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RESEARCH ARTICLE'

Biventricular Reverse (Inverted) Takotsubo/Stress Cardiomyopathy in a Male Patient

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ABSTRACT

This report describes the rare occurrence of biventricular reverse takotsubo cardiomyopathy in a male patient who accidentally rolled his tractor trapping his right leg and left chest for 8 hours before being found. At admission, laboratory studies were remarkable for elevated serum troponin, creatine kinase and lactate levels and for acute kidney injury with hyperkalemia and metabolic acidosis. An echocardiogram demonstrated severe biventricular systolic dysfunction with relative preservation of contractility at the apex of both ventricles. Cardiac catheterization showed mild coronary atherosclerosis. The patient was critically ill and hypotensive, requiring vasopressor support and intravenous fluid replacement. He later became anuric with refractory acidosis and hyperkalemia from acute kidney injury due to rhabdomyolysis. Renal replacement therapy was initiated. The patient ultimately expired to multi-system organ failure. Reverse biventricular takotsubo cardiomyopathy is a rare variant of stress cardiomyopathy. Our case suggests that it likely occurs in the setting of a major physical trigger and is associated with severe hemodynamic compromise requiring intensive management, and associated with poor outcomes.

Keywords: Takotsubo Cardiomyopathy; Stress Cardiomyopathy; Heart Failure

Introduction

Takotsubo (stress) cardiomyopathy is an increasingly recognized syndrome characterized by transient regional systolic dysfunction, typically involving the mid and apical segments of the left ventricle (hence the term "takotsubo cardiomyopathy" or "apical ballooning syndrome") [1]. Uncommon variants are the mid-ventricular, reverse (inverted, basal), isolated segment, or global [2]. Right ventricular involvement is present in approximately 10-30% of cases [3-5]. The syndrome was initially described in response to emotional triggers (hence the term "broken heart syndrome") and later observed in a variety of physical illnesses accompanied by increased adrenergic activation (hence the term "catecholamine induced cardiomyopathy"). Although the condition predominantly affects postmenopausal elderly women, it does infrequently occur in middle-aged men and younger women [6]. Clinical presentation frequently mimics acute myocardial infarction [7,8] and resolves with supportive treatment. A minority of patients develop acute heart failure and cardiogenic shock that requires intensive therapy [2,9]. This case report describes the rare occurrence of biventricular reverse (inverted) takotsubo/stress cardiomyopathy in an elderly male patient, which occurred in the setting of a major physical trigger and resulted in severe hemodynamic compromise with a poor outcome.

History of Presentation

A 71-year-old man with a past medical history of hypertension and hyperlipidemia was brought to our emergency department by Emergency Medical Services after accidentally rolling his tractor and trapping his right leg and left chest for 8 hours. At the time of the initial encounter, the patient was hypotensive (systolic blood pressure 75 mm Hg), tachycardic (heart rate 112 beats per minute) and hypoxic (oxygen saturation 88% on ambient air). Physical examination revealed distant cardiac sounds but no murmurs, rubs or gallops. Lung auscultation revealed diminished left-sided breath sounds. Abdomen was distended. Examination of the extremities showed a tense, swollen right thigh.

Differential Diagnosis

Initial differential diagnosis after primary and secondary survey included cardiac tamponade, pneumothorax, hemothorax, hollow viscus injury, solid organ laceration and crush injury.

Investigations

Electrocardiography (Figure 1) showed a normal sinus rhythm with nonspecific ST-T wave changes and a prolonged corrected QT interval of 495 milliseconds. Laboratory studies were remarkable for an elevated high-sensitivity troponin T of 747 ng/L (reference value < 15 ng/L), lactate of 6.0 mmol/L, creatinine of 2.2 mg/dL, potassium of 7.6 mmol/L, creatine kinase of 63,230 U/L, low pH of 7.06 and bicarbonate of 13 mEq/L.

