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Takotsubo syndrome in status epilepticus – case report

Zespół takotsubo w przebiegu stanu padaczkowego – opis przypadku

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Abstract

Takotsubo syndrome, also known as stress cardiomyopathy, apical ballooning syndrome or "broken heart syndrome," is a sudden, transient cardiac condition in which left ventricular dysfunction occurs. Stressors that can induce takotsubo syndrome include both emotional and physical triggers of any kind. The authors present a case of a male patient with non-convulsive status epilepticus and symptoms suggesting takotsubo syndrome. Echocardiographic examination revealed akinesis of the midsegment and apical segment of the left ventricle, and impaired left ventricle function, but no coronary artery disease was found on cardiac angiography. The clinical symptoms, and echocardiographic and laboratory abnormalities, resolved gradually simultaneously with neurological improvement.

Keywords: Takotsubo syndrome, epilepsy, status epilepticus

Streszczenie

Zespół takotsubo, nazywany także kardiomiopatią stresową, zespołem balotowania koniuszka lub zespołem „złamanego serca", jest ostrym stanem kardiologicznym, w którym dochodzi do odwracalnej hipokinezy, akinezy lub dyskinezy segmentów środkowych i koniuszka lewej komory. Czynnikiem wyzwalającym zespół takotsubo jest silny stres emocjonalny lub fizyczny. Autorzy przedstawiają przypadek chorego z niedrgawkowym stanem padaczkowym, w przebiegu którego doszło do wystąpienia objawów ostrego zespołu wieńcowego. Badanie echokardiograficzne wykazało cechy zespołu takotsubo, a w badaniu koronarograficznym nie stwierdzono zmian miażdżycowych. Objawy kliniczne, echokardiograficzne i laboratoryjne uszkodzenia mięśnia sercowego stopniowo się wycofały, równolegle z poprawą stanu neurologicznego chorego.

Słowa kluczowe: zespół takotsubo, padaczka, stan padaczkowy

CASE REPORT

A 71-year-old male was admitted to our neurological department due to prolonged post-epileptic confusion. According to his daughter, an hour before admission she found her father lying on the floor seizuring. The seizure continued until the paramedics' arrival. Diazepam was administrated to the patient for seizure inhibition, but post-epileptic confusion and sleepiness were still present.

According to the patient's family, he was a recovering alcohol addict. A few months before the current admission, he was hospitalised in a detoxification ward with success (according to the family members, he managed to achieve abstinence). Afterwards, the patient was hospitalised in a rehabilitation facility due to physical impairment (no details were available, but toxic polyneuropathy or myelopathy was suspected). A year earlier, recurrent limb shaking was observed by the patient's family members, but without a disturbance of consciousness. No other epileptic incidents were present.

On admission, psychophysical slowness was visible, and the patient did not answer any questions nor performed any tasks given. Neurological examination did not reveal significant abnormalities except for left-sided Babinski sign. Another convulsive seizure appeared during the admission procedures, and diazepam was administrated again, attaining successful seizure control, but without an improvement of consciousness disturbances. Brain computed tomography (CT) scan revealed vast post-traumatic lesions in both frontal lobes (Fig. 1). Electroencephalography (EEG) revealed continuous epileptic activity in the right frontoparietal region, with slow waves and sharp-and-slow-wave complexes which sometimes propagated to the right temporal and left frontal regions (Fig. 2).

Valproic acid (VPA) was given intravenously (i.v.), and because of its ineffectiveness phenytoin (PHT) was given as

a second drug. After that treatment, the patient's convulsive seizures disappeared, but consciousness disturbances persisted, and were accompanied by involuntary oromandibular movements. Ultimately, the patient was intubated and thiopenthal was introduced with good clinical and electroencephalographic results (Fig. 3). The treatment with VPA and PHT, administered orally, was continued.

Laboratory findings on admission were within normal ranges, but an increased level of C-reactive protein (CRP) and leukocytosis were detected the next day. Chest CT revealed parenchymal densities in the right upper lobe and both lower lobes, with fluid present in both pleural cavities (no other abnormalities were found within the visible abdominal internal organs, adrenal glands included). Cerebrospinal fluid (CSF) analysis results were normal. Sputum and blood cultures were collected, but did not reveal any specific infection. Empirical antibiotic therapy was introduced.

