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Takotsubo cardiomyopathy secondary to elective sclerotherapy for varicose veins

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SUMMARY

A man in his 70s presented to the emergency department with ongoing chest pain, which started directly after receiving sclerotherapy for the treatment of varicose veins. This was on a background of experiencing short-term chest pain twice previously following sclerotherapy. By the time he was seen, his pain had reduced significantly. ECG showed subtle ischaemic changes. Troponins were significantly raised. A transthoracic echocardiogram demonstrated apical akinesis. Coronary arteries were patent on angiography. A repeat echocardiogram in 4 weeks showed complete resolution of ventricular dysfunction. This represents the first reported case of Takotsubo cardiomyopathy following sclerotherapy in the UK. This case provides a useful learning opportunity for clinicians, to consider immediate investigation in the context of chest pain following sclerotherapy, and how to practically distinguish between Takotsubo cardiomyopathy and myocardial infarction in the differential diagnosis.

BACKGROUND

Sclerotherapy as treatment for varicose veins is known to be a relatively safe procedure, with few side effects.¹ However, here, we detail the first reported case in the UK of Takotsubo cardiomyopathy (TC) following sclerotherapy. Knowledge of how it presents may be of significance to vascular surgeons who undertake these procedures regularly, and clinicians who review cases of chest pain postprocedure.

CASE PRESENTATION

A man in his 70s experienced central chest pain and palpitations directly after receiving sodium tetradecyl sulphate foam as sclerotherapy in a private elective clinic, for the treatment of left leg varicose veins. He felt sweaty and lightheaded within the

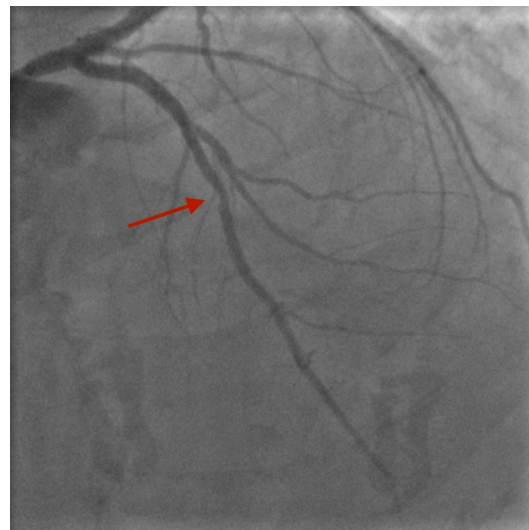


Figure 2 Mid-left anterior descending artery stenosis of less than 50% (arrow).

first hour postprocedure, which then evolved into constant chest discomfort with no other symptoms. The vascular surgeon observed him for 3 hours, and then advised the patient to present to the emergency department (ED) if the symptoms did not resolve by the time he got home, and discharged him. On returning home, the chest pain had not resolved, and the patient decided to drive to the local district general ED.

When he presented, the pain had reduced in severity to 1 out of 10 on the Visual Analogue Scale within 6 hours from onset, from 5 out of 10 initially. The pain was not pleuritic, and did not have any radiation to limbs or jaw. He was neither short of breath nor had any symptoms suggestive of a deep vein thrombosis (DVT). During history taking, he revealed that this had been his third session of sclerotherapy, as his varicose veins were resistant to treatment. Each time after receiving sclerotherapy he had experienced chest pain, but never sought medical attention as these episodes were not severe and self-resolved within 4 hours. His medical history included age-related macular degeneration, hypertension treated with losartan and multiple myeloma, managed well for over 4 years with regular carfilzomib/dexamethasone infusions. He had no smoking history and drank alcohol infrequently.

On examination, his observations were temperature 37°C, heart rate 82, respiratory rate 16, oxygen saturation 98% on air, blood pressure 169/104 mm Hg. He had normal vesicular breath sounds with fine crepitations in both lung bases, and his heart

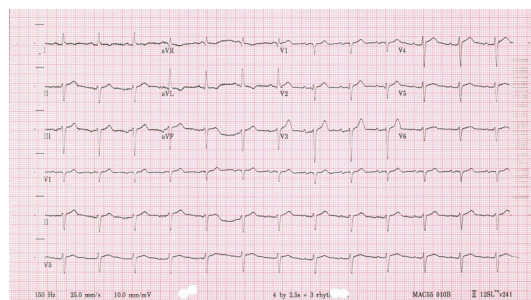


Figure 1 ECG from day 1, on admission. T wave inversion in leads I and aVL, upright T waves in aVR, 1 mm ST elevation in V1, 2, 3.



