CASE REPORT

Takotsubo syndrome in a premenopausal patient

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SUMMARY

Takotsubo syndrome is a rare clinical condition, with a pathophysiology that is not fully understood. Characterised by an acute and usually reversible heart failure, the condition is often preceded by a stressful event. For the diagnosis of Takotsubo syndrome to be possible, the absence of coronary artery disease as a cause is required. We report a case of Takotsubo syndrome in a 47-year-old woman of fertile age. Electrical and echocardiographic presentations were classical in the patient. However, abnormally elevated cardiac biomarkers were registered. The patient showed signs of clinical improvement, with a follow-up angiography excluding coronary artery disease and therefore leading to a diagnosis of Takotsubo syndrome.

BACKGROUND

First described in Japan in 1990, Takotsubo syndrome is an acute and usually reversible heart failure. Despite similar characteristics to acute coronary syndromes in its initial presentation, Takotsubo syndrome does differ. Samples of Asian and Western populations indicate that 1%–2% of patients with suspected acute coronary syndrome can eventually be diagnosed with Takotsubo syndrome. This diagnosis occurs predominantly in postmenopausal women (~90% of reported cases).[1–3] 'Takotsubo' owes its name to the Japanese octopus traps, due to the shape taken on by the left ventricle at the end of the systole.

Although the syndrome is classically associated with a stress event, this trigger is no longer essential for diagnosis.[1 2 4] The current diagnostic criteria were published in 2015 by Heart Failure Association of the European Society of Cardiology.[1] The pathophysiology of Takotsubo syndrome is still not well established; however, it is thought that an acute catecholaminergic myocardial stunning mechanism may be involved.[1] Takotsubo syndrome encompasses several anatomical variants. The main clinical manifestations of this syndrome are precordialgia, which in the most severe cases may be accompanied by syncope, acute pulmonary oedema, cardiogenic shock, dyspnoea and palpitations with ECG alterations mimicking acute coronary syndrome.

In its initial stages, Takotsubo syndrome is indistinguishable from an acute coronary syndrome.[1 2 5] Complications include acute mitral regurgitation, ventricular arrhythmias, left ventricular outflow tract obstruction and ventricular mural thrombus with potential embolisation.[6]

The present case is of interest due to its occurrence in a premenopausal patient under the age of 50 (<10% of reported cases), in addition to the rarity of reporting of Takotsubo syndrome in cases of meningitis or encephalitis.[7]

CASE PRESENTATION

The patient was a 47-year-old premenopausal Caucasian woman, with a prior traumatic brain injury with a fracture of the petrous part of the temporal bone and pneumococcal meningitis at the age of 19 years.

The patient was found unconscious at home. The prehospital emergency service was deployed and the emergency medical team confirmed respiratory arrest, successfully reversed through ventilator support with an artificial manual breathing unit. The patient recovered from a Glasgow Coma Score of 6 and was intubated, sedated, ventilated and transported to the emergency department at a Central Hospital.

Influenza and otalgia were reported the week before hospitalisation. No potential triggers such as physical or emotional distress were reported (either by the patient or the patient's family).

INVESTIGATIONS

Right otomastoiditis and bacterial meningitis were assumed at the emergency department following a CT, MRI and a cytological and biochemical examination of the cerebrospinal fluid.

The patient was admitted to the Neurocritical Intensive Care Unit and underwent direct treatment, requiring vasopressor and ventilator support. Electrocardiographically, the patient initially showed changes suggestive of a lateral wall ischaemia (figure 1).

Troponin I (high sensitivity) reached a maximum of 12 891 pg/mL (<15.6), and natriuretic peptide type B (BNP) was also found to be 655 pg/mL (<100).

The patient underwent a transthoracic echocardiogram on admission, showing a hypokinesis of the left ventricular lateral wall, with a discrete dilation of the same area.

