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CASE REPORT
Heart failure

Dynamic change of mitral regurgitation after myocardial reverse remodelling: a case report

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Background Chronic mitral regurgitation can be primary (degenerative) or secondary (functional); each has its own aetiology, treatment approach, and prognosis. A combination of the two types of regurgitation can lead to unexpected haemodynamic changes.

Case summary A 72-year-old woman presented to our hospital with dyspnoea on exertion, moist cough, and orthopnoea. At admission, transthoracic echocardiography (TTE) findings revealed severely reduced left ventricular ejection fraction, dilation of the left ventricle and left atrium, mild mitral regurgitation with prolapse of the posterior leaflet, and bilateral leaflet tethering. She was diagnosed with idiopathic cardiomyopathy with mild mitral regurgitation. After compensation of heart failure, angiotensin-receptor blocker and beta-blocker treatment were initiated, and the dose was subsequently titrated. At 7 months after initiating medical therapy, TTE showed significant improvement of the left ventricular ejection fraction, disappearance of left ventricular dilation (reverse remodelling), and mitral valve tethering. However, posterior leaflet prolapse became apparent, and mitral regurgitation blowing became more severe. Chordal lengthening, leaflet thickening, and degeneration were observed, but there were no ruptured chordae. Successful surgical repair of the mitral and tricuspid valves was performed.

Discussion In this unusual mitral regurgitation case, the regurgitation worsened following an improvement of cardiac function due to the loss of tethering from a reduction of the left ventricular diameter and an increase in closing force by increasing the left ventricular contractile force. Eventually, mitral regurgitation prolapse became apparent. Therefore, we should consider that reverse remodelling may exacerbate mitral regurgitation.

Keywords Case report • Mitral regurgitation • Mitral valve tethering • Prolapse • Myocardial reverse remodelling

ESC Curriculum 2.2 Echocardiography • 4.3 Mitral regurgitation

Learning points

- Multiple factors are involved in the establishment of mitral regurgitation.
- Reverse remodelling of left ventricular function, loss of tethering, and increased closing force can cause mitral valve prolapse and enhance mitral regurgitation.

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Introduction

Mitral regurgitation (MR) is the most common valve disease worldwide.[1] Chronic MR can be primary (degenerative) or secondary (functional), and both have several mechanisms, treatment approaches, and prognoses.[2]

Primary MR is caused by the impairment of one or more of the valve components, with the most common cause being mitral valve prolapse. Mitral regurgitation causes chronic volume overload, which may lead to left ventricular (LV) enlargement, LV ejection fraction (LVEF) decline, left atrium enlargement, and atrial fibrillation, which ultimately result in heart failure.[2]

In chronic secondary MR, there is no abnormality in the mitral valve complex itself. Severe LV dysfunction is an important cause of secondary MR and leads to LV dilation, causing leaflet tethering that prevents mitral valve coaptation.[2] It has been well reported that the combination of MR and LV dysfunction exacerbates the worsening of heart failure. If both primary and secondary MR occur together, MR is expected to deteriorate and become difficult to manage.[3]

On the other hand, evidence-based medical and device therapies can promote LV reverse remodelling, defined as an improvement of LVEF and reduction in LV size, in cases of dilated cardiomyopathy, which may lead to the improvement of secondary MR and better prognosis.[4]

Herein, we present a valuable case, in which MR was accentuated by a combination of primary and secondary MR elements, despite an improvement in cardiac function and the resolution of impaired functional elements.

Timeline

Before admission	Dyspnoea on exertion appeared at 2 weeks before admission and gradually worsened.
Admission Day 1	Admission with decompensated congestive heart failure with severely reduced LVEF and mild MR with posterior leaflet prolapse.
Day 3	Dyspnoea and congestion disappeared. Optimal medical therapy started.
Day 24	After cardiac rehabilitation, she was discharged without any complications. The LVEF was improved mildly.
Month 7	Though LVEF was improved to normal, MR blowing was worsening and dyspnoea on exertion had reappeared.
Month 9	MV repair and tricuspid valve repair were performed.