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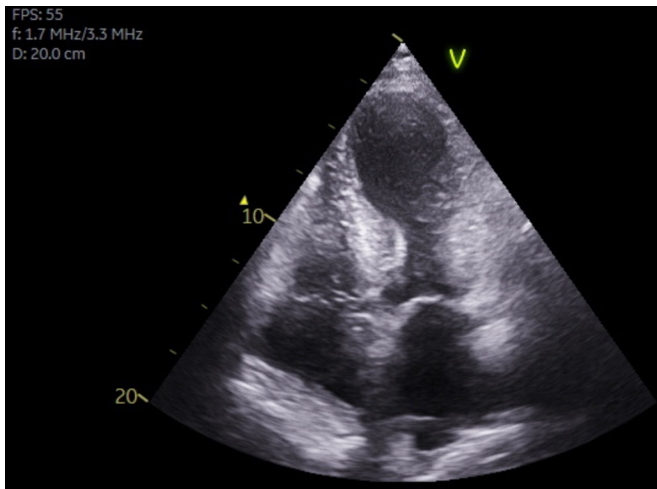


Figure 3 Initial transthoracic echocardiogram showing apical akinesis (mid-systole).

sounds were normal. His left leg had a compression stocking in situ. No clinical signs of a DVT were present on both lower limbs.

INVESTIGATIONS

ECG (figure 1) showed a normal sinus rhythm with a rate of 82, T wave inversion in leads I and aVL, upright T waves in aVR and 1 mm ST elevation in V1, V2 and V3. Chest radiograph showed clear lung fields. High sensitivity troponin T taken at the initial clerking was 890 ng/L, which dropped to 674 ng/L after 4 hours. A d-dimer level was 1.08 $\mu\text{g/mL}$, and all other blood tests were normal.

DIFFERENTIAL DIAGNOSIS

Initial suspicions of anaphylaxis from the sclerosing agent were low given the lack of signs in the clinical picture, hence not pursued in diagnostic tests. Similarly, suspicions of infectious myocarditis were also low, given the onset of symptoms following sclerotherapy. Myocardial infarction (MI) was the most likely differential given the significant troponin rise and ECG changes, and the patient was initially treated with fondaparinux (2.5 mg), aspirin (300 mg) and clopidogrel (600 mg). A CT pulmonary angiogram was performed to rule out pulmonary embolism and aortic dissection, and was negative. The patient then underwent coronary angiography (figure 2), which revealed patent coronaries, with two points of <50% stenosis seen at the left anterior descending artery and right coronary artery. A bedside transthoracic echocardiogram (TTE) was used to assess cardiac function, as well as to rule out cardiomyopathy or pericardial pathologies. This showed apical akinesis with a reduced ejection fraction of 42%, suggestive of TC (figure 3). Over the patient's 4-day admission, daily ECG traces showed a progressive T wave inversion (figure 4). The final contending differential diagnoses were TC or MI with non-obstructive coronary arteries (MINOCA). Given that the patient was well and pain-free for over 72 hours, he was discharged on dual antiplatelet therapy, statin and beta-blocker, with follow-up.

OUTCOME AND FOLLOW-UP

A TTE was repeated as an outpatient, 4 weeks after discharge. This showed that his ejection fraction had returned to normal (60%) and there were no regional wall movement abnormalities,

