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Case Report

Takotsubo Syndrome Associated with Isolated Hyponatremia: Case Report

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ABSTRACT

Background: Electrolyte disorders have been exceptionally associated with the development of takotsubo syndrome (TTS).

Case Presentation: A 73-year-old healthy and active woman was admitted to the Emergency Department for acute dyspnea and chest pain. She had no medical history, except for arterial hypertension successfully controlled by lisinopril. Laboratory investigations revealed marked and isolated hyponatremia, consistent with a syndrome of inappropriate antidiuretic hormone (SIADH) secretion. The diagnosis of takotsubo syndrome (TTS) was based on the echocardiogram and coronary angiography findings.

Conclusion: Lisinopril appeared to be the most likely triggering factor of SIADH and hyponatremia, possibly deepened by a recent and transient increase of water intake. The mechanism linking hyponatremia and TTS is not fully understood.

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Introduction

Takotsubo syndrome (TTS) is associated with a sudden and profound systolic dysfunction that can affect, according to the different variants, the apex and/or midventricular segments of the left ventricle, or can be characterized by other wall motion abnormalities, also involving the right ventricle. The syndrome is usually drastically reversible and numerous triggering factors have been identified. Among them, electrolyte disorders are exceptionally observed. We describe a case of TTS following isolated hyponatremia that was consistent with a drug-induced syndrome of inappropriate antidiuretic hormone (SIADH) secretion.

Case Presentation

A 73-year-old woman with a history of arterial hypertension was admitted to the Emergency Department with dyspnea, chest pain and general malaise. Her blood pressure was usually well controlled by lisinopril (20 mg/day) that was started several years before (first 10 mg/day, then 20 mg/day since 2016). The patient was usually fit and very active physically. Symptoms started two days before hospital admission.

No other medication had been recently introduced. Additional history revealed that she had mildly increased fluid intake over the last days due to muscular cramps while she was walking over a longer distance. At physical examination, heart rate was 150/min, blood pressure 155/85 mmHg, respiratory rate 30/min, oxygen saturation 85% on room air. The patient was well oriented to time and place. Bilateral crackles were found on lung auscultation. There was no peripheral edema. Chest-X-ray showed bilateral pleural effusion and pulmonary congestion. Pulmonary embolism was ruled out by computed tomography (CT) pulmonary angiogram. Laboratory investigations revealed a marked hyponatremia (sodium level 118 mmol/L) and hypo-osmolality (248 mOsm/kg); chloride and potassium levels were respectively 82 mmol/L and 3.66 mmol/L. Troponin-T concentration was 223 pg/ml (<30), NT pro-BNP 16131 pg/ml (<301) and arterial lactate 3.4 mmol/L (0.5-2.2). Urine osmolality was 524 mOsm/kg and natriuresis 24 mmol/L. Adrenal and thyroid function tests were normal.

The electrocardiogram (ECG) on admission showed sinus tachycardia (133/min) with an absence of progression of R-wave from V1 to V5. Echocardiogram revealed a large apical akinesia extending to the middle lateral and septal wall (Video 1). Coronary angiography was strictly

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normal, while the ventriculogram confirmed the extensive midventricular and apical akinesia with an ejection fraction at 36% (Figure 1). The patient was managed with oxygen, diuretic therapy, fluid restriction and pleural drainage (-1300 ml, proteins 21.6 g/L, normal cellularity). Retrospectively, it was found from previous laboratory analyses that serum sodium level was sometimes around 130 mmol/L when the patient was consulting for her routine control of arterial blood pressure. There was a progressive correction of sodium levels up to 131 mmol/L on day 3 when the patient was transferred to the cardiology ward. Due to the suspicion of the lisinopril-related syndrome of inappropriate antidiuretic hormone (SIADH) secretion, losartan and carvedilol were progressively introduced instead of lisinopril. A complete recovery of left ventricular function was noted at follow-up. The patient tolerated long-term losartan therapy without hyponatremia.

The video link is: https://youtu.be/kCNxyiS_Vd8

Video 1: Echocardiography (four-chamber view) on admission with a large apical akinesia extending to the middle lateral and septal wall.

