

Case Report

# Association of Posterior Reversible Encephalopathy Syndrome and Transient Apical Ballooning Syndrome (Takotsubo): First Case Report of a Man and Review of the Literature

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## Keywords

Posterior reversible encephalopathy syndrome · Takotsubo cardiomyopathy · Catecholamines

## Abstract

**Introduction:** An association of posterior reversible encephalopathy syndrome (PRES) and takotsubo is rare. We present the first case of a male patient. **Case Report:** A 69-year-old man presented to the hospital in a persistent comatose state following a generalized tonic-clonic seizure with high blood pressure. The electrocardiogram revealed transient left bundle branch block. Troponin and BNP were elevated. Cardiac ultrasound showed large apical akinesia with altered left ventricular ejection fraction, and the left ventriculogram showed characteristic regional wall motion abnormalities involving the mid and apical segments. Brain MRI showed bilateral, cortical, and subcortical vasogenic edema predominant in the

posterior right hemisphere. The lumbar puncture and cerebral angiography were normal. Paraclinical abnormalities were reversible within 2 weeks with a clinical recovery in 3 months, confirming the takotsubo and the PRES diagnoses. **Discussion:** Several theories hypothesize the underlying pathophysiology of takotsubo or PRES. Circulating catecholamines are up to 3 times higher in patients with takotsubo causing impaired microcirculation and apical hypokinesia. An association of both takotsubo and asthma crisis and PRES and asthma crisis underlines the role of catecholamines in the occurrence of these disorders. **Conclusion:** Early recognition of this rare association, in which heart and neurological damage may require rapid intensive care support, is needed.

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## Introduction

Only one study reported the association of posterior reversible encephalopathy syndrome (PRES) and transient apical ballooning syndrome (takotsubo cardiomyopathy) and described a series of 6 women in the United States [1]. Five other cases of women were reported separately [2–6]. We present here the first case of a male patient with this rare association.

## Case Report

A 69-year-old Caucasian man was admitted to intensive care unit because of a persistent comatose state (Glasgow Coma Scale scored at 6) following a generalized tonic-clonic seizure requiring intubation. His high blood pressure (>190/110 mm Hg) required intravenous infusion of nicardipine. Brain CT scan and MRI (with DWI, FLAIR, T2, and T2\*) showed no abnormalities. He had a past medical history of oral cancer treated in 2007 with surgery and radiotherapy. He had a comorbid condition of obesity and dyslipidemia. Electrocardiogram (ECG) revealed transient left bundle branch block (Fig. 1a) which normalized a few hours later. Troponin and BNP were elevated to 35 ng/mL ( $n < 0.05$ ) and 600 pg/mL ( $n < 100$ ), respectively. Cardiac ultrasound showed large apical akinesia with altered left ventricular ejection fraction (LVEF). Angiography showed no occlusive lesion or stenosis, and left ventriculogram showed regional wall motion abnormalities involving the mid and apical segments, characteristic of takotsubo cardiomyopathy (Fig. 1b).

After 3 days, the patient's consciousness improved. However, he continued to have persistent left-sided hemiparesis predominantly in the upper limb. Electroencephalogram showed slight slowing of cerebral activity in the right hemisphere without paroxysmal activity. The CSF analysis was normal (biochemistry, bacteriology, virology, pathology). A second brain MRI was performed on day 3 (Fig. 1c) and displayed bilateral, cortical, and subcortical vasogenic edema with a right posterior predominance, suggesting the diagnosis of PRES. A cerebral angiography performed on day 12 showed no abnormalities and in particular no stenosis that could have been in favor of a reversible cerebral vasoconstriction syndrome.

Troponin, BNP, LVEF, and cardiac kinetics normalized a few days later as would be expected in transient apical ballooning syndrome. A brain MRI obtained 15 days after admission (Fig. 1d) showed complete resolution of the vasogenic edema confirming the diagnosis of PRES. The patient recovered fully within 3 months.