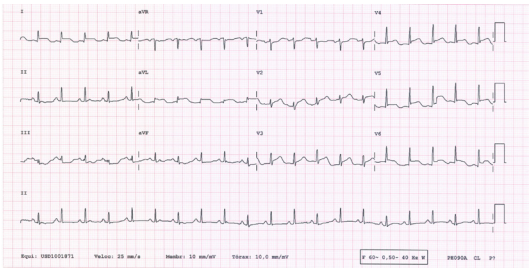

Figure 1 Initial ECG—ST segment elevation in DI, aVL and V5–V6.

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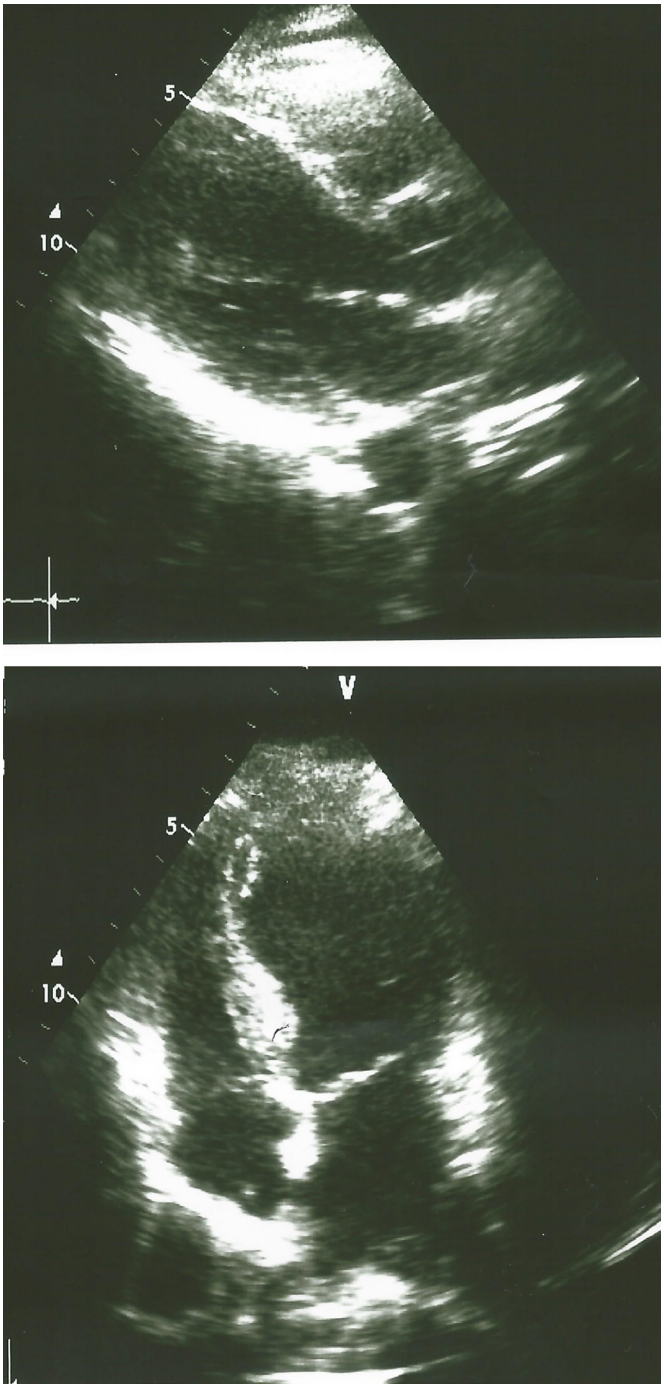

Figure 2 Transthoracic echocardiogram. (A) Long left parasternal axis with dilated left ventricle, hypercontractility of basal segments of the posterior wall and IVS. The remaining segments are hypokinetic. (B) Apical plane: apical dilation. Hypercontractility of basal wall segments lateral and IVS. IVS, inter ventricular septum.