Case presentation

A 72-year-old Japanese woman was admitted to our hospital with dyspnoea on exertion, moist cough, and orthopnoea. She had no medical history except an electrocardiogram abnormality observed on her medical examination. She had been asymptomatic and had therefore not examined closely. Dyspnoea during exertion had appeared 2 weeks before and gradually worsened. She had oedema of the lower legs 4 days before admission, and orthopnoea had appeared the night before her visit to the hospital. On admission, her physical examination findings were as follows: pulse rate, 135 b.p.m.; blood pressure, 138/79 mmHg; oxygen saturation, 95% in room air; pansystolic murmur at Levine grade II/VI; bilateral coarse crackles in the lower lung field; and oedema in both lower legs. The patient's electrocardiogram showed sinus tachycardia at 140 b.p.m.; inverted T waves in leads I, V5, V6, II, III, and aVF; and an abnormal Q wave in leads V1 to V3. Radiographic examination of the chest showed enlargement of the cardiac shadow, bilateral peripheral effusion, and pulmonary congestion (Supplementary material online, *Figure S1*).

The patient's initial transthoracic echocardiography (TTE) revealed a severely reduced LVEF (19%, calculated by the modified Simpson method), dilation of the LV and left atrium, and mild MR with prolapse of the posterior leaflet and bilateral leaflet tethering (*Figure 1* and *Video 1*). Moreover, her B-type natriuretic peptide (BNP) level was elevated at 1627.3 pg/mL (normal range: <18.4 pg/mL).

A diagnosis of decompensated congestive heart failure with reduced ejection fraction was made; a continuous infusion of dobutamine and carperitide and oral spironolactone administration (25 mg) were initiated on the day of admission. Dyspnoea and congestion cleared within a few days. Treatment with telmisartan, which was selected because of intolerance of angiotensin-converting enzyme inhibitor and treatment of hypertension, and bisoprolol was initiated and subsequently titrated to maximal doses (i.e. 20 and 2.5 mg, respectively). Coronary angiography findings did not detect significant stenosis in the coronary arteries. Cardiac magnetic resonance imaging findings showed an LVEF reduced to 14% and no late gadolinium enhancement. Though MR was identified, a detailed quantitative evaluation was not performed because the regurgitation and valve deviation were mild. Because of the first onset of acute heart failure and LV dysfunction without coronary artery disease, an endomyocardial biopsy from the right ventricle was performed to exclude secondary cardiomyopathy and acute myocarditis. Hypertrophy of cardiomyocytes and mild fibrosis were observed; however, no specific findings were revealed. Given these findings, the patient was diagnosed with idiopathic cardiomyopathy with mild MR. After cardiac rehabilitation and optimization of medication, she was discharged on hospitalization Day 24 after her BNP level (normal range: <18.4 pg/mL) had decreased to 245 pg/mL without any complications. At discharge, the patient's LVEF had slightly improved to 28%, and a TTE showed that the MR was still mild.

After 7 months of receiving optimal medical therapy after discharge, her dyspnoea on exertion reappeared. Her BNP level (normal range: <18.4 pg/mL) was 49.3 pg/mL, an electrocardiogram showed sinus with 60 b.p.m., and the negative T waves had