In the history there was no record of a stressful physical or emotional event preceding the onset of the patient's symptoms. Biological samples and abdomen/pelvic CT scan found no evidence of thyroid dysfunction or pheochromocytoma.

## Discussion

Takotsubo cardiomyopathy refers to transient apical dyskinesia with normal coronary angiogram mimicking acute coronary syndrome. It presents mainly in middle-aged and elderly women and is often preceded by physical and/or emotional stress. ECG displays ST segment elevation and T wave abnormalities. Troponin may be elevated. Cardiac ultrasound shows left ventricular dysfunction with apical akinesia or dyskinesia and hypercontractility of basal segments, resulting in the expression "octopus trap" (takotsubo in Japanese) morphology of the ventricles. Complications can be severe with acute pulmonary edema or death. Takotsubo cardiomyopathy/physiopathology is not fully understood yet. Several pathological mechanisms have been proposed, including coronary artery vasospasm, coronary microcirculation dysfunction, obstruction of the left ventricular outflow tract, and catecholamine overload [7]. Blood catecholamine levels are up to 3 times higher in takotsubo patients compared to patients with acute coronary syndrome. Thus, catecholamine overload might play a central role in the development of this disorder. Published data suggest that elevated plasma catecholamine levels seen in stress cardiomyopathy patients could be particularly relevant and result in catecholamine-related toxic effects [8]. Stress cardiomyopathy is characterized by morphological alterations that are similar to those following catecholamine cardiotoxic effects reported previously [9] and is thought to be due to changes in microcirculation. Cardiac SPECT analysis shows apical ischemia despite normal coronary arteries [10]. Clinical parameters resolve completely in 1–3 weeks.

PRES is characterized by neurological symptoms including headache, altered mental status, visual disturbances, and seizures in conjunction with reversal of findings on imaging. Brain MRI usually shows subcortical white matter vasogenic edema typically in the parietal and occipital lobes and less frequently in the frontal lobes, cerebellum, basal ganglia, or brainstem [11]. The incidence is moderately higher in females with a mean age of 44 years. Comorbid conditions are hypertension, malignancy, autoimmune diseases, kidney diseases, dialysis-dependent renal insufficiency, and organ transplantation. PRES physiopathology is not yet fully understood as well. Several theories hypothesize on the underlying pathophysiology of PRES: the "vasogenic" theory (with increased systemic blood pressure), the "cytotoxic" theory (toxins responsible for endothelial dysfunction), the "immunogenic" theory (T-cell activation increasing endothelial permeability), and the "neuropeptide" theory (release of vasoconstrictors leading to vasospasm) [12].

Takotsubo cardiomyopathy is commonly described in patients with subarachnoid hemorrhage, status epilepticus, ischemic stroke, craniocerebral trauma, encephalitis, myelitis, Guillain-Barré syndrome, following neurosurgical procedures, acute hydrocephalus, but an association of PRES and takotsubo has rarely been reported. All these situations might be considered as stressful events for the organism and cellular activities. They all might cause an acute dysregulation of cerebral vascular tone because of a sympathetic hyperactivity, endothelial dysfunction, and oxidative stress, but the precise mechanisms remain unknown. To this day, we do not know for certain that catecholamine overload is involved in all the situations associating takotsubo cardiomyopathy and cerebral injuries, but all the data we have reported suggest that it could be particularly relevant. A "catecholaminergic storm"

might lead to myocardial apical hypokinesia (high levels of circulating epinephrine trigger a switch in intracellular signal trafficking, from G<sub>s</sub> protein to G<sub>i</sub> protein signaling through the β<sub>2</sub> receptors [13]), blood pressure elevation, and alteration of cerebral microcirculation. Moreover, the association of both takotsubo and an asthma crisis [14] and of PRES and an asthma crisis [15] also underlines the hypothetical role of catecholamines in the occurrence of these disorders.

