Takotsubo Cardiomyopathy in the Setting of Severe Hyponatremia and Beer Potomania: A Case report and Review of Literature

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Abstract

Takotsubo Cardiomyopathy (TC), an acute cardiac event accounting for about 1-2% of all acute coronary syndromes is often associated with acute emotional stress usually in the setting of the other cardiovascular risk factors.This case report reviews a trigger of TC (severe hyponatremia) and the link between them.

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Abstract

Takotsubo Cardiomyopathy (TC), an acute cardiac event is often associated with acute emotional stress, usually in the setting of cardiovascular risk factors. This case report attempts to review one of the triggers of TC (severe hyponatremia) as well as imaging findings, that shows the link between severe hyponatremia and TC.

Background

Takotsubo Cardiomyopathy (TC), first described in Japan in 1990, is an acute cardiac condition that involves transient systolic dysfunction due to ballooning of the apex and/or mid segments of the left ventricle. [1] TC is also known as "apical ballooning syndrome", "stress-induced cardiomyopathy", "broken heart syndrome", and "ampulla cardiomyopathy". The name Takotsubo was derived from the Japanese word for octopus emblematic of the appearance of the left ventricle on ventriculography during an acute attack. The typical TC includes apical ballooning during systole due to hypokinesis or akinesis of the apex or mid ventricle and hyperkinesis of the basal walls. Atypical variants of TC include hypokinesis of the mid-ventricle alone [2], hypokinesis of the base, and global hypokinesis. [3]

TC patients are typically postmenopausal Asian or Caucasian women. Gianni et al reported that 88.8% of 286 reported TC patients were women. The mean age ranges from 61-76 years. [4] The exact prevalence of TC is unknown, but researchers have reported that 1.7-2.2% of suspected ACS patients have TC. [5-7]

TC is usually but not always brought on by an acute medical illness or an intense mental or physical stressor. [8] TC patients typically present with symptoms similar to ACS, including chest pain with echocardiographic changes and elevated cardiac markers. However, upon angiography no significant coronary artery obstruction is appreciated. Sadamatsu et al reported two cases with apical wall abnormalities and reduced coronary flow without coronary stenosis. [9]

We report a case of Takotsubo cardiomyopathy in a patient who initially presented with severe hyponatremia from beer potomania. This patient did not present with chest pain however, the apical ballooning and negative coronary artery disease was discovered on left heart catherization and ventriculogram.

Case presentation

A 56-year-old African American male with medical history significant for Hypertension, Hyperlipidemia, and alcohol dependence who presented with incoherent speech with altered mentation. He reported dyspnea with

mild exertion. He denied chest pain, orthopnea, paroxysmal nocturnal dyspnea, or pedal swelling. He has been binge drinking several cans of beer, about 24 of 24 -Oz can, prior to presentation. This was, following, a sudden incarceration and imprisonment of his wife. Patient had his last drink 5 hours prior to presentation to the Emergency room.

Examination revealed a disheveled middle age African American male who was confused and inebriated. His Vital signs revealed blood pressure 129/67mmHg, pulse 73beats/minute, and body temperature 99.4F. He was somnolent but easily arousable, and oriented to person, place but not to time or situation. Neurologic examination showed no focal neurological deficits. The rest of his physical examination yielded no addition findings.

Laboratory investigations including biochemical and hematologic results obtained in the ER is listed below (Table 1). This revealed serum sodium 102mmol/L, serum osmolality 245mOsm/L, urine osmolality 44mOsm/L, urine sodium 7mmol/L, blood alcohol level 221mg/dL, and creatine kinase 7,810units/L. Random urine drug screen was positive for opiates. Initial electrocardiogram showed normal sinus rhythm (Figure 2). Chest x ray showed no acute cardiopulmonary process (Figure 1). About 45 minutes after presentation at the Emergency department, he experienced violent incessant episodes of generalized clonic-tonic seizure episode involving all limbs. This was concerning for status epilepticus and required sedation with phenobarbital and intubation for airway protection at the medical intensive care unit at our community hospital. Nephrology, critical care, and neurology consultation was subsequently placed.

Patient was given hypertonic saline with close monitoring of his serum sodium and electrolytes. The rise in serum sodium was 0.5-1mmol/L/h, serum sodium gradually improved to 120 over 2 days. The patient's chest x-ray demonstrated possible right middle lobe pneumonia and he was started on broad spectrum antibiotics of ceftriaxone and azithromycin intravenously. The patient continued to be on mechanical ventilation and multiple attempts at extubating failed.

