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Case Report

Takotsubo Cardiomyopathy in Aneurysmal Subarachnoid Hemorrhage with an Atypical Clinical Presentation: A Case Report

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Abstract

Takotsubo cardiomyopathy can masquerade as an acute coronary syndrome and present clinically with chest pain and dyspnea, electrocardiogram changes of cardiac ischemia and elevation of cardiac enzymes. Such changes are particularly relevant in cases where Takotsubo cardiomyopathy is associated with subarachnoid hemorrhage, and treatment of acute coronary syndrome with antiplatelet drugs is contraindicated. We describe a case of a 68-year-old woman, who developed ventricular changes consistent with Takotsubo cardiomyopathy following an aneurysmal subarachnoid hemorrhage. The patient presented with collapse and vomiting, initial workup revealed anterior ST-elevation electrocardiogram changes, increased troponin I, and a chest radiograph suggestive of acute cardiac failure. In light of this, the patient was managed initially as an acute coronary syndrome with antiplatelet medication. An echocardiogram showed acute left ventricular systolic dysfunction with apical ballooning. After 3 days of hospitalization, she became increasingly drowsy with a worsening headache. Computed tomography of the head revealed intracerebral hemorrhage and bilateral subarachnoid hemorrhage and computed tomography angiography demonstrated a 9 × 5 mm A2 aneurysm. She subsequently underwent embolization to treat the ruptured aneurysm. She recovered well neurologically, and subsequent cardiac imaging revealed a complete resolution of her prior issues.

Introduction

Takotsubo syndrome (TTS) or Takotsubo cardiomyopathy is characterized by reversible left ventricular apical ballooning in the absence of angiographically significant coronary artery disease. It is thought to be caused by a surge in catecholamines and is classically preceded by acute emotional stressors, leading it to also be known as broken heart syndrome.[1] However, there are increasing reports of TTS being triggered by catecholamine release during an aneurysmal rupture. So much so, that neurogenic stress cardiomyopathy, which includes TTS, is now a recognized complication of aneurysmal subarachnoid hemorrhage (aSAH).[2] aSAH associated with TTS is often misdiagnosed owing to limited clinical awareness of these coexistent diseases and has a mortality of 30–50%.[3] This case report intends to raise awareness of Takotsubo cardiomyopathy mimicking acute coronary syndrome (ACS), and to consider aSAH in patients with relevant neurological findings and electrocardiogram (ECG) changes suspicious of myocardial ischemia.

Keywords: Takotsubo cardiomyopathy; Subarachnoid hemorrhage; Stroke; Heart failure; Acute coronary syndrome.

Abbreviations: ACS, acute coronary syndrome; aSAH, aneurysmal subarachnoid hemorrhage; CT, computed tomography; ECG, electrocardiogram; ED, emergency department; STEMI, ST-elevation myocardial infarction; TTS, Takotsubo syndrome.

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Case presentation

A 68-year-old woman, presented to the emergency department (ED) having collapsed at home with transient loss of consciousness. After regaining consciousness, she had several episodes of vomiting as well as neck pain and headache. She reported that her neck pain and headache were longstanding and most likely due to cervical spine degenerative disease. There was no history of chest pain, palpitations, or breathlessness. She had a history of hypertension controlled with lercanidipine. On examination, the patient was alert but appeared clinically dehydrated and peripherally cool. Cardiovascular examination was otherwise normal, with a normal, regular heart rate, and clear chest bilaterally on auscultation. There was no neurological deficit. Within 1 h of being admitted to the

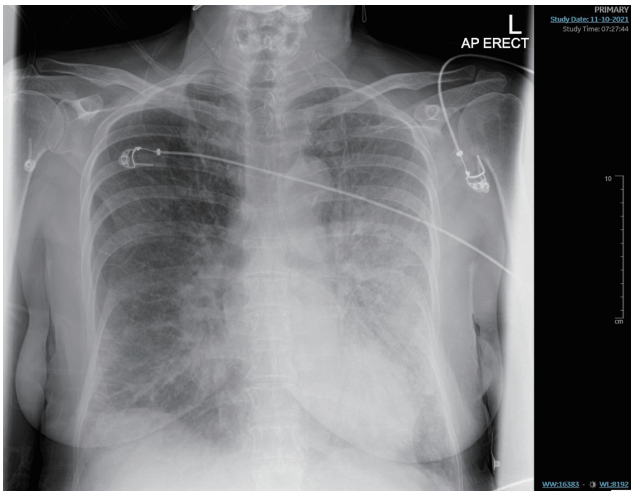

Fig. 1. Chest X-ray showing acute pulmonary edema.