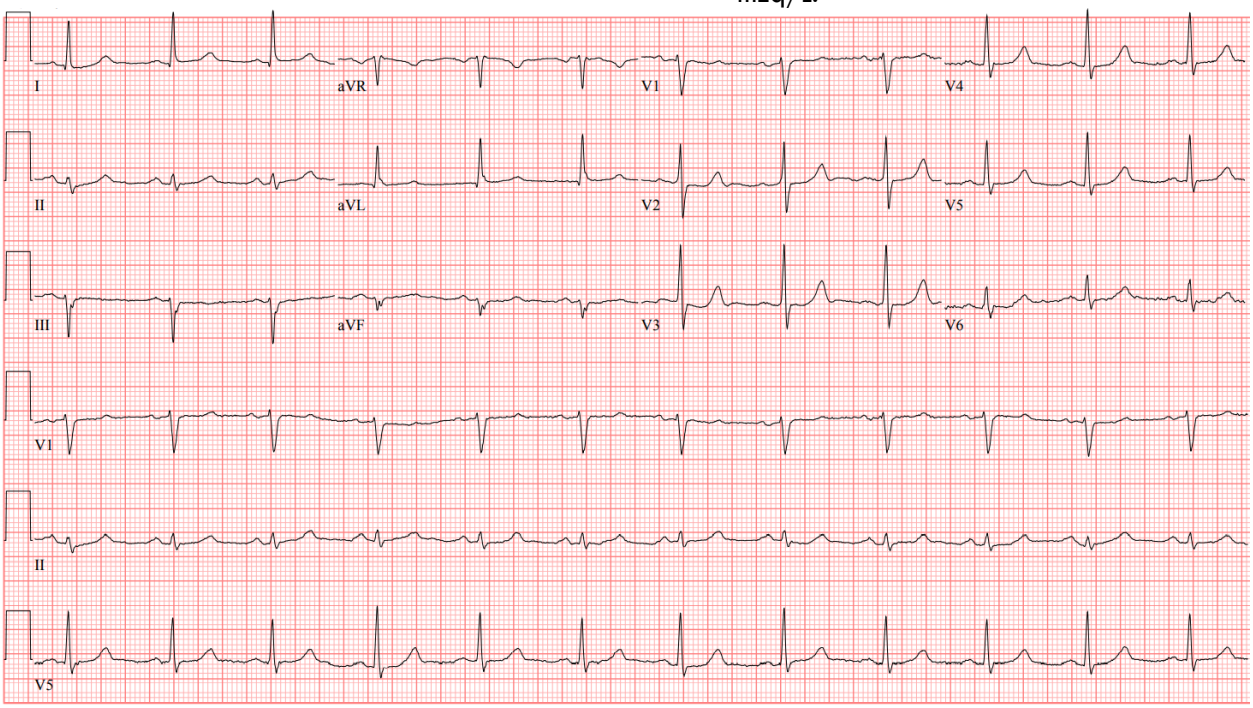

Figure 1. Initial electrocardiogram showed a normal sinus rhythm with nonspecific ST-T wave changes and a prolonged corrected QT interval of 495 milliseconds.

Management

The patient was critically ill and hypotensive, requiring norepinephrine support and large-volume intravenous fluid replacement to treat the rhabdomyolysis and worsening renal function. A transthoracic echocardiogram (Figure 2, Video 1) demonstrated severe diffuse biventricular systolic dysfunction with relative preservation of contractile function at the apex of both the left and right ventricles. The estimated left ventricular ejection fraction was 25%. The pattern of regional wall motion abnormality was suggestive of the potential diagnoses of a major acute myocardial infarction, fulminant myocarditis or reverse/inverted takotsubo cardiomyopathy with biventricular involvement.