Over the next 24 to 48 hours, a change was noted on telemetry monitoring concerning for ST elevation and a 12-lead electrocardiogram showed early repolarization abnormalities in the left lateral leads (Figure 3). Follow up cardiac enzymes done showed troponin of 4.30 mg/mL, creatine kinase- MB 50U/L, creatine kinase 1293U/L." The ST elevations did not qualify for classification as STEMI, however, he required urgent treatment for NSTE-ACS. The patient was, subsequently transferred to a neighboring hospital with percutaneous coronary intervention and cardiac catheterization capability.

He stayed on mechanical ventilation several days. Echocardiogram done prior to the left heart catherization showed left ventricular ejection fraction of 30% with severe mid-distal and apical hypokinesis and ballooning, relaxation abnormality of left ventricular hypertrophy with mild concentric left ventricular hypertrophy were also appreciated (Movie 1). The patient received aspirin, metoprolol and lisinopril orally with heparin intravenously as medical therapy.

The Left Heart Catheterization (LHC) done, showed no evidence of obstructive CAD (Figure 4). There was no evidence of coronary vasospasm. LV angiogram showed apical ballooning and hypokinesis of anteroseptal Left ventricle concerning for Takotsubo cardiomyopathy (Figure 5). The patient was monitored closely after the LHC. Troponin peaked at 33.0mg/mL and subsequently trended down 0.04mg/mL, 3 days after the LHC.

He remained on hypertonic saline with increases of his serum sodium to 123mmol/L. The hypertonic saline was stopped when his serum sodium increased to 129mmol/L. The sodium remained stable at 128 – 130mmol/L. He was successfully extubated, after 4 days of mechanical ventilation. His mental status slowly improved and began to respond to commands. Patient made steady improvement in his clinical condition, antibiotics was discontinued and was discharge after 6 days of hospital stay.

An Echocardiogram done a month post admission during a follow up clinic visit to our hospital showed left ventricular ejection fraction of 55% with resolution of apical hypokinesis and ballooning (Movie 2).

Discussion

The patient's initial presentation of a low serum sodium of 101mmol/L raised the possibility of number of differential diagnoses including syndrome of inappropriate anti diuretic hormone (SIADH), dehydration, congestive heart failure, chronic kidney disease, cerebral- wasting syndrome, psychogenic polydipsia, and beer potomania. Low urine osmolarity and low urine sodium levels excluded dehydration, SIADH and cerebral wasting syndrome as the cause of this patient's hyponatremia [34]. The patient's denial of drinking excessive water, also ruled out psychogenic polydipsia. This patient's noncontributory initial physical examination, along with chest x-ray without any acute intrathoracic process with a normal BNP and renal function essentially ruled out congestive heart failure and renal insufficiency.

His history of alcohol abuse, including clinical presentation of lethargy and disheveled appearance, along with his laboratory work up of low serum osmolarity, urine osmolarity and low urine sodium results and absence of possible explanation, led us to the possibility of beer potomania accounting for the patient's hyponatremia.

Our eventual working diagnosis of the patient's hyponatremia was likely related to alcohol, and hence, the patient possibly, had beer potomania evidenced by low urine sodium and severe hyponatremia. This together led to the Status epilepticus our patient experienced. We hypothesize that his severe hyponatremia may have cause the Takotsubo cardiomyopathy (TC), especially in the context of epileptic seizures. The TC evidenced by the absence of coronary artery stenosis on LHC and presence of apical ballooning on ventriculogram and echocardiogram. This was buttressed by a low left ventricular ejection fraction of 30% and its eventual improvement to 55% over a relatively short period of time of a month.

The pathogenesis of TC is not fully understood but the proposed mechanisms include endogenous catecholamine excess, multi-vessel coronary artery vasospasm, and microvascular dysfunction. The most favored mechanism is endogenous catecholamine excess leading to microvascular spasm or dysfunction resulting in myocardial stunning [8]. Others have also discussed a direct toxicity of cardiomyocyte from the large amount of circulating catecholamines [19].