ED, she began desaturating, requiring 12 L of high-flow oxygen. Chest radiography showed bilateral hazy perihilar opacity bilaterally, but predominant over the left lung field. The findings were reported as suggestive of heart failure with pulmonary edema; however, atypical pneumonia could not be excluded (Fig. 1). Serology revealed markedly elevated troponin I of 13,239 ng/L (normal: < 40 ng/L), a positive D-Dimer of 2,709 ng/mL (normal: < 300 ng/mL), increased white cell count of 22.2 × 10^9/L (normal: 4.5–11.0 × 10^9/L), but a normal C-reactive protein of < 4 mg/L. Empirical intravenous antibiotics were initially given (piperacillin and tazobactam) in response to the leucocytosis and chest radiograph changes. An ECG revealed a new right bundle branch block with Q waves in V1 to V5, III and aVF, and ST elevation in V4 and V5 (Fig. 2). Given the elevated cardiac enzymes, ECG changes consistent with anterior ST-elevation myocardial infarction (STEMI), and pulmonary edema; ACS treatment with oral aspirin, ticagrelor, and subcutaneous fondaparinux, as well as intravenous furosemide was started. She was transferred to the cardiology ward, where she was closely monitored and remained stable. A bedside echocardiogram at this point showed severe left ventricular systolic dysfunction with mid and apical akinesis (Fig. 3).

On the third day of hospitalization, the patient deteriorated, with a worsening frontal headache and reduced Glasgow Coma Scale of 13/15 (E3, V4, M6). She was hypotensive, with a blood pressure of 93/54 and had a heart rate of 62 beats per minute. Head computerized tomography (CT) carried out at this point showed an acute intracranial bleed with a right frontal anterior hematoma, subdural hematoma, and bilateral subarachnoid hemorrhage (Fig. 4). Repeat blood chemistry revealed worsening renal function, with a urea of 17.7 mmol/L (normal: 2.5–7.8 mmol/L), a new acute stage 1 kidney injury, and slightly increased C-reactive protein of 23 mg/L (normal: < 4 mg/L). Antiplatelet medication was suspended. Cerebral CT angiography confirmed a medium-size 9 × 5 mm aneurysm of the A2 segment right anterior cerebral artery, which likely ruptured and caused the aSAH and intracerebral hematoma (Fig. 5).

She was started on nimodipine and intravenous fluids to manage the aSAH and was transferred to a neurosurgical specialty unit where embolization of the ruptured pericallosal aneurysm was performed. Following embolization, the patient had mild left-side weakness, mild inattention, and mild cognitive impairment, which continued to improve with rehabilitation on the ward. A repeated echocardiogram at week 3 revealed normal left ventricular cavity size with concentric left ventricular hypertrophy. Left ventricular ejection fraction was severely impaired at about 25% of the normal level. She was started on dapagliflozin and spironolactone, transferred to the local stroke unit, and improved over the next few days to a point where she could mobilize with a Nordic pole and manage her diet and hygiene. She was discharged home approximately 1 month after her original admission. At her 6-month review, a follow-up echocardiogram showed complete recovery of left ventricular function, and some degree of left ventricular hypertrophy remained (Fig. 6). Subsequent CT angiography showed no evidence of coronary artery disease. Her heart failure symptoms improved and her medications were eventually stopped. She was managed for hyper-

