

Unusual combined cause of Takotsubo cardiomyopathy: Hyponatremia and seizure

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ABSTRACT

Takotsubo cardiomyopathy (TTC) is characterized by transient systolic dysfunction of the left ventricle and changes of electrocardiographic or cardiac markers resemble an acute coronary syndrome. Although the etiology of TTC is unknown, there is a wide variability in the psychological and physical triggers for TTC. In this article, we describe the case of 69-year-old woman with epilepsy history who presented in the emergency room with new onset generalized tonic-clonic seizure activity. After her biochemistry results indicated severe hyponatremia, a diagnosis of TTC was established through echocardiography and angiography.

Keywords: Apical ballooning syndrome; hyponatremia; seizure; Takotsubo cardiomyopathy.

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Takotsubo cardiomyopathy (TTC) is characterized by transient systolic dysfunction of the left ventricle and changes of electrocardiographic or cardiac markers resemble an acute coronary syndrome. TTC mostly occurs after emotional or physical stress in the absence of obstructive coronary disease or without angiographic evidence of acute plaque rupture [1–4]. The pathophysiology of TTC is unclear. An excessive release of catecholamines following emotional or physical stress seems to have a pivotal role in the development of TTC [5]. Meanwhile, TTC can be triggered by some non-cardiac clinical conditions such as hyponatremia and seizure [6–10]. In this paper we describe a case of TTC which was developed after seizure and severe hyponatremia.

CASE REPORT

A 69-year-old woman with a history of epilepsy was presented to the emergency room with a new onset general-

ized tonic-clonic seizure activity. On admission, she had no chest pain or any cardiac symptoms. In her medical history she had a hypertension and epilepsy and treated with indapamid, carbamazepine, and levetiracetam. Her physical examination was unremarkable. Routine laboratory values revealed serum sodium level was 112 mmol/L, initial troponin was 7.13 ng/ml (normal range 0.0–0.06 ng/ml) and serum carbamazepine concentration was 7.1 ng/ml (therapeutic range 4–12 ng/ml). The first electrocardiogram (ECG) showed sinus rhythm with diffuse upsloping 1-mm ST-segment elevation (Fig. 1). Transthoracic echocardiography (TTE) demonstrated apical hypokinesia with an estimated ejection fraction (EF) was 36% (Fig. 2). Although initial clinical findings suggested TTC, she underwent coronary angiography to rule out coronary artery disease. Coronary angiography revealed no stenosis in any coronary arteries (Fig. 3) and left ventriculography showed anteroapical, inferoapical and apical akinesis (Fig. 4).



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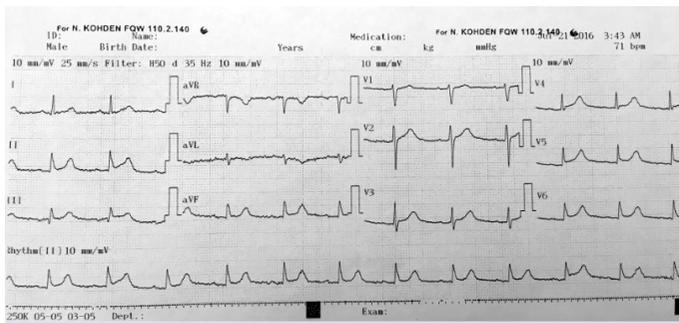


FIGURE 1. Electrocardiogram showed sinus rhythm with diffuse 1-mm upsloping ST-segment elevation.

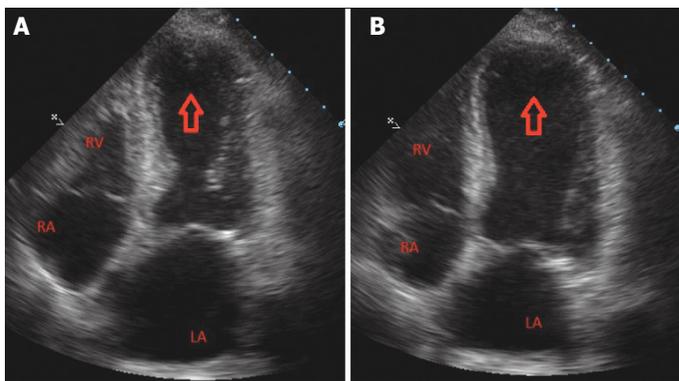


FIGURE 2. Transthoracic echocardiography demonstrated apical hypokinesia with an ejection fraction estimated 36% in apical 4 chamber. **(A)** left ventricle systole **(B)** left ventricle diastole, red arrow; apical hypokinesia. (LA: Left atrium; RA: Right atrium; RV: Right ventricle).