In support of the endogenous catecholamine excess hypothesis, a mouse model showed that a high level of epinephrine had negatively inotropic effect on cardiomyocytes due to a switch from beta-2 adrenoceptor Gs protein signaling to Gi protein signaling. It is speculated that the effect is greatest on the apex of the myocardium because of a higher density of beta-2 adrenoceptors. [20]

Additionally, Ellison et al found that high doses of isoproterenol cause diffuse death of myocytes while sparing cardiac stem cells in rats allowing for rapid recovery of the myocardium. [21]

Akashi et al in another study, reported that TC patients had an increased myocardial ^{123}I-metaodobenzlguanide (^{123}I-MBG) washout rate which indicates an increased norepinephrine release from sympathetic nerve endings or increased clearance of ^{123}I-MBG by extra neural tissues. Ultimately the increased wash out rate correlated to increased plasma norepinephrine levels in TC patients. [22]

There are a few case reports of TC in the setting of moderate to severe hyponatremia described in the body of literature. [10,12,30-33]

Hyponatremia has not been thought to be linked to Takotsubo cardiomyopathy but perhaps may have an indirect causal relationship. The prevailing theory of this indirect causal relationship is a stress induced catecholamine storm causing a direct toxic effect on the myocardium or indirect effect by coronary vasculature constriction. The mechanistic connection is still not clear; however, it has been suggested that hyponatremia could interfere with myocardial inotropy by modifying the cardiomyocytic sodium-calcium exchange pump resulting in myocardial swelling associated with hypotonicity. [10]

Indeed, transient positive inotropic effects on the myocardium were observed in rat hearts, and the degree of positive inotropy correlated with the degree of hyponatremia [11]. There have been cases reported of Takotsubo cardiomyopathy in the setting of "isolated hyponatremia" and it has been suggested that in post-menopausal women presenting with acute coronary syndrome-like symptoms and hyponatremia, Takotsubo cardiomyopathy should be considered within the differential diagnoses. [12]

Takotsubo cardiomyopathy arising as a direct consequence of hyponatremia is an unexplored mechanism for this poorly understood disease process. The prevailing theories for the pathogenesis of TC involves excessive catecholamine action on the myocardium causing stunning either directly or through ischemia by causing multi-vessel epicardial or microvascular spasm. [13]

There has also been a long-recognized connection between TC and stress, particularly strong emotional stress, which suggests that there may be a neurohumoral connection that precipitates TC. Interestingly, TC has been found in cases of subarachnoid hemorrhage and stroke, and neurologists have advanced the idea "neurogenic stunning" to describe this reversible cardiomyopathy in the setting of brain injury in the absence of coronary artery disease [13] Norepinephrine release in the myocardium is increased as a result of hypothalamic ischemia from a subarachnoid hemorrhage, and may be the cause of the myocardial injury observed [14]

Furthermore, this neurogenic stunning effect is dampened when there is a disruption of neural innervation of the myocardium as in diabetes or heart transplant [15]. Neurocardiac lesions also occur in adrenalectomized animals, but to a lesser extent, further strengthening the neurogenic stunning theory. [16]

Although ischemia as a direct cause of TC is still being debated, the dysfunctional myocardium in TC follows a neural rather than vascular distribution, as there is a much higher concentration of adrenergic receptors in areas around myocardial arterioles than in areas adjacent to epicardial coronary arteries. [17]

Conclusions

TC's preferential effects on the sub-endocardial myocytes manifests as an increased propensity for arrhythmia; this combined with excessive catecholamines, which can induce arrhythmia even in healthy myocardium, may be a major cause of sudden death in neurologic disease including subarachnoid hemorrhage, stroke, head trauma and increased intracranial pressure. With the wealth of evidence connecting the brain's effect on the heart, perhaps hyponatremia indirectly causes TC by first causing cerebral edema. The resulting neurological disturbance results in excessive catecholamine action on the myocardium which manifests as TC.

Availability of data and materials

Available on demand

Abbreviations

ACS: Acute coronary syndrome

CAD: Coronary artery disease

CK: Creatine kinase

CKMB: Creatine Kinase Myocardial Band

DM: Diabetes Mellitus

EKG: Electrocardiogram

HTN: Hypertension

HLD: Hyperlipidemia

LHC: Left Heart Catherization

LV: Left Ventricle

MI: Myocardial Infarction

NSTE-ACS: Non ST Elevation Acute Coronary Syndrome

PCI: Percutaneous Coronary Intervention

STEMI: ST Elevation Myocardial Infarction

TC: Takotsubo Cardiomyopathy

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Author Contributions

SND conceived the case report, acquired the progress reports, drafted the initial manuscript, reviewed, and revised the manuscript. SND, AAS, NT, RAA, MLW reviewed and revised the manuscript. All authors read and approved the final manuscript.

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Ethics approval and consent to participate.

