE II and Society of Thoracic Surgeons scores, and these scores may not necessarily be valid in patients with cardiac amyloidosis. Several case reports have suggested poor outcomes after coronary artery bypass surgery, mainly through the occurrence of a low cardiac output state.[9–11] In addition, there is evidence of increased risk following surgical valve replacement in patients with aortic stenosis and cardiac amyloidosis, although some studies have not reported a significant increase in perioperative mortality.[12,13] Interestingly, reversal of cardiac AL amyloidosis-related left ventricular dysfunction may occur with treatment, with improvement in longitudinal strain.[14,15] Speckle-tracking imaging allows for monitoring this improvement in cardiac function. Whether it allows improving outcomes in patients requiring cardiac surgery remains to be determined. In the present case, the clinical remission including symptoms, NT-proBNP, and haematologic improvement, together with the near normalization of the longitudinal strain led us to consider surgery as a valid option.

Conclusion

Papillary fibroelastoma and cardiac amyloidosis are relatively rare and most likely unrelated entities. To the best of our knowledge, this is the first report of PFE in a patient with cardiac amyloidosis. Concomitant presentation of both conditions in the same patient presents a unique therapeutic challenge as outcomes of cardiac surgery are negatively affected by the presence of cardiac amyloidosis. By

allowing the improvement in cardiac function following amyloidosis treatment to be monitored, speckle-tracking echocardiography might be instrumental in optimizing the surgical timing.

Lead author biography



Ivan Dimov studied medicine at the Université Libre de Bruxelles in Belgium. He began his residency in internal medicine in 2016 and subspecialty training in cardiology in 2019. He is currently physician in residency in the Department of Cardiology at the Centre Hospitalier Universitaire Saint-Pierre in Brussels, Belgium.

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 authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

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