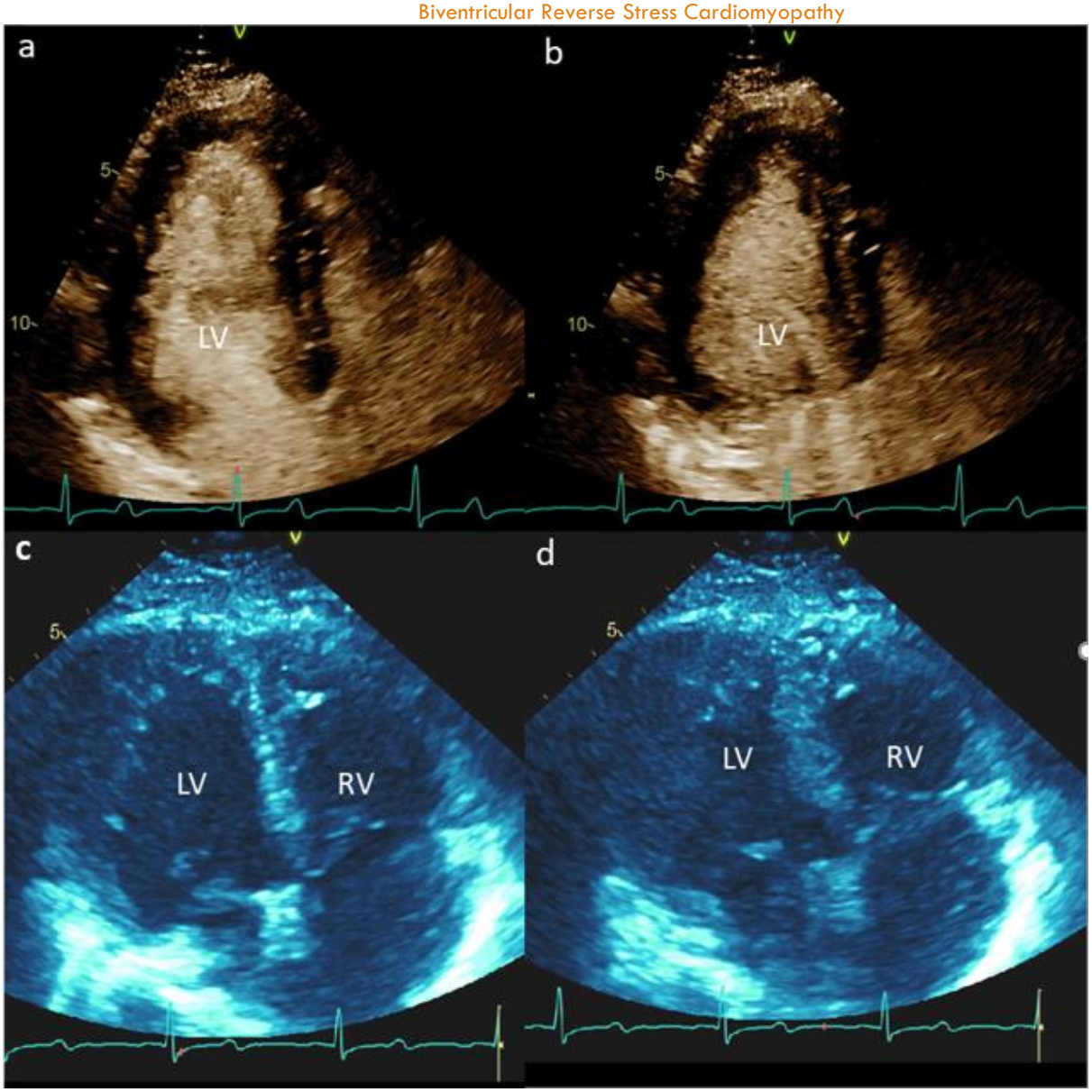

Figure 2. Apical four-chamber view in end-diastole (a) and end-systole (b) demonstrating reduced basal and mid left ventricular function and relatively preserved apical function (arrows), ejection fraction 25%. Right ventricular focused views in end-diastole (c) and end-systole (d) demonstrating right ventricular enlargement and reduced systolic function.

Video 1. Echocardiography in apical four-chamber view demonstrating absent basal and mid left ventricular contraction and relatively preserved apical function, ejection fraction 25%. Right ventricular views demonstrating right ventricular enlargement and similar pattern of regional wall motion abnormality.

Video 2. Coronary angiography in the left anterior oblique view showing mild atherosclerosis in the left coronary artery.

Video 3. Coronary angiography in the right anterior oblique view showing mild atherosclerosis in the right coronary artery.

In view of the need for inotropic and vasopressor support and high-volume fluid replacement, a Swan-Ganz catheter was inserted to assess and monitor hemodynamics. On norepinephrine infusion, it showed a mean right atrial pressure of 17 mm Hg, mean pulmonary artery pressure of 30 mm Hg, and a pulmonary capillary wedge pressure of 17 mm Hg, consistent with severe elevation in right-sided filling pressures and mild elevation in left-sided filling pressures. Cardiac index was normal at 2.8 L/min/m^2 and systemic vascular resistance was 576 dynes/sec/cm^{-5} (normal 900-1200 dynes/sec/cm^{-5}). Coronary angiography was performed to exclude obstructive coronary artery disease. There was mild coronary atherosclerosis (Video 2 and 3) supporting the diagnosis of takotsubo cardiomyopathy.