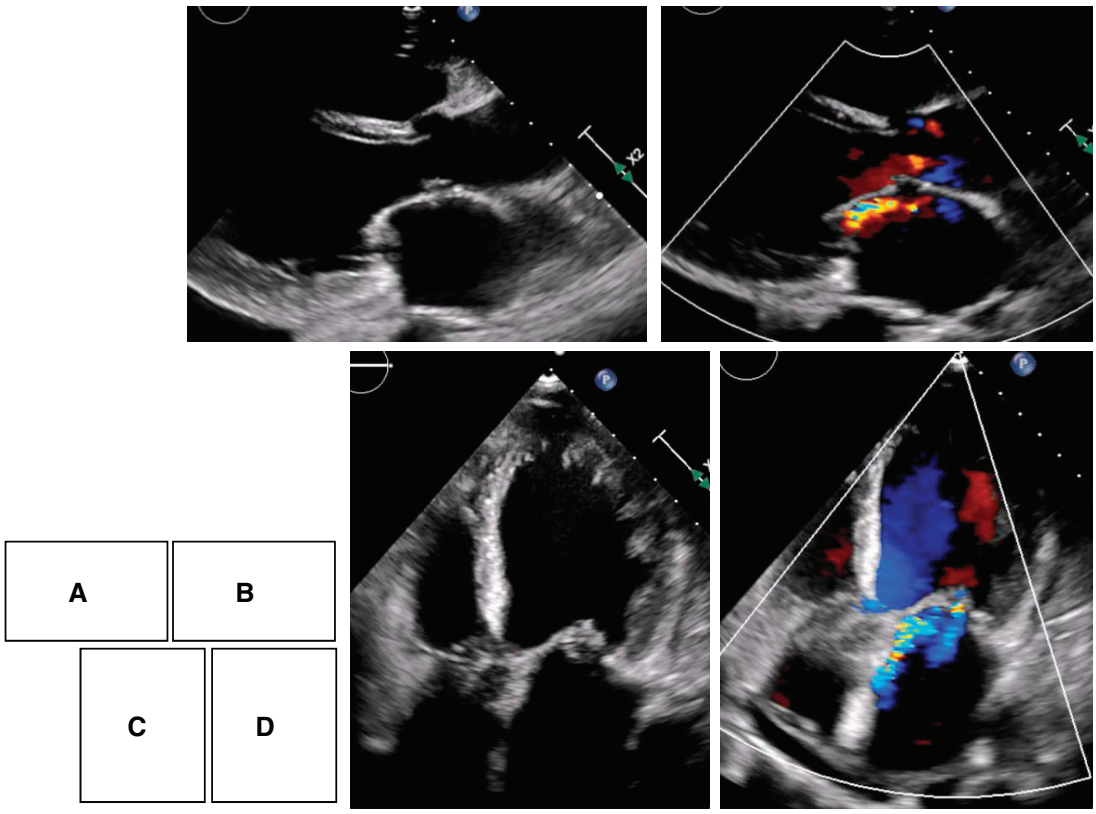
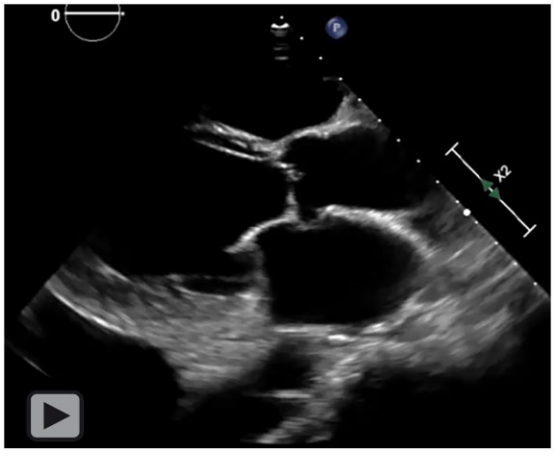


Figure 1 Transthoracic echocardiogram on admission presenting (*A*) left ventricular dilation, tethering of both leaflets, and posterior leaflet prolapse; (*B*) a mild mitral regurgitation jet; (*C*) the grey-scale four-chamber view; and (*D*) the colour Doppler imaging four-chamber view.



Video 1 Transthoracic echocardiography on admission.

disappeared. Radiographic image findings of the chest showed a reduced cardiac shadow, and that the lung congestion and pleural effusion had disappeared (Supplementary material online, *Figure S2*). Transthoracic echocardiography showed significant improvement in LVEF to 64%, a normalized LV wall motion, and that the LV dilation and mitral valve tethering had disappeared. However, posterior leaflet prolapses became apparent, and MR blowing was getting worse (*Figure 2* and *Video 2*). Transoesophageal echocardiography showed massive prolapse of P2 and P3 with a severe MR jet blow. The regurgitant volume was 138 mL and the effective regurgitant orifice area, measured using the proximal isovelocity surface area method, was 0.87 cm^2. Chordal lengthening, leaflet thickening, and degeneration were observed. There were no ruptured chordae (*Figure 3* and *Video 3*). We decided that mitral valve surgery should have been performed to treat the symptomatic severe primary MR.

After 2 months, successful surgical repair of the mitral and tricuspid valves was performed. The postoperative course was satisfactory, the MR disappeared, and the LV wall motion was maintained. Her dyspnoea on exertion had disappeared. At 2 years after the operation, the patient has not experienced any subsequent exacerbation of heart failure.