Due to hemodynamic instability with hypotension poorly responsive to catecholamine infusion cardiac biomarker tests were also ordered on the second day of hospitalisation. Elevated creatine kinase myocardial band (CK-MB), troponin I (cTnI) and creatine kinase (CK) levels were present with a further increase within a few hours [cTnI 23.50 vs. 16.30 ng/mL (normal range <0.16), CK-MB activity 55.4 vs. 51.2 U/L (normal range <25.0), CK 1314.3 vs. 1000.5 U/L (normal range <190.0)]. Electrocardiography (ECG) revealed the sinus rhythm of 98/min, low QRS voltage in limb leads, ST depression of 0.5 mm in II and aVF leads, lack of R-wave progression in V1–V3 leads, and J-point elevation in precordial leads. An echocardiogram was obtained on the same day. Akinesis of the apex, apical segments of the anterior, lateral and inferior walls as well as mid lateral and mid inferior segments was visible, with good basal segments contractility. The ejection fraction (EF) was 45%. No other significant abnormalities were detected.

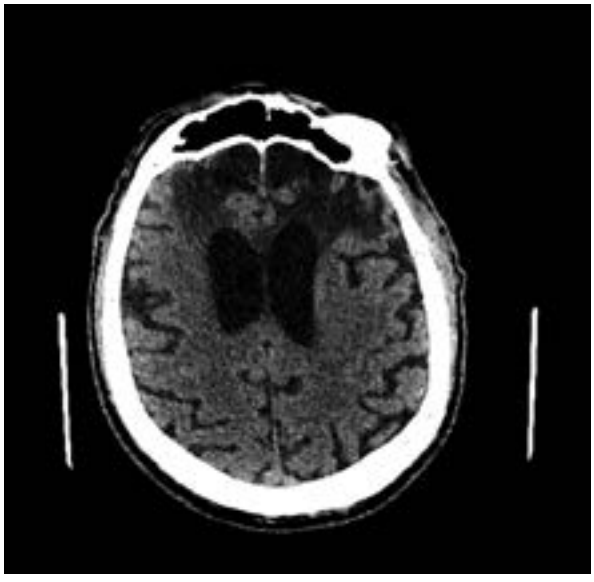

Fig. 1. CT scan performed on admission showing vast post-traumatic lesions in both frontal lobes

The patient was transferred to the cardiology department for further diagnostics and treatment. On discharge, he was still intubated, and thiopental infusion was maintained.

According to the discharge summary from the cardiology ward, coronary angiography was performed, but no atherosclerotic coronary stenosis was found. Echocardiography was repeated, revealing severe left ventricular contractility impairment and left atrium enlargement with EF of 20–25%. General medical management, antibiotic therapy and antiepileptic drug treatment were continued with additional parenteral midazolam.

Midazolam was withdrawn, and the patient was extubated after EEG normalisation. Although no seizures were observed, the patient experienced hallucinations and visual illusions, especially in the evening. Withdrawal syndrome from benzodiazepines was considered, and quetiapine was introduced symptomatically, producing a good clinical response. The CRP level, leukocytosis, and cardiac panel tests were gradually normalising. The patient required higher doses of antiepileptic drugs, as the serum levels were under the therapeutic range. Follow-up echocardiography revealed no abnormalities seen on the previous examination apart from left atrium enlargement. The EF was 60%. Physical rehabilitation was introduced, and full mobility was achieved.

DISCUSSION

Takotsubo syndrome (TTS), also known as stress cardiomyopathy, apical ballooning syndrome or "broken heart syndrome," is a sudden, transient cardiac condition in which left ventricular dysfunction occurs (caused by apical akinesis and/or left ventricular – LV midsegments dyskinesis). It can mimic acute coronary syndrome and lead to acute systolic heart failure. It was first described in Japan in 1990 by Sato et al.

Although the precise pathophysiological mechanisms underlying TTS are not completely understood, it is suspected that stress-induced catecholamine release may lead to sympathetically mediated epicardial spasm, microcirculatory dysfunction, coronary endothelial dysfunction or stunning of the myocardium caused by catecholamine toxicity (Boland et al., 2015; Ghadri et al., 2018). These stressors may include both emotional and physical triggers of any kind (e.g. personal or interpersonal conflicts, anxiety, natural disaster, intense physical activities, acute medical conditions or exacerbation of a chronic disease, medical procedures, or use of or withdrawal from illicit drugs or alcohol) (Ghadri et al., 2018).

Clinically, it is very hard to distinguish patients with TTS from patients with acute coronary syndrome. Most patients with TTS present with chest pain and dyspnoea (although palpitations, nausea, vomiting or syncope also may be reported).