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Consent for publication

Written informed consent was obtained from the patient for publication of this case report.

and any accompanying images. A copy of the written consent is available for review by

the Editor-in-Chief of this journal.

Competing interests

The authors declare that they have no competing interest to disclose.

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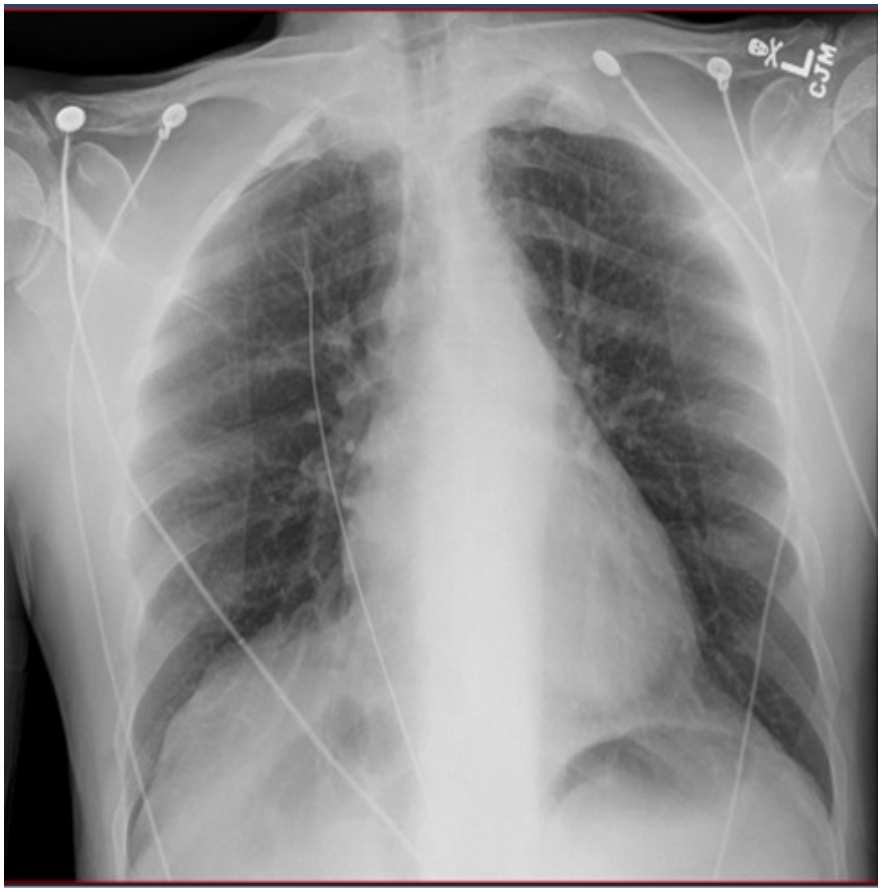
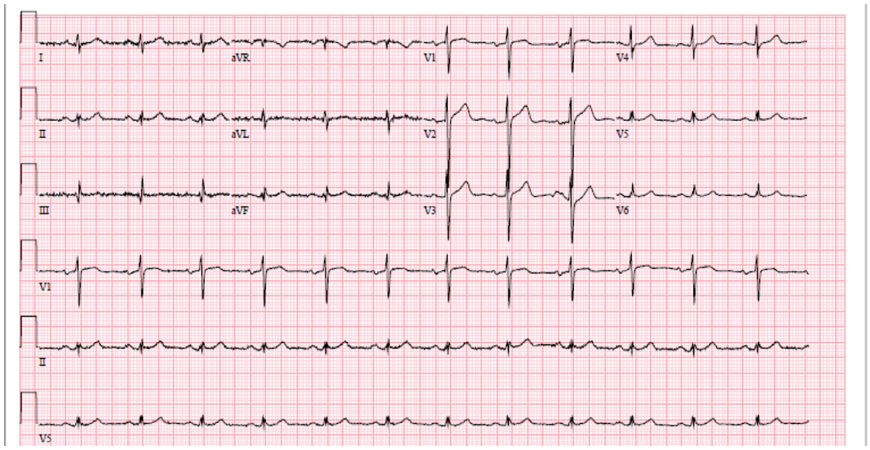
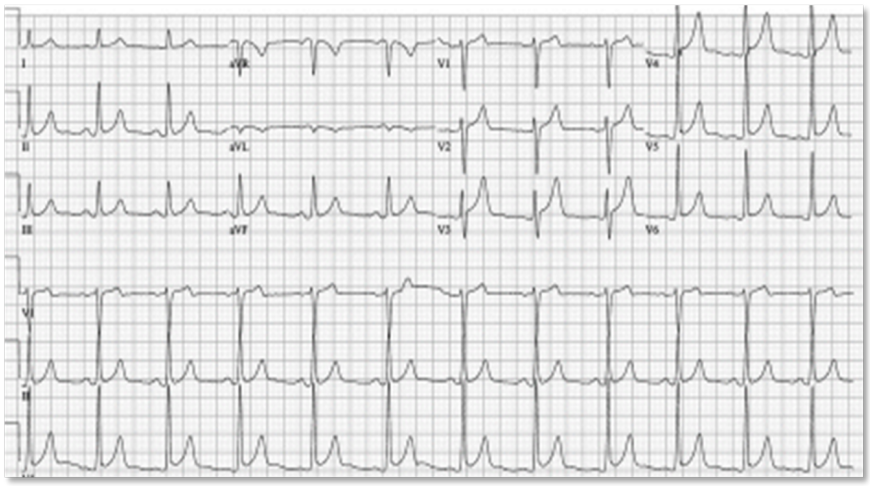