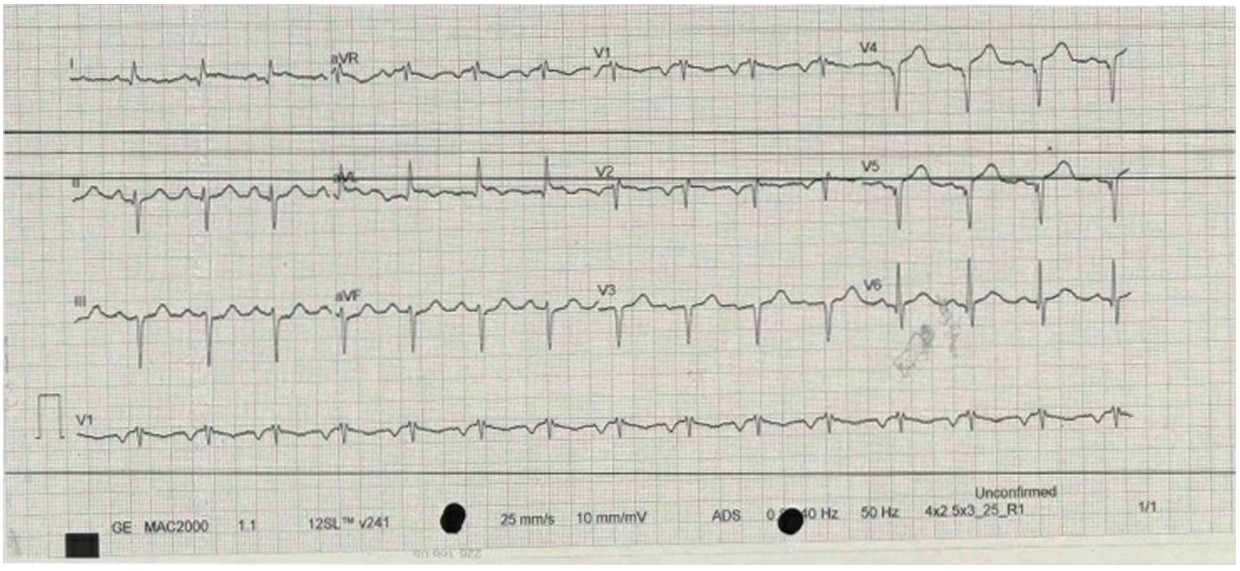

Fig. 2. Electrocardiogram changes consistent with anterior STEMI, Q waves in V1 to V5, III and aVF, and ST elevation in V4 and V5. STEMI, ST-elevation myocardial infarction.

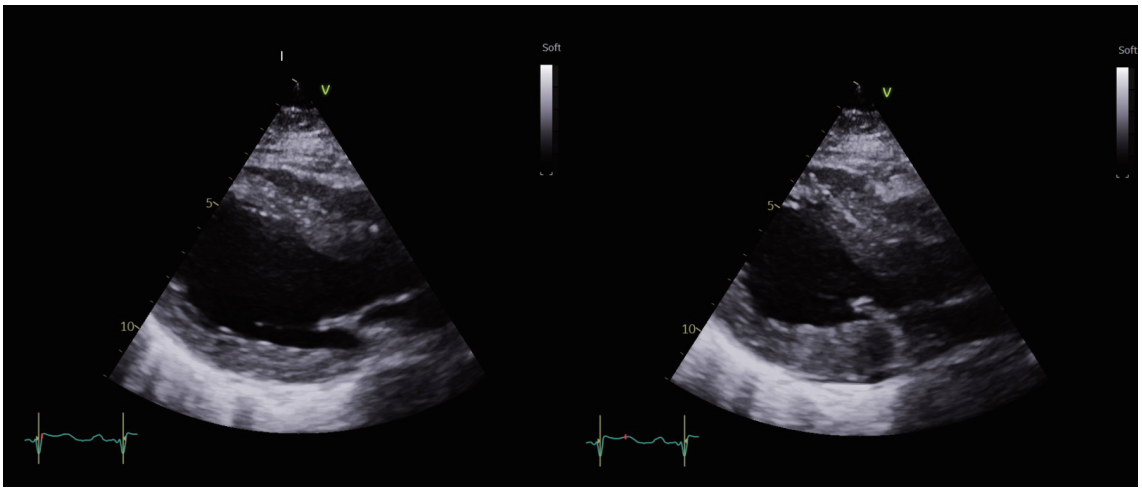

Fig. 3. Echocardiogram showing apical ballooning and dilation, with basal segment contraction.

tension as per the usual community protocol. She continued to make good neurological recovery in the ensuing weeks.