Takotsubo syndrome affects approximately 1–3% of all patients with suspected ST elevation myocardial infarction (STEMI) (Prasad et al., 2014; Redfors et al., 2015), and

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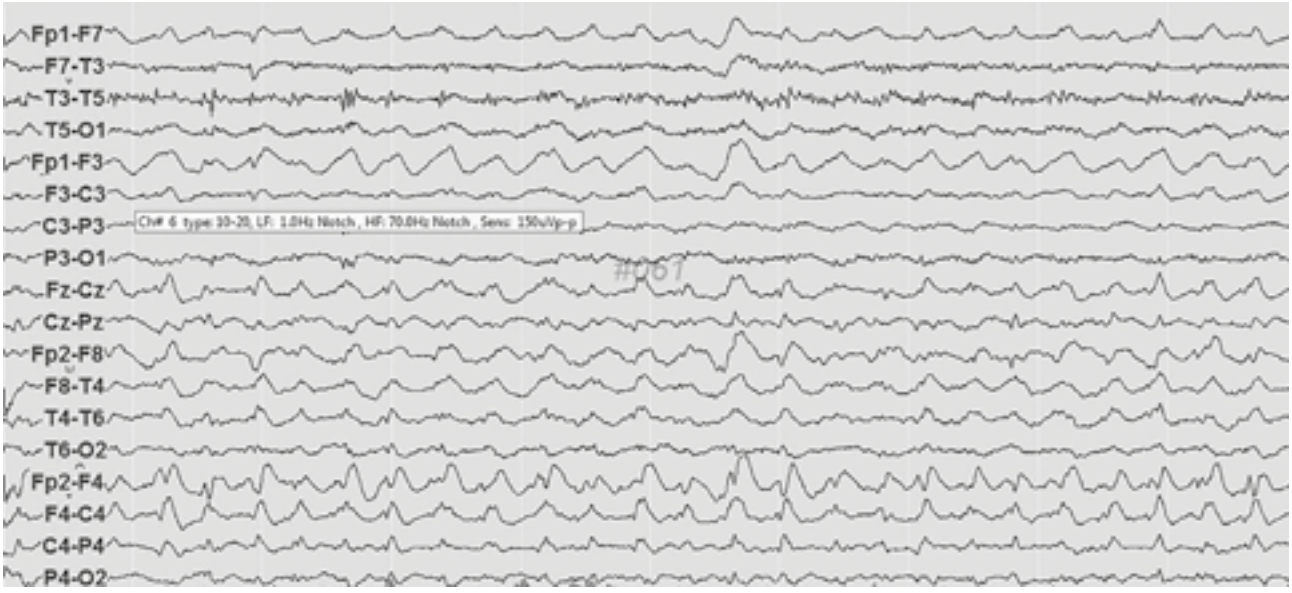

Fig. 2. Continuous epileptic activity in the right frontoparietal region, with slow waves and sharp-and-slow-wave complexes propagating to the right temporal and left frontal regions

about 90% of TTS patients are women with a mean age of 67–70 years (Schneider et al., 2013; Templin et al., 2015). Despite its sudden course and potential risk of complications (such as left heart failure, cardiogenic shock, ventricular arrhythmias or LV free-wall rupture) the prognosis in TTS is usually good, with nearly 95% of patients achieving complete recovery within 4–8 weeks (Pilgrim and Wyss, 2008).

Classical Mayo diagnostic criteria of TTS include transient hypokinesia, akinesia or dyskinesia of the LV apical or midsegments, regional wall motion abnormalities (extending beyond a single epicardial vascular distribution), absence of obstructive coronary artery disease, new electrocardiographic abnormalities (e.g. ST-segment elevation, ST-segment depression, T-wave inversion, and QTc prolongation) or troponin and creatine kinase elevation, absence of pheochromocytoma and myocarditis (Prasad et al., 2008). The criteria were revised in 2018 by Ghadri et al. who proposed an update with InterTAK Diagnostic Criteria which alongside the above-mentioned conditions emphasised the presence of emotional, physical, or combined triggers (including neurologic disorders and pheochromocytoma) and the fact that most TTS patients are post-menopausal women. It was also stated that significant coronary artery disease

