CASE REPORT

Can aldosterone break your heart? Takotsubo cardiomyopathy in a patient with newly diagnosed primary aldosteronism

Dominika M Zoltowska,¹ Yashwant Agrawal,² Jagadeesh K Kalavakunta³

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¹Department of Internal Medicine, Western Michigan University, School of Medicine, Kalamazoo, Michigan, USA

²Department of Internal Medicine, Western Michigan University Homer Stryker School of Medicine, Kalamazoo, Michigan, USA

³Department of Cardiology, Borgess Medical Center, Michigan State University, Kalamazoo, Michigan, USA

Correspondence to

Dr Dominika M Zoltowska, dominika.zoltowska@med.wmich.edu

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SUMMARY

We report a case of a 47-year-old Caucasian woman with medical history of hypertension and hypokalemia, who presented to Emergency Room with symptoms resembling acute coronary syndrome ST-segment elevation myocardial infarction. Coronary angiogram revealed clear coronary arteries and left ventriculogram confirmed the diagnosis of Takotsubo cardiomyopathy. She was treated conservatively with good clinical outcome. Subsequent testing revealed underlying primary aldosteronism.

BACKGROUND

Takotsubo cardiomyopathy (TCM), also described as broken heart syndrome, represents transient left ventricular dysfunction in the absence of coronary vessel obstruction.¹ Discrimination of TCM from acute coronary syndrome is crucial in initial diagnostic approach.² This unique form of acute heart failure is classically developed in response to intense emotional or physical stress. Nevertheless, increasingly often, TCM is being linked to endocrine disturbances. Presented case reveals episode of TCM in the context of newly diagnosed primary aldosteronism (PA). Pathophysiology of heart injury in hyperaldosteronism and potential causative relationship of hyperaldosteronism and TCM has been discussed.

CASE PRESENTATION

A 47-year-old Caucasian woman presented to Emergency Room (ER) complaining of non-exertional, gradually increasing chest pain, which started within the previous 24 hours. Pain was localised in right upper chest and was associated with bilateral upper extremity discomfort, described as tingling. About 1 week prior to admission, she underwent outpatient stress echocardiogram for intermittent chest pain, which came back negative.

Medical history was significant for well-controlled hypertension with amlodipine and hypokalemia of unclear aetiology, for which she was taking potassium supplementation.

In the ER, initial vital signs and physical examination did not reveal any abnormalities. Patient was administered 325 mg of aspirin and single dose of sublingual nitroglycerine before further diagnostic studies were pursued.

INVESTIGATIONS

Initial laboratory tests including troponins were within normal limits except mild hypokalemia (K 3.1 mEq/L). ECG showed normal sinus rhythm (figure 1). Shortly thereafter, patient's chest pain significantly intensified. Urgent ECG showed new onset ST elevation in the inferior leads and T wave inversion in V4–V6 (figure 2). Repeat troponin came back significantly elevated at 20 ng/mL. She underwent emergent coronary angiogram which showed mild luminal irregularities without any significant coronary artery obstruction (figure 3). Left ventriculography revealed left ventricle systolic dysfunction with estimated ejection fraction (EF) of 40%–45% with inferoapical hypokinesis consistent with the diagnosis of focal type of TCM (see video 1 in the online Supplementary data).

In the context of unexplained hypokalemia along with the history of hypertension, patient underwent screening for PA, which came back positive. Serum aldosterone (SA) was 17 ng/dL, plasma renin activity (PRA) 0.3 ng/mL, which gave SA/PRA > 20 (positive screening when SA > 15 ng/dL and SA/PRA > 20). Intravenous normal saline infusion test failed to suppress SA (SA 27 ng/dL in supine position, cut-off < 10 ng/dL), which confirmed the diagnosis of PA.³ Hypercortisolaemia and pheochromocytoma have been excluded by normal level of 24 hours urine cortisol and not elevated serum metanephrine. Patient underwent CT of abdomen with and without contrast. It showed mild bilateral nodular enlargement of adrenal glands which led to diagnosis of adrenal hyperplasia as the cause of her primary aldosteronism.

DIFFERENTIAL DIAGNOSIS

The most important initial differential diagnosis included acute coronary syndrome with ST elevation (acute coronary syndrome ST-segment elevation myocardial infarction).