Discussion

This was a very unusual case, in which MR worsened following improvement of cardiac function because of the exacerbation of posterior leaflet prolapse. Given this patient's clinical course, we excluded other possible causative factors of rapid MR exacerbation, such as infective endocarditis, myocardial infarction, and connective tissue

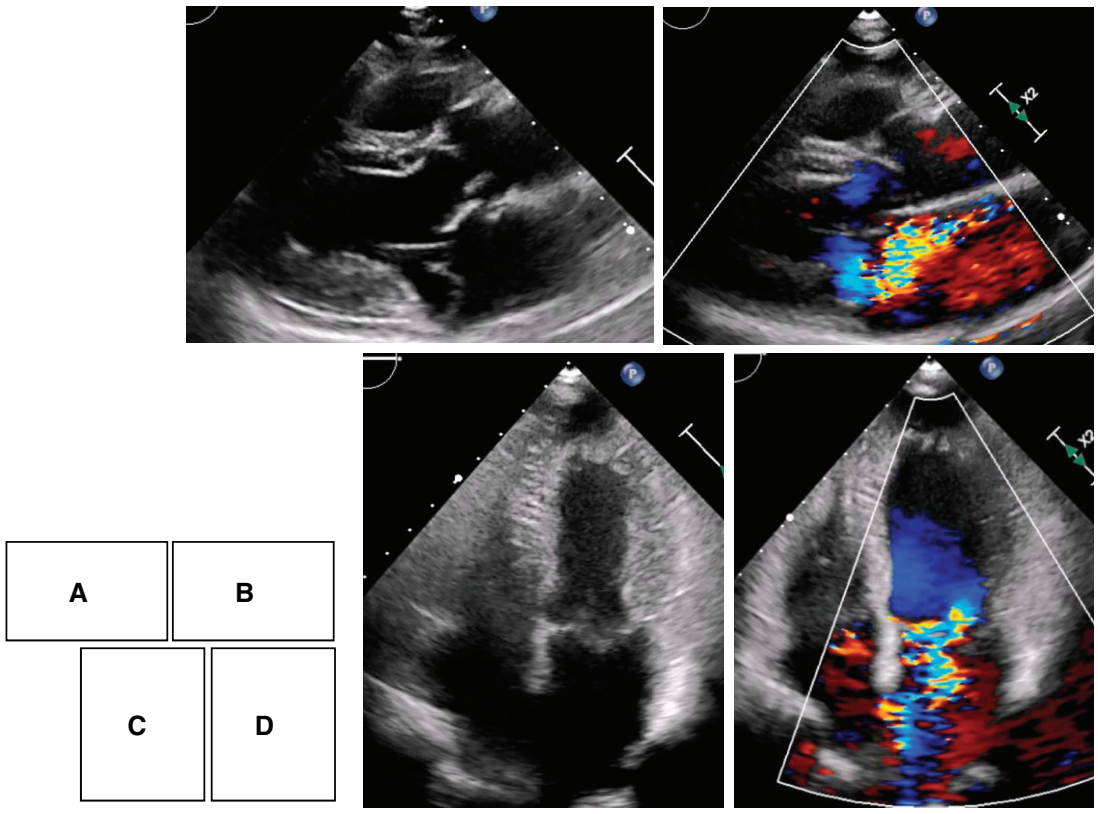
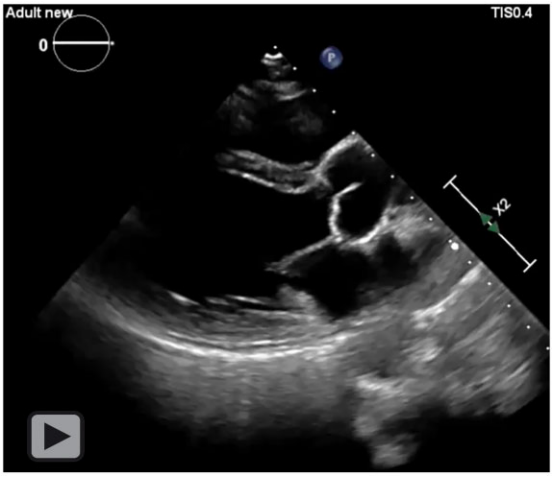


Figure 2 The transthoracic echocardiogram after 7 months of medical therapy showing (*A*) that ejection fraction improved to 64%, left ventricular volume reduced, and anterior leaflet tethering disappeared compared with the corresponding in the acute phase. Posterior leaflet prolapse worsened; (*B*) mitral regurgitation was exacerbated; (*C*) the grey-scale four-chamber view; and (*D*) the colour Doppler imaging four-chamber view.



