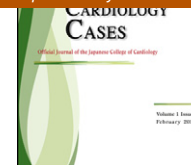




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Case Report

Renal thromboembolism in tako-tsubo cardiomyopathy in spite of anticoagulation

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KEYWORDS

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Summary An elderly lady was admitted with chest pain and an electrocardiogram depicting ST segment elevation, indicative of a myocardial infarction. She was treated with intra-venous tissue plasminogen activator. On coronary angiography there was a dilated and akinetic left ventricular apex but no significant coronary artery disease. She was diagnosed with tako-tsubo cardiomyopathy. An echocardiogram performed two days later demonstrated a thrombus in the left ventricular apex. Despite immediate anticoagulation with intravenous unfractionated heparin, she sustained a renal thromboembolic phenomenon.

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Introduction

Tako-tsubo cardiomyopathy (TTC) is an uncommon condition first described in Japan. Presentation mimics a myocardial infarction, with electrocardiogram (ECG) changes and an associated troponin and creatinine kinase (CK) rise. There is dilatation of the apex of the left ventricle, which may predispose to thrombus formation, with the risk of embolisation, resulting in end organ damage [1,2]. Anticoagulation plays an important role in thrombus lysis [3], however guidelines on anticoagulation are lacking.

Case report

A 67-year-old lady presented with a 5-h history of left upper limb numbness and central compressive chest pain associated with nausea and sweating. She had a blood pressure of 125/80 mmHg, heart rate of 75 beats/min, and a central temperature of 37 °C. She had passed through a very emotionally traumatic period following the death of her son who had Down's syndrome. He died secondary to metastatic testicular carcinoma one year previously. Her initial ECG showed a normal sinus rhythm and no ischaemic changes. A subsequent ECG, performed 2 h later, revealed ST segment elevation in leads I, aVL, V5, V6. A diagnosis of ST segment elevation myocardial infarction (STEMI) was made. She was thrombolysed with intra-venous tissue plasminogen activator and treated with intravenous unfractionated heparin for 48 h. CK level rose to 510 U/L, with CK-MB ratio of 7%. A complete blood count was normal, except for a mild thrombocytosis (platelet $450 \times 10^9/L$). Coronary

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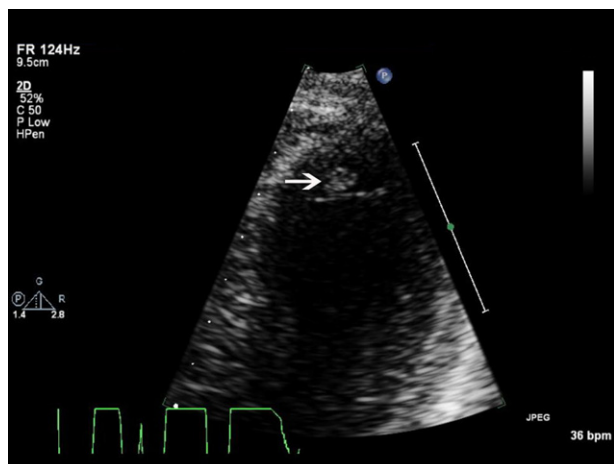


Figure 1 Echocardiogram with thrombus in the apex of the left ventricle.

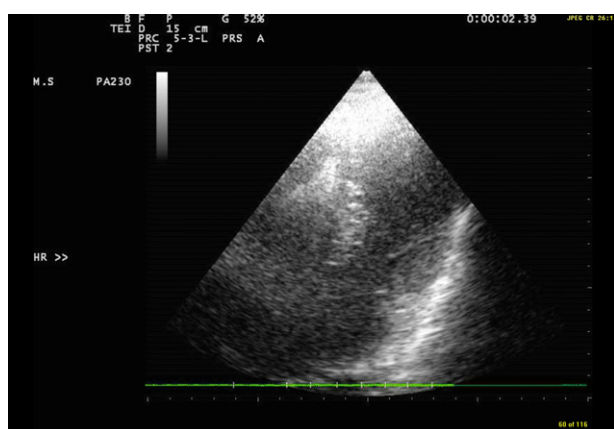


Figure 2 Echocardiogram depicting a dilated left ventricle in systole.



Figure 3 Echocardiogram depicting a dilated left ventricle in diastole.

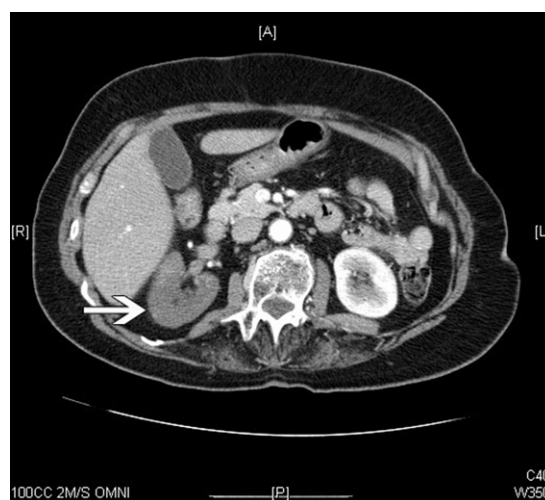


Figure 4 Computed tomography of the abdomen showing no contrast uptake by the lower pole of the right kidney.

angiography was performed 2 days after admission. The left ventriculogram showed a dilated and akinetic apex with bulging out of the left ventricular apex and moderate mitral regurgitation. There were non-significant lesions involving the mid-left anterior descending coronary artery and the diagonal arteries. Heparin was stopped prior to the coronary angiogram, and not re-started following the exclusion of STEMI. An echocardiogram performed on the same day showed a dilated akinetic apex with normal contractility of the basal segment. Significant mitral regurgitation was noted with a flaccid cusp of the posterior segment of the mitral valve. The echocardiogram (Figs. 1–3) was repeated 3 days later and an apical mural thrombus was detected. Anticoagulation was initiated immediately with intravenous unfractionated heparin and also with oral warfarin.