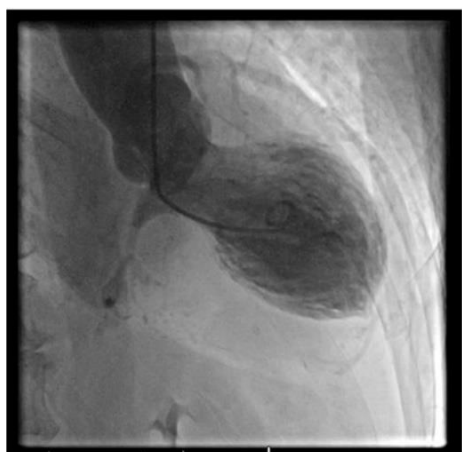


Figure 1: Left ventriculogram revealing a marked akinesia of the mid and apical segments.

Discussion and Conclusion

Several factors have been identified as potential triggering factors for the development of TTS. These triggers can be emotional, physical, medical, surgical, neurological or pharmacological. The particularity of the present observation is that no clear triggering factor could be found, with the exception of isolated hyponatremia. There was a temporal relationship between changes in natremia and installation and recovery of TTS. Among metabolic or electrolyte derangements, hyponatremia has been occasionally associated with TTS [1-6]. The pathophysiological link between hyponatremia and TTS is not evident. It can be speculated that hyponatremia, whatever its etiology, would induce an excessive catecholamine release secondary to brain dysfunction. In some case reports, hyponatremia was also complicated by seizures preceding the observation of TTS [2, 3]. Another suggested mechanism is that hyponatremia could interfere with myocardial inotropism by modulation of cardiomyocyte $\text{Na}^+/\text{Ca}^{2+}$ exchange which results in hypotonicity-induced myocardial swelling [3, 4].

Common causes of hyponatremia include diuretic therapy, SIADH, polydipsia, dehydration, hypothyroidism, adrenal insufficiency, nephrotic syndrome and liver cirrhosis. In the present observation, we

suspected lisinopril as a possible precipitating factor for SIADH. Even if the patient was under lisinopril therapy for a period of several years, this does not totally exclude the responsibility of lisinopril. SIADH is a rare but possible complication of therapy with lisinopril and other angiotensin-converting enzyme (ACE) inhibitors [7, 8]. It was hypothesized that ACE inhibitors in low to moderate doses might block the conversion of angiotensin I to angiotensin II in the peripheral circulation, but not in the brain. The presence of angiotensin II in the brain may stimulate the release of antidiuretic hormone. Hyponatremia may appear several years after the introduction of lisinopril when water intake is incidentally increased [7].

In the case reported by Jha *et al.* of TTS in a patient with SIADH, lisinopril was also found among the patient's medication [9]. As most of the patients receiving ACE inhibitors also have congestive heart failure, the precise role of the drug as the cause of SIADH is usually difficult to establish. Our patient was only suffering from arterial hypertension, with a normal cardiac function. She admitted having recently increased water intake after physical exercise. Finally, our patient did not develop hyponatremia under losartan therapy, even if losartan has been exceptionally associated with hyponatremia [10].

In conclusion, profound hyponatremia may trigger TTS in some patients. Among drug-related SIADH, ACE inhibitors may occasionally cause inappropriate antidiuresis and subsequent hyponatremia, particularly when other conditions (polydipsia, diuretics) are also present.

Conflicts of Interest

None.

Funding

None.

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.

Availability of Data and Materials

Not applicable.

Author Contributions

JV wrote the draft of the manuscript and performed echocardiography. PH and PFL were the ICU supervisors and revised the final version of the paper. CL supervised the follow-up of the patient and had also a significant contribution in writing the manuscript. All authors read and approved the manuscript.

Abbreviations

ACE: Angiotensin-Converting Enzyme

CT: Computed Tomography

ECC: Electrocardiogram

SIADH: Syndrome of Inappropriate Antidiuretic Hormone

TTS: Takotsubo Syndrome

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