Video 2 Transthoracic echocardiography after reverse remodeling.

disease (Marfan syndrome). In our case, the MR mechanism was described using Carpentier's classification, which classifies MR according to the movement of the mitral valve.[5] A clear posterior leaflet prolapse (type II) was identified on the TTE in the acute and compensatory periods of heart failure. In the acute phase of heart failure, LV enlargement was observed, both anterior and posterior mitral valves were tethered, and MR at this point contained functional (type IIIb) elements. After the improvement in cardiac function, the size of the left ventricle normalized, and mitral valve tethering disappeared. In the acute phase, in which type II and IIIb (functional MR) elements should have been involved, the degree of MR were mild. After the improvement in cardiac function (after type IIIb elements were eliminated), MR worsened and unexpectedly became severe because of the exacerbation of the type II element.

Generally, during systole, the mitral valve is closed by a balance between a closing force that pushes the mitral valve from the LV side and a tethering force that pulls the mitral valve to the LV side.[6] In this case, the regurgitation mechanism can be explained as follows: the tethering force attributed to LV enlargement was enhanced, and the posterior leaflet was pulled to the LV side, thus, reducing the degree of prolapse (instead of the appearance by which the tip of the posterior cusp with reduced deviation covered the gap between the anterior and posterior leaflets). This mechanism decreased both the gap and closing force on the mitral valve, contributing to the MR jet attenuation. After reverse remodelling, the loss of tethering and increased closing force resulted in mitral valve prolapse and MR enhancement (*Figure 4*).

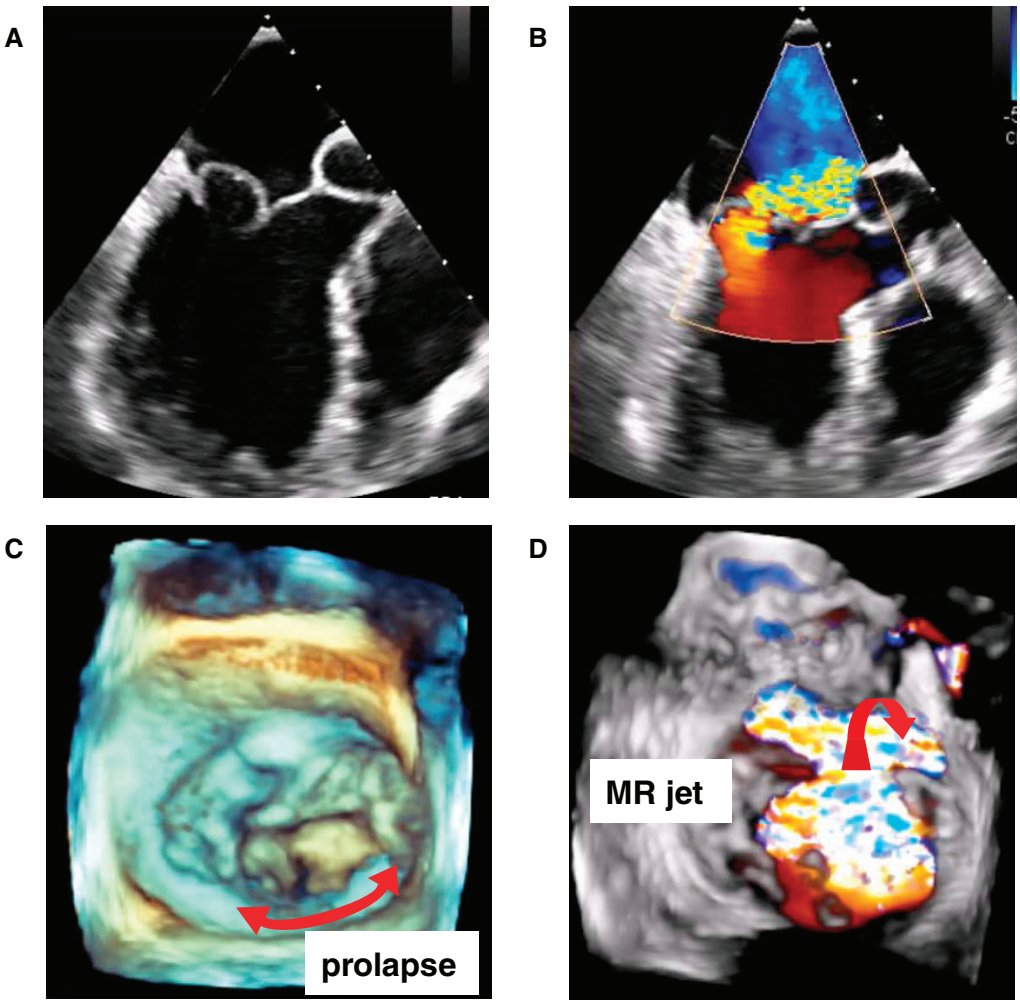
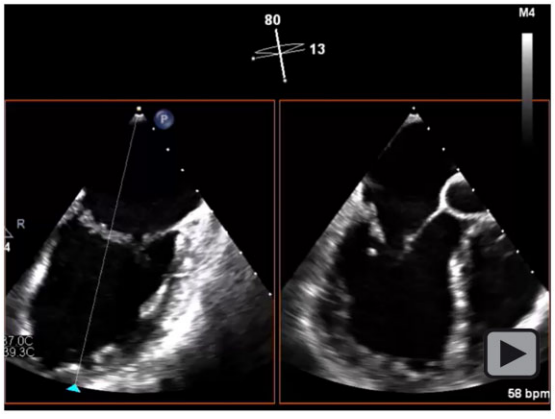