Discussion

We present the clinical details of a postmenopausal woman, previously in quite good functional health with controlled hypertension, who developed signs and symptoms indicative of acute myocardial infarction soon after hospital admission. This was preceded by symptoms suggestive of, but not entirely characteristic of, subarachnoid hemorrhage. Atypical pneumonia was briefly considered as a differential because of a new oxygen requirement, raised white cell count, and bilateral haziness on the chest radiograph. Considering the ECG changes and a markedly high troponin, cardiac failure secondary to ACS was thought to be more likely and she was started on oral antiplatelets and intravenous diuretics, with good effect. Despite the presenting complaint of collapse and headache, the presence of these significant cardiac findings, combined with a normal neurological exam led away from an intracranial cause as a main differential, therefore CT scan of the head was not considered at first. Three days afterward, when she developed worsening neurological symptoms, imaging confirmed the presence of an anterior cerebral artery aneurysm with subarachnoid and intracerebral hemorrhage. Chest radiography at presentation, serial ECGs, and clinical progress showed changes consistent with Takotsubo cardiomyopathy, which explained the cardiac symptoms. Other differentials could include viral illness-induced encephalitis and myocarditis, or acute decompensated heart failure.

Initial and subsequent investigations and clinical progress helped confirm the presence of Takotsubo cardiomyopathy. As defined by the European Heart Failure Association, the following

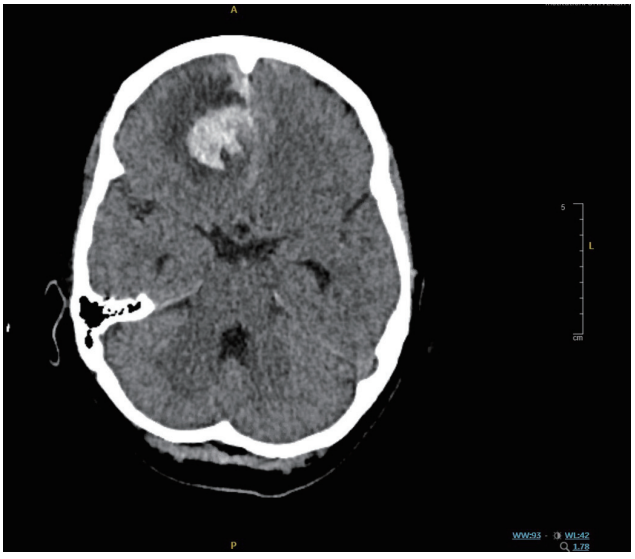

Fig. 4. Computed tomography head showing bilateral subarachnoid hemorrhage, and right frontal lobe Intracranial hemorrhage.

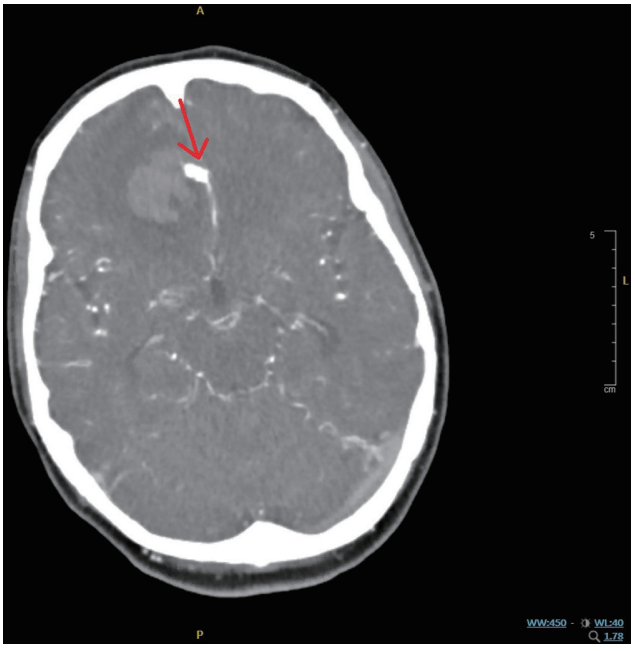

Fig. 5. Computed tomography angiography showing opacified aneurysm in the right anterior cerebral artery.