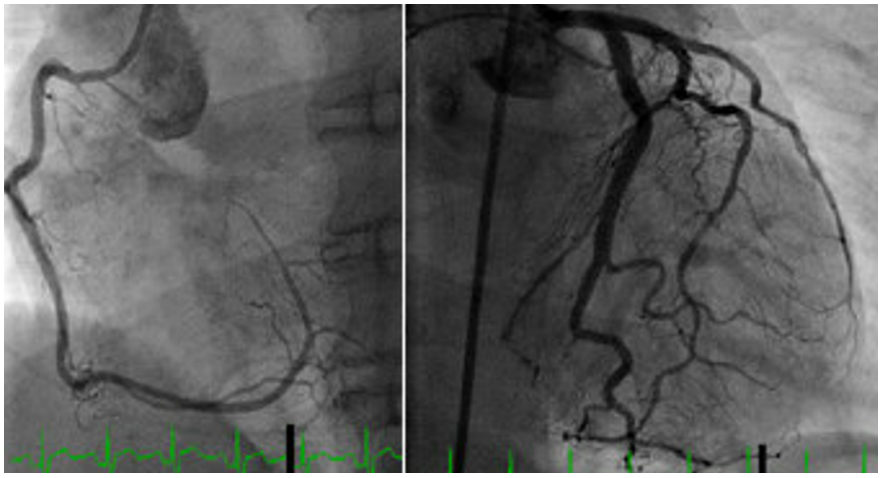
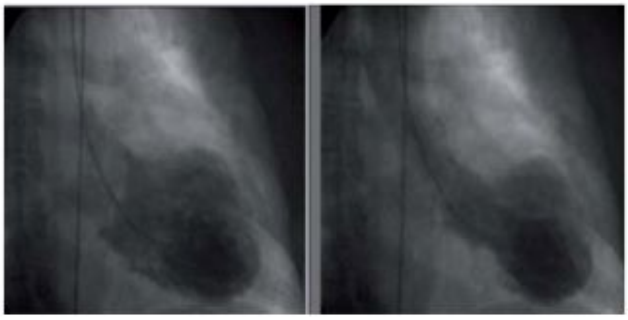


Figure 5- Ventriculogram imaging showing the apical and mid segment left ventricular

Akinesis and ballooning, taking the shape of the proverbial Japanese octopus. Takotsubo Cardiomyopathy



Left image: apical left ventricular akinesis and ballooning

Right image: Mid-segment left ventricular ballooning

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Table 1- Laboratory investigations.docx available at https://authorea.com/users/501217/articles/581819-takotsubo-cardiomyopathy-in-the-setting-of-severe-hyponatremia-and-beer-potomania-a-case-report-and-review-of-literature

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Movie 1-Echo apical ballooning consistent with TC (1).mp4 available at https://authorea.com/users/501217/articles/581819-takotsubo-cardiomyopathy-in-the-setting-of-severe-hyponatremia-and-beer-potomania-a-case-report-and-review-of-literature

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Movie 2- follow up Echo resolution of apical ballooning.mp4 available at https://authorea.com/users/501217/articles/581819-takotsubo-cardiomyopathy-in-the-setting-of-severe-hyponatremia-and-beer-potomania-a-case-report-and-review-of-literature