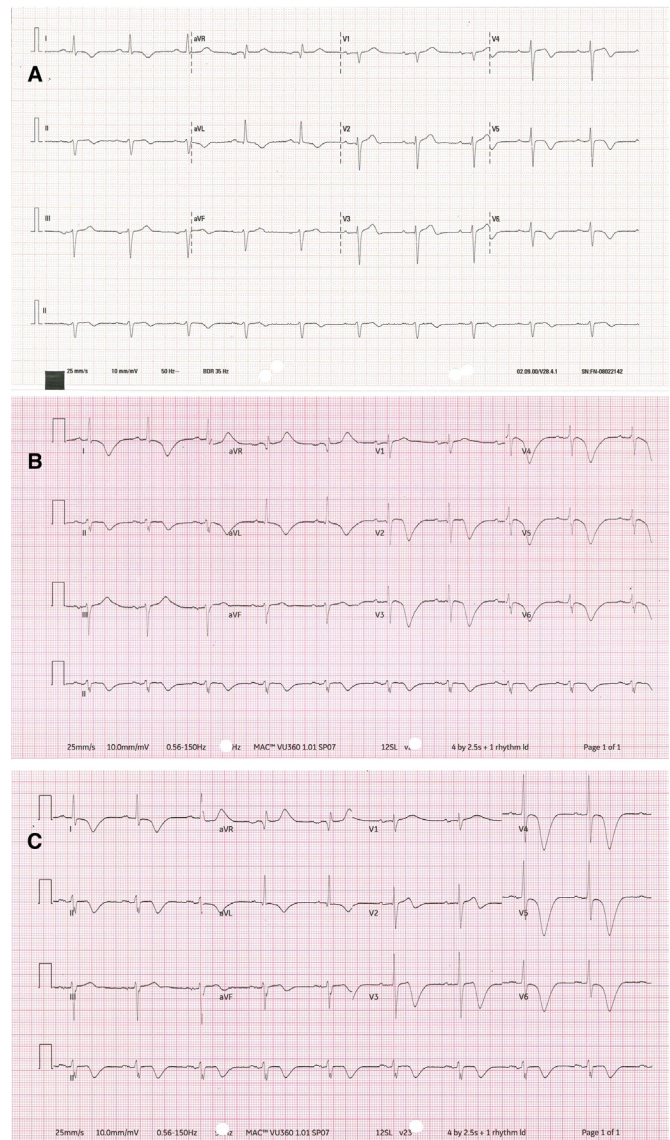


Figure 4 (A) ECG from day 2 admission. New T wave inversion in leads II, V4, 5, 6. Deepened inverted T waves in leads I. (B) ECG from day 3 admission. New T wave inversion in V2, 3. Deepened inverted T waves overall. (C) ECG from day 4 admission. Progressive deepened T wave inversion.

including at the apex. The patient's cardiac medications were stopped, and he was discharged with advice not to undergo sclerotherapy again.

The final diagnosis was TC.

DISCUSSION

We performed a literature search on PubMed, and found three similar cases of TC following sclerotherapy. Two of the cases occurred in patients where the agent of use was polidocanol,^{2,3} and the other, sodium tetradecyl sulphate foam.⁴ In all three cases, patients experienced chest pain shortly after receiving sclerotherapy, followed by ECG changes and elevated troponins. All cases demonstrated apical hypokinesis on TTE, with normal coronaries on cardiac catheterisation. Our case is similar in terms of onset of symptoms, presentation and investigation findings. One case described the use of cardiac MRI to rule out acute ischaemia, and conducted a follow-up cardiac MRI that

Table 1 International Takotsubo diagnostic criteria (InterTAK diagnostic criteria)

1. Patients show transient* left ventricular dysfunction (hypokinesia, akinesia or dyskinesia) presenting as apical ballooning or midventricular, basal or focal wall motion abnormalities. Right ventricular involvement can be present. Besides these regional wall motion patterns, transitions between all types can exist. The regional wall motion abnormality usually extends beyond a single epicardial vascular distribution; however, rare cases can exist where the regional wall motion abnormality is present in the subtended myocardial territory of a single coronary artery (focal takotsubo syndrome).†
2. An emotional, physical or combined trigger can precede the takotsubo syndrome event, but this is not obligatory.
3. Neurological disorders (eg, subarachnoid haemorrhage, stroke/transient ischaemic attack or seizures) as well as pheochromocytoma may serve as triggers for Takotsubo syndrome.
4. New ECG abnormalities are present (ST-segment elevation, ST-segment depression, T-wave inversion and QTc prolongation); however, rare cases exist without any ECG changes.
5. Levels of cardiac biomarkers (troponin and creatine kinase) are moderately elevated in most cases; significant elevation of brain natriuretic peptide is common.
6. Significant coronary artery disease is not a contradiction in takotsubo syndrome.
7. Patients have no evidence of infectious myocarditis.†
8. Postmenopausal women are predominantly affected.