On the third day, the patient was again submitted to echocardiographic evaluation, which documented a much enlarged left ventricle with decreased global systolic function, apex akinesia and hypokinesia of all other walls with hypercontractility of the basal segments and no obstruction to the left ventricle exit chamber (figure 2).

The patient was submitted to an initial empirical antibiotic treatment with vancomycin and ceftriaxone which, after the isolation of *Streptococcus pneumoniae* in cerebrospinal fluid with no bacteraemia, was adjusted to ceftriaxone only. The patient also underwent a right myringotomy and the insertion of transtympanic tubes.

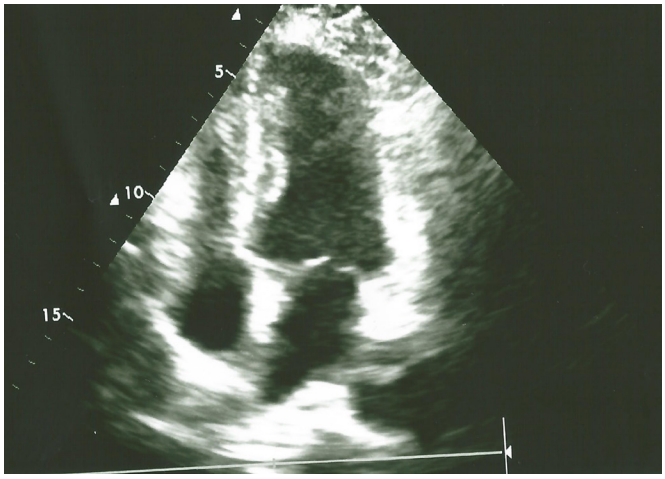

Figure 3 Transthoracic echocardiogram. Apical plane: left ventricle of normal dimensions with preserved global and segmental systolic function.

The patient showed signs of clinical improvement, with no behaviour or personality changes, although a slight psychomotor retardation was noted. An electroencephalogram was performed, showing scarce paroxistic activity. The patient was treated with valproic acid and levetiracetam, with a control electroencephalogram indicating no paroxistic activity. Imaging studies were performed, with CT unchanged from admission.

With no need of organ support, the patient was transferred to the Internal Medicine ward on the 13th day, where she continued asymptomatic and did not manifest any signs or symptoms of heart failure or focal or cognitive neurological deficits.

OUTCOME AND FOLLOW-UP

On the 20th day, the patient was in the infirmary and was submitted to a new echocardiographic evaluation, which emphasised a normalisation of the global and segmental systolic function (figure 3).

Electrocardiographically, only the inversion of the T waves in the anterolateral derivations was noted (figure 4).

On the 25th day, a coronary angiography was undertaken. No changes were noted, corroborating the Takotsubo syndrome hypothesis.

Asymptomatic, the patient was discharged on the 27th day of hospitalisation.

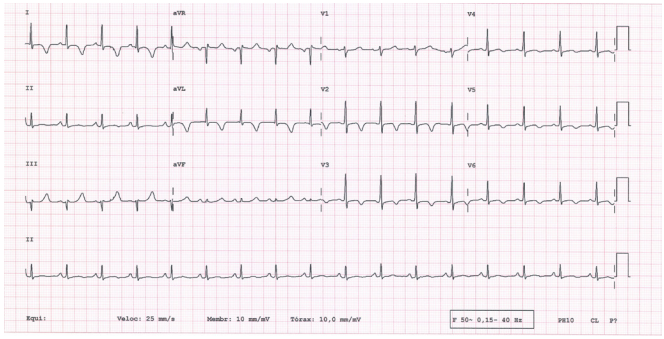

Figure 4 ECG at discharge—negative T waves in anterolateral derivations (**V2–V6**).

DISCUSSION

Cardiac dysfunction (either neurogenic stunned myocardium or stress-induced myocardiopathy—Takotsubo syndrome) has been well documented in patients with central nervous system infection, traumatic brain injury, sepsis, stroke, intracranial haemorrhage, postcardiac arrest, etc.[8 9]

In this case, electrocardiographic changes, associated with elevated cardiac biomarkers, initially raised the diagnostic hypothesis of acute coronary syndrome.