Outcome

The patient initially responded to supportive therapy but later became anuric with refractory acidosis and hyperkalemia from acute kidney injury due to rhabdomyolysis. Over the course of 24-48 hours following admission, the cardiac index decreased to 1.31 L/min/m^2 and SVR increased to 3982 dynes/sec/cm^{-5}, consistent with cardiogenic shock. Mechanical circulatory support was discussed but not initiated. Hemodialysis was initiated. The patient continued to decompensate and ultimately expired to multi-system organ failure and pulseless electrical activity.

Discussion

Takotsubo cardiomyopathy is an important differential diagnosis of acute myocardial infarction. It accounts for

2% of cases initially suspected of an acute myocardial infarction. Hence recognizing the unique clinical characteristics of takotsubo cardiomyopathy are essential, especially in the context of complex clinical scenarios such as major trauma or acute medical illnesses. Our case represents the rare confluence of three infrequent clinical characteristics of this unique cardiomyopathy in one patient, namely biventricular dysfunction, the reverse variant, and elderly male. Biventricular involvement occurs in about 10-30% of cases [3-5], the reverse (inverted) variant occurs in only 2% of cases [2], and only 10% of patients are males [6,10]. There is the potential of such cases being misdiagnosed as acute myocardial infarction or acute myocarditis.

Two small case series have compared the clinical characteristics of the inverted variant to the classic apical ballooning pattern of regional wall motion abnormality [11,12]. Both reported that the inverted variant occurs in younger patients, typically under the age of 60 years. Our patient was atypical in this regard. Another distinctive aspect of the variant is that all cases were associated with a physical or emotional trigger, whereas no trigger was identified in 1 out of 4 cases of the classic apical ballooning. This circumstantial evidence suggests that more potent stressors, with potentially a larger catecholamine surge, are needed to cause the inverted form of the cardiomyopathy, as was the case in our patient. This is underscored by a recent case report of inverted Takotsubo in a patient with pheochromocytoma [13].

The Mayo Clinic diagnostic criteria do not explicitly mention the possibility of right ventricular involvement, but the more recent International Takotsubo (InterTAK) diagnostic criteria explicitly state that right ventricular involvement may be present [8,14] (Table 1). Involvement of the right ventricle is associated with a sicker cohort of patients. Patients with biventricular takotsubo cardiomyopathy have lower left ventricular ejection fraction, more acute heart failure and shock, and complex hospitalization course compared to those without right ventricle involvement. In general, the distribution of right ventricular regional wall motion abnormality mirrors that of the left [5,15]. Recent larger multicenter national registries have confirmed the findings of the original single center reports, except that the incidence of biventricular takotsubo cardiomyopathy has been estimated to be lower at approximately 10-15% of cases [3,4]. Thus, systematic imaging of the right ventricle should be performed at presentation, and if dysfunction is present, identifies a higher risk subset of patients.

Table 1. Diagnostic Criteria of Takotsubo Cardiomyopathy.