Figure 3 Transoesophageal echocardiography showing (*A*) P2 prolapse, (*B*) the mitral regurgitation jet blowing from the same site on colour Doppler imaging, (*C*) three-dimensional imaging from the left atrial side showing P2–P3 prolapse, and (*D*) colour Doppler imaging showing the severe mitral regurgitation jet from the prolapse part shifting to the front of the left atrium.



Video 3 Transesophageal echocardiography showing P2 prolapse.

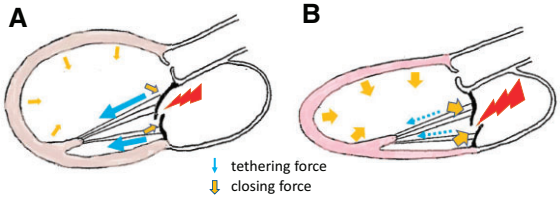


Figure 4 Schematic representation of the proposed mechanism of the patient's heart activity. (*A*) In the acute phase, the closing force to the mitral valve was weakened, and the tethering force increased. As a result, the gap of the mitral leaflets decreased, and mitral regurgitation jet was attenuated. (*B*) After reverse remodelling, the closing force was enhanced, and the tethering force decreased. Accordingly, prolapse of posterior leaflet and exacerbation of mitral regurgitation were observed.

We speculated that the decongestion and improvement of neurohormonal blockade, together with reverse remodelling may have contributed to alleviating the heart failure while worsening the MR.

Our study had a limitation. Although mitral valve prolapse was observed because MR was mild and jet deviation strong, quantitative evaluation of MR was not performed in the acute phase. Therefore, the severity of MR may has been underestimated.

Conclusions

This case presents an unusual course of mitral valve prolapse and MR enhancement due to reverse remodelling of the LV function, loss of tethering, and increase in closing force. To the best of our knowledge, this is the first report of MR exacerbation after improvement of LV function based on the mechanism described above. Our study presents that reverse remodelling may exacerbate mitral valve prolapse.

Lead author biography

Mami Morioka is a 33-year-old doctor working in Kumamoto University, Kumamoto, Japan. She performed a fellowship in Kumamoto University, Kumamoto, Japan. Her areas of interest include heart failure and valvular heart disease.

Supplementary material

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

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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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