* Wall motion abnormalities may remain for a prolonged period of time or documentation of recovery may not be possible. For example, death before evidence of recovery is captured.

† Cardiac MRI is recommended to exclude infectious myocarditis and diagnosis confirmation of takotsubo syndrome.

demonstrated a resolution of the cardiac abnormality.² Another used nuclear stress testing to rule out ischaemia, but was inconclusive.³ Two cases effectively ruled out ischaemia by demonstrating near normal coronary arteries on angiography.^{3,4} Our case considered the possibility of MINOCA, given the instances of <50% stenosis seen in two vessels on the coronary angiogram and the ECG changes over the course of the admission.⁵ Follow-up TTE demonstrating a resolution of ventricular function effectively ruled this out and provided the final diagnostic step. It is also worth noting that this was similarly demonstrated in one case, which saw a return to normal left ventricular function on TTE within 3 days.⁴

TC, otherwise known as transient left ventricular apical ballooning syndrome,⁶ is defined as a reversible cardiomyopathy with clinical presentation indistinguishable from MI.⁷ The European Society of Cardiology recently published an international consensus on the diagnostic criteria of TC (table 1),⁸ taking into account previous work by cardiologists from the Mayo Clinic.⁶

The prevalence of TC is estimated to be approximately 2%–3% in all patients presenting with suspected acute coronary syndrome, though this is likely to be underestimated.⁹ Theories of the aetiology of TC include multivessel vasospasm and direct catecholamine-mediated myocardial stunning.¹⁰ Theories for the development of TC after sclerotherapy are thus similar, and are hypothesised to be as a result of vasospasm either from direct interaction of the sclerosant to vessel walls or via mast cell degranulation, or from catecholamine release as a result of the discomfort of procedure or from direct interaction of the sclerosant with vessel walls.^{2,4} Sclerotherapy has also been linked with strokes and transient ischaemic attacks, further suggesting a possible vasospastic aetiology.^{4,10}

A number of published cases can be found of MI following sclerotherapy, though all are associated with a pre-existing

Patient's perspective

Initially, I was not worried as the pain was not severe. I didn't think it was serious because the chest pain had happened before, each time after sclerotherapy. But when the troponins came back high, I was actually interested in what was going on, and slightly disappointed to have to stay in hospital. Throughout my stay in hospital, I was actually more concerned about how this would affect my other treatments and conditions, like my myeloma. I'm ultimately glad that someone has taken an interest in my case, and I hope people will be able to learn from this case as well.

Learning points

- ▶ Takotsubo cardiomyopathy following sclerotherapy is rare.
- ▶ In patients experiencing chest pain following sclerotherapy, even if chest pain is self-limiting and relatively short, a cardiac pathology needs to be suspected and investigated accordingly.
- ▶ In the context of differentiating between myocardial infarction (MI) and Takotsubo's, treating a suspected MI and following up with an outpatient echocardiogram to exclude, is a realistic management compared with cardiac MRI or stress nuclear imaging.

patent foramen ovale (PFO).^{11–14} Rather than vasospasm, the aetiology is thought to be as a result of microemboli, caused by the procedure, crossing the PFO and causing coronary artery embolisation.¹⁴ We could find no published cases of MI, without pre-existing PFO, following sclerotherapy. This may be something for clinicians to consider when differentiating between a diagnosis of MI or TC in patients who experience chest pain postprocedure.

Contributors RA-M is first author of this case reports, as he was involved in the patient's direct clinical care, the case report conception and design, the literature search and review, the initial article drafting and subsequent revisions. He has given final approval of this manuscript. YM was instrumental in the case report design, the literature search and review and the manuscript drafting and revisions. He has given final approval of this manuscript. KHGL was instrumental in the manuscript drafting and revisions. He has given final approval of this manuscript. SB is the consultant physician who supervised the writing of this case report. He was involved in the case report design and the article revisions. He has given final approval of this manuscript.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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