Mayo Clinic Criteria for Apical Ballooning Syndrome [8]	**International Takotsubo Diagnostic Criteria (InterTAK Diagnostic Criteria)** [14]
1. Transient hypokinesis, akinesis, or dyskinesis of the left ventricular mid segments with or without apical involvement; the regional wall motion abnormalities extend beyond a single epicardial vascular distribution; a stressful trigger is often, but not always present.*	1. Patients show transient[a] left ventricular dysfunction (hypokinesia, akinesia, or dyskinesia) presenting as apical ballooning or midventricular, basal, or focal wall motion abnormalities. Right ventricular involvement can be present. Besides these regional wall motion patterns, transitions between all types can exist. The regional wall motion abnormality usually extends beyond a single epicardial vascular distribution; however, rare cases can exist where the regional wall motion abnormality is present in the subtended myocardial territory of a single coronary artery (focal TTS).[b]
2. Absence of obstructive coronary disease or angiographic evidence of acute plaque rupture.†	2. An emotional, physical, or combined trigger can precede the takotsubo syndrome event, but this is not obligatory.
3. New electrocardiographic abnormalities (either ST-segment elevation and/or T-wave inversion) or modest elevation in cardiac troponin.	3. Neurologic disorders (e.g. subarachnoid haemorrhage, stroke/transient ischaemic attack, or seizures) as well as pheochromocytoma may serve as triggers for takotsubo syndrome.
4. Absence of: Pheochromocytoma Myocarditis	4. New ECG abnormalities are present (ST-segment elevation, ST-segment depression, T-wave inversion, and QTc prolongation); however, rare cases exist without any ECG changes.
	5. Levels of cardiac biomarkers (troponin and creatine kinase) are moderately elevated in most cases; significant elevation of brain natriuretic peptide is common.
	6. Significant coronary artery disease is not a contradiction in takotsubo syndrome.
	7. Patients have no evidence of infectious myocarditis.[b]
	8. Postmenopausal women are predominantly affected.
*In both of the above circumstances, the diagnosis of ABS should be made with caution, and a clear stressful precipitating trigger must be sought. There are rare exceptions to these criteria such as those patients in whom the regional wall motion	[a]Wall motion abnormalities may remain for a prolonged period of time or documentation of recovery may not be possible. For example, death before evidence of recovery is captured.

Mayo Clinic Criteria for Apical Ballooning Syndrome [8]	International Takotsubo Diagnostic Criteria (InterTAK Diagnostic Criteria) [14]
abnormality is limited to a single coronary territory. †It is possible that a patient with obstructive coronary atherosclerosis may also develop ABS. However, this is very rare in our experience and in the published literature, perhaps because such cases are misdiagnosed as an acute coronary syndrome.	[b]Cardiac magnetic resonance imaging is recommended to exclude infectious myocarditis and diagnosis confirmation of takotsubo syndrome.

Older men presenting with elevated and rising troponin levels are generally suspected of having obstructive coronary artery disease due to its high prevalence. Conversely, 90% of takotsubo cardiomyopathy cases occur in women. Therefore, misdiagnosis is more likely to occur in men. Men developing takotsubo cardiomyopathy typically present with a physical trigger, have a lower ejection fraction, and are generally in a critical condition with a concomitant non-cardiac diagnosis [6]. Differentiation from acute myocardial infarction requires the exclusion of obstructive coronary artery disease by angiography and the recognition of the typical patterns of regional wall motion abnormality.

The patient was critically ill in the context of major trauma, with mixed shock, in part due to the severe biventricular systolic dysfunction. Cardiogenic shock is seen in up to 10% of patients with stress cardiomyopathy [2,9]. Due to the potential role of catecholamines in the pathophysiology of takotsubo cardiomyopathy, the use of inotropes is generally minimized or avoided. Mechanical circulatory support is the preferred therapy when there is marked left ventricular dysfunction associated with severe hypotension and shock. The cardiac index was low normal initially but declined in our patient even with supportive therapies. The severe crush injury to the lower limb and chest was a relative contraindication for mechanical circulatory support including intra-aortic balloon counterpulsation. Extracorporeal membrane oxygenation was also not considered in our case due to the patient's age and multisystem organ failure.

Takotsubo cardiomyopathy represents an acute heart failure syndrome with substantial morbidity and mortality both during and after the acute phase of the disease [2]. The rates of severe in-hospital complications including cardiogenic shock and death in stress cardiomyopathy are similar to those in acute coronary syndrome [2,16]. Consistent with our case, physical triggers, high troponin levels, a low left ventricular ejection fraction and involvement of the right ventricle are independent predictors of in-hospital complications [2,5].

Conclusion

Biventricular reverse takotsubo cardiomyopathy is a rare variant of stress cardiomyopathy. It may be associated with severe hemodynamic compromise and poor outcomes and requires early detection and intensive management. The adverse outcomes are frequently related to the associated triggering illness and comorbidities.

Conflict of interest: The authors declare that there is no conflict of interest relevant to the contents of this manuscript.

Abstract presentation: The manuscript content was previously presented as a Complex Clinical Case at the 71st Annual Scientific Session of the American College of Cardiology in Washington, D.C., on April 3, 2022.

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