The following day the patient, in spite of anticoagulation (activated partial thromboplastin time ratio of 2.1, international normalized ratio 1.1), sustained severe abdominal pain in the right iliac fossa and right loin associated with feeling faint. A computed tomography scan of the abdomen revealed an embolus in the right renal artery, with an avascular area of the right lower one-third of the kidney (Fig. 4). A right sided pyelogram was carried out via a right femoral

artery puncture. Dual right renal arterial supply was noted. The upper and middle poles of the nephrogram were seen, whilst the lower pole (main renal artery) was not vascularized (Fig. 5). Intra-arterial lysis of the avascular lower pole of the right kidney was unsuccessfully attempted, since the thrombus was not visualized. It is most probable that the thrombus had already fragmented and moved into the distal renal arterioles. Serum creatinine level rose to a maximum value of 110 $\mu\text{mol/L}$. On repeat echocardiography 24 h after the renal infarction the apical mural thrombus was absent, suggesting that the thrombus had embolized out of the left ventricle.

A follow up echocardiogram performed 24 days after the initial event, showed marked improvement in the apical akinesia. No thrombus was visualized in the left ventricle. The flaccid posterior leaflet had resolved, however there was transient systolic anterior leaflet motion of the mitral valve with septal contact and left ventricular outlet obstruction, resulting in mild mitral regurgitation. This resolved completely on echocardiogram performed 3 months after the event. She was advised to continue warfarin for up to one year. Her serum creatinine level returned to normal range at 84 $\mu\text{mol/L}$. A 2-methoxy isobutyl isonitrile scan performed



Figure 5 Right renal pyelogram demonstrating infarcted lower pole of right kidney.

6 months after this event did not reveal any significant ischaemia related to the coronary lesions.

Discussion

To our knowledge, this is the first described case of TTC complicated by a thrombo-embolic phenomenon, despite anticoagulation.

TTC, also known as transient apical ballooning, is a type of non-ischaemic cardiomyopathy where there is a sudden temporary weakening of the myocardium, often triggered by emotional or physical stress. The typical presentation is sudden onset congestive heart failure or chest pain with ECG changes suggestive of STEMI, including ST elevation and/or T wave inversion. Q waves are often present. They may also present with cardiogenic shock [4], ventricular fibrillation, or atrial fibrillation. The left ventricular apex bulges out, with a hypercontractile base of the left ventricle. A coronary angiogram usually does not reveal any significant coronary artery occlusion. Risk factors for TTC include physical or emotional stress, especially in post menopausal women [5], such as the death of a loved one (broken heart syndrome), intracranial events (bleeding, trauma, or ischaemic stroke), acute medical illnesses, surgical procedures, overproduction of catecholamines and administration of exogenous catecholamines [6].

The main treatment is generally supportive. Hypotension should be treated with inotropic agents or an intra-aortic balloon pump. The left ventricular function normalizes within two months. Patients with persistent left ventricular dysfunction at discharge should be treated with a diuretic and an angiotension-converting enzyme inhibitor or angiotension receptor blocker until left ventricular function returns to normal [7]. Repeat echocardiography should be performed prior to hospital discharge and after 1–3 months in patients with persistent left ventricular dysfunction.

TTC is susceptible to left ventricular thrombus formation, due to the hypokinetic ventricular wall motion. Thrombus is detected through echocardiography and should be immedi-

ately treated by anticoagulation [3]. Up to 8% of patients with TTC may have a thrombus in the left ventricle. This may be present at the initial presentation, or may occur later [8]. An elevated C-reactive protein and thrombocytosis may indicate a higher risk for thrombus formation [8]. Sasaki reported a case where a patient was diagnosed with TTC and treated with anti-platelet therapy due to development of heart failure. Four weeks after anti-platelet therapy was terminated, she was re-admitted with acute renal infarction and a left ventricular thrombus was detected. The thrombus was lysed with urokinase and warfarin [9]. Evidence of thromboembolism in TTC has been documented in the form of embolic strokes [1], and embolic occlusion of the distal right popliteal and anterior tibial arteries [2]. In the majority of cases, thrombi occur in the left ventricular apex, however they may also form adjacent to the papillary muscles, so this area needs to be assessed carefully during echocardiography [8].

In TTC with thrombus formation, all reported cases were treated with some form of anticoagulation. Urokinase, warfarin [9], low molecular weight heparin (LMWH) have all been used with success. One case was initiated with aspirin and intravenous unfractionated heparin and switched to LMWH two days later [10]. The reported duration of anticoagulant treatment varied from 7 days up to 3 months, depending on the time of follow up for thrombus resolution [8].

Conclusion

The incidence of thrombus formation is low in TTC. However, the effects of thromboembolism are serious. Further research is required to establish whether or not initiating anticoagulation is required in all patients presenting with TTC, or only once a thrombus has been detected. The best form, dose, and duration of anticoagulation in TTC also remains unclear.

Conflict of interest

We declare that there is no financial support and no relationships that may pose a conflict of interest.

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