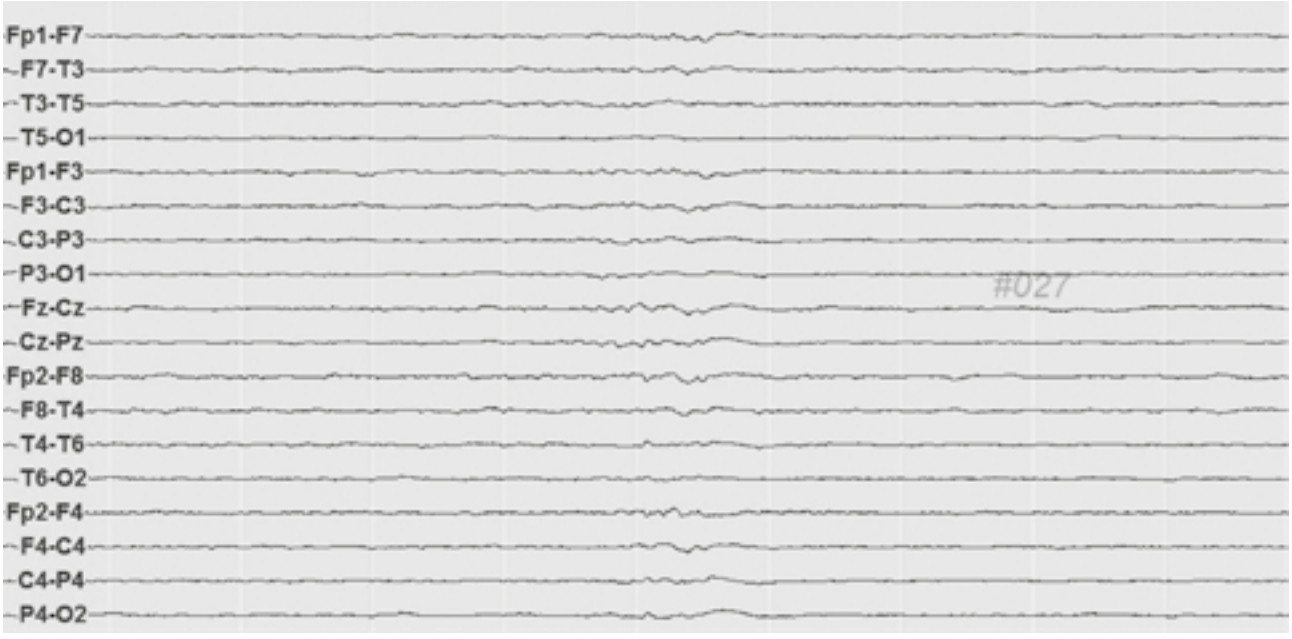

Fig. 3. EEG low voltage record with no paroxysmal abnormalities

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was not a contradiction for the presence of TTS (Ghadri et al., 2018). Moreover, it did not include pheochromocytoma and myocarditis exclusion.

Multiple case series and literature reviews have examined associations between various neurological disorders and TTS. Even though the strongest correlations were seen with subarachnoid haemorrhage and status epilepticus (SE) (or seizures), there are several other neurological disorders which may result in TTS (e.g. transient global amnesia, meningoencephalitis, migraine, intracerebral haemorrhage and ischemic stroke) (Morris et al., 2019). Despite these reports, the connection between the brain and the heart in TTS patients remains unclear, and activation of the sympathetic nervous system, limbic system excitation or neuroendocrine changes in the hypothalamus–pituitary–adrenocortical (HPA) axis are suspected to be responsible for this unusual clinical stress response (Wang et al., 2020).

Although epilepsy-related TTS is rare condition with 0.1% frequency among epilepsy admissions, it is associated with higher all-cause in-hospital mortality and complications rate due to both cardiac (e.g. arrhythmia, cardiogenic shock, cardiac arrest) and cerebral (e.g. stroke) causes (Desai et al., 2020). Moreover, some authors speculate that TTS is one of the possible mechanisms of sudden unexpected death in epilepsy (SUDEP) (Dupuis et al., 2012), but it is still a matter of debate (Finsterer and Bersano, 2015).

Seizure-triggered TTS may appear at any age in patients with or without history of epilepsy. In the study by Desai et al. (2020), most patients with epilepsy-related TTS were women (60%). Generalised tonic-clonic seizures were the triggers in 60% of patients, followed by generalized SE (32%) and complex partial seizures (6%). As far as SE is concerned, both convulsive and non-convulsive SE were reported in epilepsy-related TTS (Nandal et al., 2019).

Our patient's case fulfilled most of the TTS diagnostic criteria (apical, apical anterior, mid-inferior and mid-lateral segments akinesis, absence of obstructive coronary artery disease, and troponin and creatine kinase elevation). Although 24-hour urine collection for creatinine, total catecholamines, vanillylmandelic acid and metanephrines (to exclude pheochromocytoma) was not performed, chest CT covered some abdominal organs, adrenal glands included (with negative result for adrenal mass). Cardiac dysfunction visible on echocardiography was transient, resolving within 2 weeks. Status epilepticus was successfully treated with antiepileptic therapy. Although bilateral pneumonia (another acute medical condition which may cause TTS) was diagnosed, the authors believe it was rather secondary to SE, as aspiration during prolonged seizures could not be excluded. Interestingly, since clinical symptoms of coronary syndrome were not possible to assess due to drug-induced coma, haemodynamic compromise in our patient was a reason for further cardiac investigation. However, this abnormal haemodynamic response might have been also mistaken for a side effect of phenytoin or thiopental. This case highlights the importance of considering serial ECG and troponin testing (and transthoracic echocardiogram, if needed) in the postictal period, especially in patients with prolonged seizure activity.

Conflict of interest

The authors do not report any financial or personal connections with other persons or organisations which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

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