Hypothyroidism and adrenal insufficiency, causes of hyponatremia, were ruled out by measuring thyroid stimulating hormone (TSH) levels (1.5 μ IU/ml (normal range 0.5–6.2 μ IU/ml) and serum cortisol levels (20 μ g/dl (normal range 10 to 20 μ g/dl). After withdrawal of both indapamide and carbamazepine, the patient was subsequently treated with an intravenous infusion of 3% saline and her sodium increased to 135 mmol/l at the end of the first week. In this context, TTC was thought to have developed by hyponatremia due to indapamide and carbamazepine. She was discharged on aspirin (100 mg/d), metoprolol (50 mg twice daily), ramipril (5 mg/d), subcutaneous enoxaparin (0.8 ml twice daily), valproic acid (500 mg twice daily) and levetiracetam (500 mg twice daily) and discontinuation of carbamazepine and indapamide treatment. TTE demonstrated full recovery of EF (60%) at two weeks of discharge (Fig. 5). Two months later, the patient was referred to hospital due to recurrent hyponatremia with

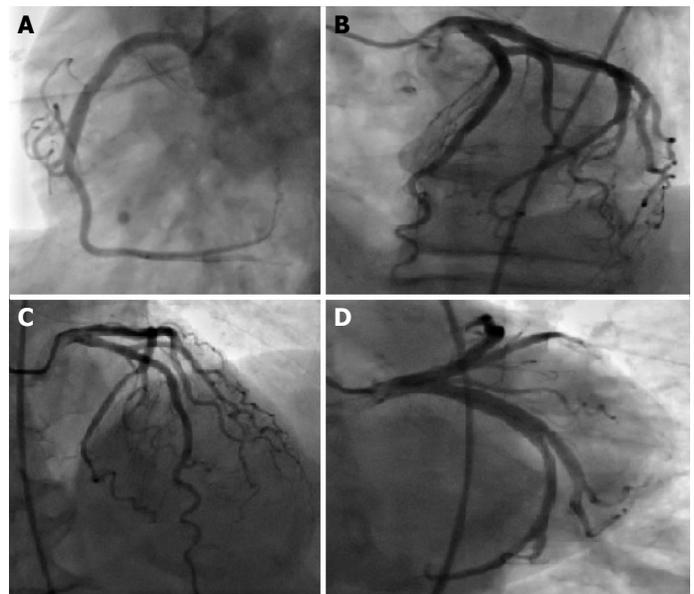


FIGURE 3. Coronary angiography showed normal coronary arteries.

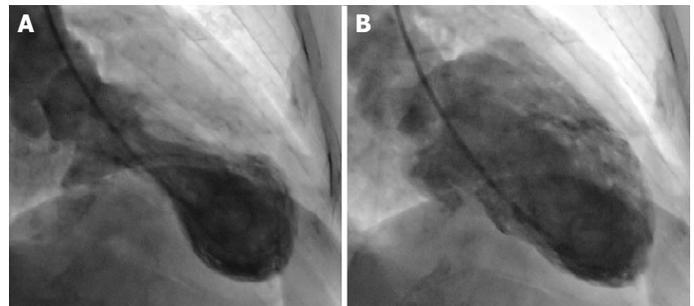


FIGURE 4. Left ventriculography demonstrated apical ballooning in right anterior oblique view. **(A)** left ventricle in systole **(B)** left ventricle in diastole.