However, it was the presence of several potential triggering physical stress events (respiratory arrest, shock and meningitis), in particular the patient's echocardiographic results (figure 2), that postulated the Takotsubo syndrome hypothesis.

The Doppler echocardiogram should be the first imaging method to be performed, which was the case. The acute phase findings consist of a large area of dysfunctional myocardium involving more than one territory of coronary artery irrigation.[1 5] The present case fits the classic pattern described, found in ~50%–80% of cases, with changes of the left ventricular segmental contractility, with apical and circumferential hypokinesia and basal hypercontractility, with the appearance of virtual apical ballooning at the end of the systole.[1] Contrary to what is described in the literature, troponin reached abnormally high values,[6] which initially raised the diagnostic hypothesis of acute coronary syndrome. BNP levels were >600 pg/mL, as expected in Takotsubo syndrome.[6] This marked elevation of troponin could have raised other diagnostic hypotheses, namely acute coronary syndrome and acute myopericarditis. Moreover, the presence of typical echocardiographic alterations of Takotsubo syndrome, accompanied by a favourable evolution without directed therapy, makes the latter unlikely.

While a coronary angiography is recommended in the event of ventricular dysfunction, in order to rule out acute coronary syndrome, this procedure was not possible in light of the patient's critical state.

The confirmation of the absence of lesions in the epicardial coronary arteries, verified through an angiography, distances the hypothesis of acute coronary syndrome. However, as it was only performed on the 25th day of hospitalisation, this could be a limitation to call it Takotsubo syndrome.

Other proposed diagnostic tests,[1] namely coronary ventriculography and cardiac MR (for the benefit of better visualisation of the right ventricle and areas of ill-clarified apical akinetics on the echocardiogram, and whose T2 weighting allows a more reliable distinction between acute coronary syndrome, myopericarditis and Takotsubo syndrome) could not be performed initially, considering that the patient was undergoing invasive ventilation with an active infectious focus that did not meet the conditions for this type of investigation or other invasive methods at an early stage.

The left ventricular ejection fraction usually recovers up to 12 weeks, whereas electrocardiographic changes and natriuretic peptide levels may take 6–12 months. In some cases, these levels may even remain altered.[1] In this specific case, there was a recovery of the global and segmental systolic function, as well as a normalisation of BNP. However, the inversion of the T waves in the anterolateral leads was maintained. In conclusion, six of the seven diagnostic criteria proposed are fulfilled[1] in this case.

In view of the written above, a Takotsubo syndrome diagnosis is more likely than the others considered at the time.

Learning points

- Cardiac dysfunction has been described in several neurological injuries.
- Although its initial presentation has similar characteristics, Takotsubo syndrome differs from acute coronary syndromes.
- Clinical suspicion is extremely important in the diagnosis of what is a rare condition that is increasingly being identified.

The case described above is of important epidemiological interest, considering the patient's profile in being premenopausal and <50 years old (<10% of cases). Moreover, Takotsubo syndrome is rarely reported in cases of meningitis or encephalitis.[7] Nevertheless, we cannot establish a causal association between these conditions, most notably due to the fact that respiratory arrest could in itself cause cardiac dysfunction.

Although paroxysmal activity can imply cortical dysfunction, the absence of parenchymal lesions in an MRI performed on a patient with a pneumococcal central nervous system infection cannot support the diagnosis of encephalitis. To this end, only meningitis can be assumed.

The importance of clinical suspicion, even without classical clinical features, is particularly relevant in cases of Takotsubo syndrome, allied to the relevance of echocardiography showing transient morphological and functional alterations and angiography proving the absence of coronary disease.[10] This allows the diagnosis of what is a rare condition that is increasingly being identified.

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Competing interests None declared.

Patient consent Obtained.

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