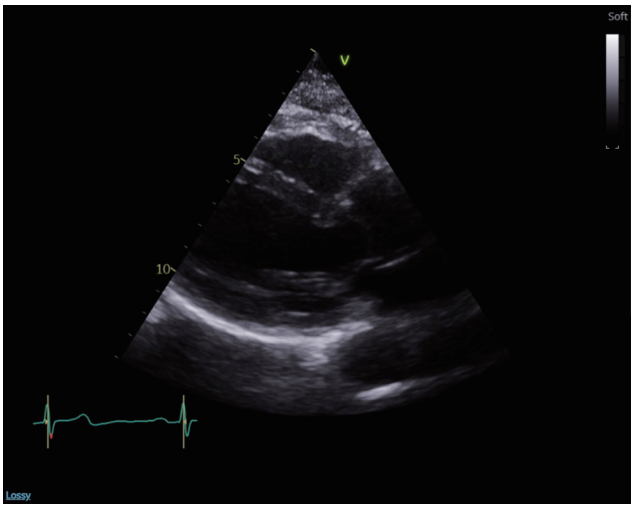

Fig. 6. Echocardiogram showing resolution of left ventricular function with some degree of left ventricular hypertrophy.

diagnostic criteria for TTS were met:

- an identifiable stressor trigger (emotional or physical);
- transient regional ventricular wall motion abnormalities confirmed on echocardiography;
- a negative CT coronary angiography demonstrating the absence of atherosclerotic coronary artery disease; and
- new ECG changes in the acute phase and complete resolution of ventricular systolic function at 3–6 months of follow-up.[4]

TTS is an interesting and unique heart failure syndrome. It was first described in Japan in 1990 and accounts for approximately 1–2% of all troponin-positive suspected ACS presentations and almost 6% of all women presenting with suspected STEMI who undergo urgent angiography.[5] Globally TTS occurs predominantly in older adults and more commonly in women, particularly those who are postmenopausal.[5] Evidence of TTS can be seen in up to 27% of subarachnoid hemorrhage cases, with severe symptomatic TTS such as in this case present in up to 8%.[6] The pathophysiology of TTS following aSAH is mostly explained by the catecholamine hypothesis.[7–9] The catecholamine surge produced by aneurysmal rupture massively increases circulating levels of adrenaline and noradrenaline. Adrenaline has a positive inotropic effect on the myocardium at normal levels though a negative effect at very increased levels (stunned myocardium), mainly affecting the apex of the left ventricle. Noradrenaline, on the other hand, has a solely positive inotropic effect, mainly affecting the base of the left ventricle. This imbalance leads to ventricular wall motion dyskinesia, hypokinesia, and focal akinesia. Compared with patients with classic TTS, patients with aSAH-induced TTS tend to be slightly younger, and present with heart failure and not chest pain. ECGs are likely to show no ST-segment elevation and more T-wave inversion, with an echocardiogram demonstrating more mid- to apical rather than basal left ventricular dysfunction. Neurogenic stress cardiomyopathy describes transient cardiac dysfunction secondary to acute neurological injury, which is a well-known complication of aSAH. Secondary cardiomyopathy, such as that of TTS manifests in up to 20–30% of patients following aSAH.[6] Therefore, it is important to consider that in some cases, the cardiac symptoms of cardiomyopathy may precede that of neurological symptoms of aSAH. Such recognition will stop therapeutic antiplatelet therapy which may aggravate intracerebral hemorrhage.

Clinical perspectives

A registry of TTS cases would help track different presentations and triggers of this condition. It would also help develop research into the exact mechanism behind the acute cardiac event and potential early cardiac protective treatment without worsening the trigger event.

Conclusions

TTS is an increasingly recognized condition characterized by transient severe acute heart failure in the absence of significant obstructive coronary artery disease. In patients presenting with syncope and collapse, despite clinical findings being highly suggestive of primary cardiac problems, evaluating the patients for central nervous system etiologies such as intracranial hemorrhage should not be overlooked, especially in those with hypertension. Clinicians should keep a low threshold for obtaining a head CT scan in these patients, as otherwise clinical conditions can progress and have poorer outcomes.

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Conflict of interest

The authors have no conflicts of interest to declare.

Author contributions

Preparation and write-up of the publication (IHYG and FQ), and supervision and review of the article write-up and clinical supervision of IHYG and FQ (RT).

Ethical statement

The study was performed in accordance with the ethical standards of the institutions to which we are affiliated and with the Declaration of Helsinki. Written informed consent was obtained from the patient for publication of this case report.

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