The literature review found 5 case reports of women [2–6]. Six others cases of women with PRES were found in a series of 224 patients with takotsubo [1]. To our knowledge, this is the first case of a male patient presenting with PRES and takotsubo. The reason for the much more common occurrence in women (and especially in postmenopausal women) has not yet been explained. One hypothesis is that sex hormones may exert important influences on the sympathetic neurohormonal axis and on vasoreactivity. Another one is that women seem to be more vulnerable to sympathetically mediated myocardial stunning and to postmenopausal alteration of endothelial function in response to reduced estrogen levels [7].

### Conclusion

This case highlights the need for early recognition of this rare association, in which heart and neurological damage may require rapid intensive care support. Catecholamine overload seems to play a major role in this phenomenon.

### Statement of Ethics

The authors have no ethical conflicts to disclose.

### Disclosure Statement

The authors declare no financial conflict of interest.

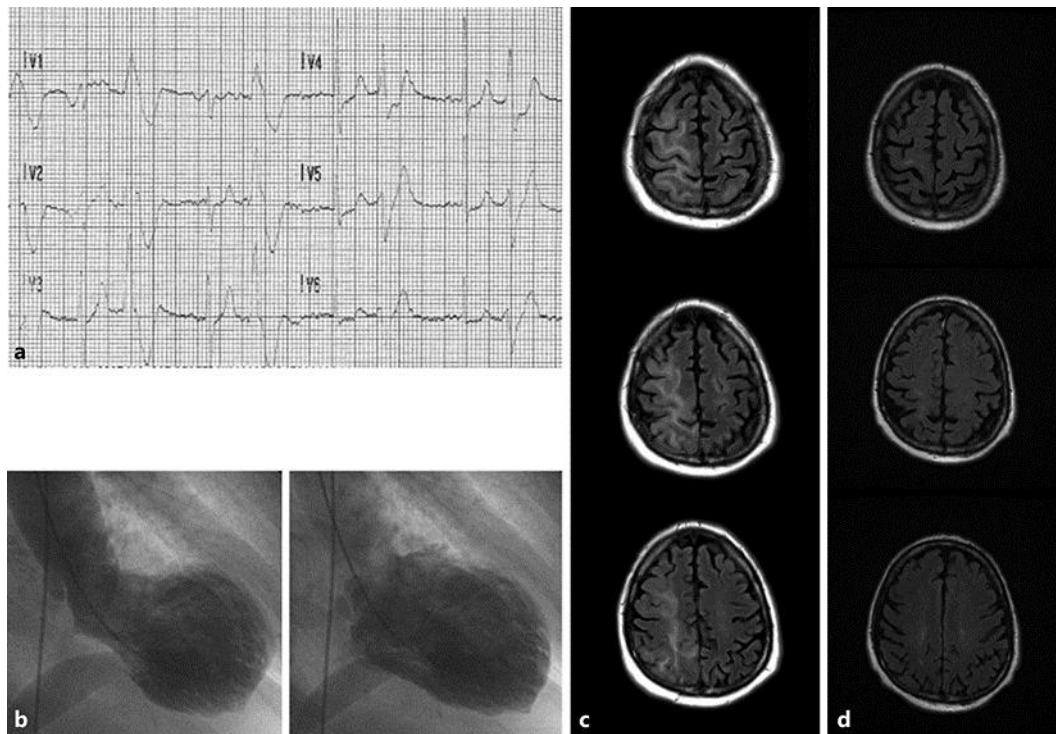
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**Fig. 1.** **a** ECG with left bundle branch block. **b** Left ventriculogram with typical stress cardiomyopathy wall motion abnormalities characterized by basal hyperkinesis and apical ballooning. **c** Brain MRI at day 3: T2 FLAIR. Bilateral, cortical, and subcortical (frontoparietal) vasogenic edema with a right posterior predominance. **d** Brain MRI at day 15: T2 FLAIR. No abnormality.