TREATMENT

Patient was started on enalapril, aspirin, metoprolol succinate and atorvastatin along with spironolactone. She was discharged home after few days of admission in stable condition and free of any cardiac symptoms.

OUTCOME AND FOLLOW-UP

During outpatient cardiology follow-up visit 4 months later, patient remained asymptomatic from cardiac standpoint and repeat transthoracic

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Figure 1 Initial ECG showing normal sinus rhythm.

echocardiogram showed normal left ventricular EF without regional wall motion abnormalities. She was continued spironolactone for PA and followed with endocrinology clinic.

DISCUSSION

TCM was first described in Japan in 1990.⁴ It was recognised as a rare phenomenon; however, since 1990, there is increasing numbers of cases registered all over the world. Unique clinical course and unclear pathophysiology is still the object of special interest in cardiology. Currently, the dominating theory proposed catecholamine-induced microvascular dysfunction that leads to myocardial stunning.^{5,6} Traditionally, TCM is associated with apical hypokinesia and this is the most commonly reported type, comprising above 80% of all cases. Less commonly occurring forms include basal (reverse), midventricular and a focal pattern of myocardial dysfunction, as diagnosed in our patient.⁷

Classically, TCM is precipitated by intense emotional or physical stress. Nevertheless, the nature of stress may vary. TCM was reported among others in response to pharmacological cardiac stress test as well.⁸

Lately, TCM is being increasingly investigated in the context of endocrine disorders. The most commonly described is hyperadrenergic state induced by neuroendocrine tumour, pheochromocytoma.⁹ Subsequently, exclusion of pheochromocytoma was incorporated into proposed Mayo Clinic Criteria for diagnosis of TCM.¹⁰ Along with pheochromocytoma, hyperthyroidism is being reported in association with TCM.¹¹ In contrary, it is being postulated that diabetes mellitus may have a protective effect in mechanism of reduced sympathetic response as the result of autonomic neuropathy and diminished catecholamine release.^{12,13}

Figure 2 Subsequent STAT ECG showing new onset ST elevation in the inferior leads and T wave inversion in V4–V6.

Figure 3 Angiogram without obstructive coronary artery disease. (A) Right coronary artery, (B) left anterior descending artery and (C) left circumflex artery.

PA previously assumed as uncommon syndrome, currently is described as the leading cause of secondary hypertension and has been identified in 5%–18% of hypertensive population.¹⁴ Importantly, aldosterone excess is considered as an independent risk factor for cardiovascular disease and increased mortality.¹⁵ Both structural and functional changes of heart have been recognised in patients with PA. Direct cardiotoxic effect is exerted by mineralocorticoid receptors in cardiomyocytes leading to excessive fibrosis and ion transport derangements. Deleterious effect of aldosterone can be potentiated by interaction with other hormones, including angiotensin II and endothelin.¹⁶ It has also been demonstrated, in both animal and human models, that PA is causing reversible transient hypersympathetic activity which can additionally contribute to cardiac toxicity.^{17,18}

Our case, revealed interesting concomitant finding of TCM and PA. Patient's history did not reveal any known triggers of TCM, which pointing towards PA as a potential cause. Interestingly, all patient's cardiac symptoms resolved since she was started on spironolactone. Aldosterone induced excessive inflammatory and hyperadrenergic state could explain its role in TCM pathogenesis. To date, there is only one more reported case of TCM linked to hyperaldosteronism.¹⁹ Nevertheless, there is still no established association in between PA and TCM and at this point any causative relationship remains a speculation. There is no current recommendation to screen patients with history of TCM for PA. It is worth pointing out though, that in presented patient, underlying PA remained undiagnosed before the admission despite classic symptoms of hypertension and hypokalemia. Diagnosis and treatment of PA are crucial to prevent increased morbidity and mortality associated with mineralocorticoid excess.

Learning points

- Importance of differentiation of Takotsubo cardiomyopathy (TCM) from acute coronary syndrome as initial approach.
- Occurrence of TCM under four forms: apical—classical, basal—reverse, midventricular and focal.
- Suspected role of endocrine disturbances as precipitators of TCM.
- Importance of recognition in patients eligible for screening for primary aldosteronism (PA).
- Implication of PA in pathophysiology of cardiovascular disease and increased mortality.

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