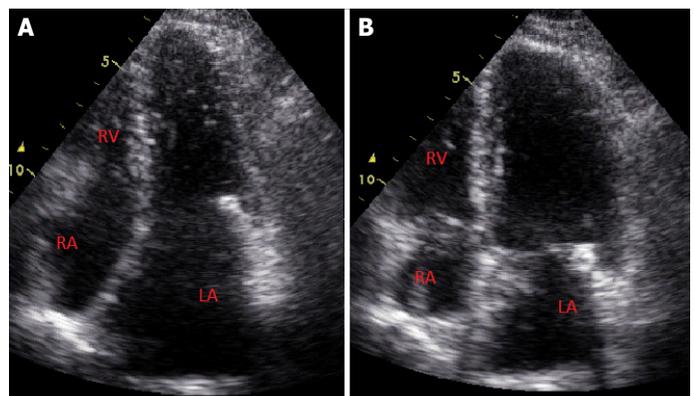


FIGURE 5. After two weeks, control TTE showed full recovery in apical 4 chamber. **(A)** left ventricle systole **(B)** left ventricle diastole.

serum sodium level was 115 mmol/L. However she had no cardiac symptoms and seizure. ECG and TTE did not show any ST-segment changes or wall motion abnormality. Although carbamazepine was stopped on first hospital admission, it had to be started and continued with a lower limit of therapeutic range (4.55 ng/ml (therapeutic range 4–12 ng/ml)) to prevent epileptic seizures.

DISCUSSION

Although pathophysiology is unclear, TTC is defined as a reversible left ventricular hypokinesis. Coronary artery vasospasm, transient obstruction of the left ventricular outflow tract and microcirculatory dysfunction have been proposed as possible causes of this disease [11].

Hyponatremia is the most common electrolyte disorder in hospitalized patients and the severity is determined based on serum sodium levels; mild (serum sodium, 130–134 mmol/L), significant (125–129 mmol/L), and severe (<125 mmol/L) [12]. While asymptomatic patients do not require immediate correction, symptomatic hyponatremia is a medical emergency which needs prompt and prudent treatment. Acute severe hyponatremia is associated with neurologic symptoms, such as seizures or coma, and should be treated meticulously to prevent cerebral edema and encephalopathy. In present case several clinical factors demonstrated that seizure is not associated with acute severe hyponatremia. First, the patient has been suffering from recurrent seizures due to epilepsy for a long time. Second, hyponatremia in this patient is chronic and recurrent. However, this patient have severe hyponatremia due to several contributing factors including drugs such as carbamazepine and indapamide. The association between hyponatremia and carbamazepine has been well described. Although the mechanisms how carbamazepine causes the hyponatremia are not fully understood. Carbamazepine may increase the secretion of antidiuretic hormone (ADH) from the posterior pituitary and sensitize the the osmoreceptors to ADH in the distal convoluted tubules [13]. Several case reports have established a causal relationship between indapamide and severe hyponatremia [14]. In this case these two drugs with different activity (carbamazepine and indapamide) are thought to cause hyponatremia.

According to the a few previous case reports, TTC is associated with severe hyponatremia in cases even the absence of adrenal insufficiency and hypothyroidism [6, 9, 10]. In our case we ruled out hypothyroidism and adrenal insufficiency. On the second admission, the pa-

tient had been taking carbamazepine without receiving indapamide since two months and eventually serum sodium level decreased similarly.

On first admission the serum sodium level was 112 mEq/L when TTC occurred, whereas it did not occur on the second admission while serum sodium level was 115 mEq/L. In this context we can postulate that recurrence of hyponatremia may not induced TTC. Singh et al. reported that there was a negative correlation between use of renin angiotensin aldosterone system blockers and recurrence of TTC [15]. We speculate that the medication started after the first TTC might have prevented the recurrence of TTC in spite of recurrent hyponatremia.

Seizure is also associated with Takotsubo cardiomyopathy [16]. The mechanism of seizure-associated TTC can be explained by excessive catecholamine release during epileptic seizures. On the first admission even if the reason of TTC was seizure instead of hyponatremia, there were many seizures in her history and we could not know whether TTC occurred together with previous seizures or not. In fact, both hyponatremia and seizure might cause TTC separately. Yet, we conclude that both hyponatremia and seizure were predisposing factors together in this case.

Informed Consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

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