Reverse or inverted apical ballooning in a case of refeeding syndrome

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Abstract

Takotsubo cardiomyopathy is characterized by the development of transient left ventricular regional wall motion abnormalities, in the absence of significant coronary artery obstruction. This syndrome usually occurs in women and is frequently associated with an intense emotional or physical stress. It usually involves apical segments, but in the recent years atypical forms have been described. Inverted or reverse Takotsubo is a variant in which the basal and midventricular segments are hypokinetic, sparing contractile function of the apex. In this report we describe the case of a 54-year-old woman, with chronic malnutrition, initially admitted because of hypoglycemia and severe electrolyte disturbance due to a refeeding syndrome. Within the next hours she experienced acute cardiac symptoms and developed heart failure with low cardiac output. Electrocardiogram (ECG), elevation of troponin and echocardiographic findings were consistent with inverted Takotsubo cardiomyopathy. To the best of our knowledge, this is the first incidence reported of inverted Takotsubo triggered by refeeding syndrome.

Key words: Apical ballooning; Refeeding syndrome; Anorexia; Atrial tachycardia; Inverted takotsubo

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Core tip: Inverted Takotsubo is a stress-induced cardiomyopathy type that could be encountered in patients suffering from varied physical or emotional triggers. In this report we describe the first case following a refeeding syndrome. There are reported cases of classical apical Takotsubo associated with nutrition disorders, but none of them presenting with the inverted variant.

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INTRODUCTION

Takotsubo cardiomyopathy (also called apical ballooning syndrome or stress-induced cardiomyopathy) is an acute cardiac syndrome characterized by transient and reversible wall-motion abnormalities of the left ventricle.

The clinical features include an onset of acute chest symptoms, electrocardiographic changes, and elevated cardiac enzymes, mimicking myocardial infarction, but in the absence of significant obstructive coronary disease.

It is estimated that this condition probably accounts for 1% to 2% of all cases of suspected acute myocardial infarction. Approximately 90% of all reported cases have been in women and the average age of onset range between 58 and 75 years, with < 3% of the patients being < 50 years[1].

In the most commonly described type of stress cardiomyopathy, the contractile function of the mid and apical segments of the left ventricular is depressed and there is hyperkinesis of the basal walls. Less common (atypical) variants include ventricular hypokinesis restricted to the mid-ventricle (mid-ventricular Takotsubo), hypokinesis of the base and mid-ventricle segments with sparing of the apex (reverse or inverted Takotsubo), and localized hypokinesis[2].

The pathophysiology remains unknown, but this syndrome is frequently triggered by intense emotional or physical stress or by an acute medical illness, so catecholamine mediated myocardial stunning is the most accepted explanation[3]. We present a case of inverted Takotsubo in a woman with chronic malnutrition who experienced a rapid oral nutrition repletion. After that she developed refeeding syndrome, a potentially lethal clinical condition characterized by severe metabolic disturbances in undernourished or starved patients undergoing refeeding. Medical complications of this syndrome include cardiovascular system, but it has not usually been described to trigger Takotsubo’s cardiomyopathy. The fact that the patient developed an atypical variant (inverted) instead of the classical type of apical stress cardiomyopathy, also makes this case remarkable.

CASE REPORT

A 54-year-old woman was admitted to our hospital on Christmas day with impaired consciousness and severe hypoglycemia (19 mg/dL). She had a past medical history significant for persistent malnutrition, although main organic causes of weight loss had been excluded. The day before admission the relatives of the patient had urged her to ingest a copious dinner on Christmas Eve.

Physical examination on admission revealed marked emaciation with a body weight of 28 kg. She was 162 cm in height and her body mass index (BMI) was 10.66 kg/m² (~45% of her ideal BMI). Her body temperature was normal, but she had bradycardia (55 beats/min) and edema in her lower limbs. Her albumin (1.5 g/dL), phosphate (2.2 mg/dL), magnesium (1.6 mg/dL) and potassium (2.7 mmol/L) levels were low. Liver dysfunctions (AST: 122 IU/L, ALT: 72 IU/L) also were noted, as well as coagulation disorders (PT: 55.9%, APTT: 43 s).

First of all, she was treated with 25 g of 50% glucose administrated intravenously, with recovery of consciousness within a few minutes. Then she started receiving specific treatment for electrolyte replacement. The initial ECG showed sinus bradycardia (Figure 1A). Some hours later, the patient referred heart palpitations and a new ECG (Figure 1B and C) was obtained, showing a supraventricular tachycardia. It was remarkable the ST segment elevation in leads II, III, aVF, V5-V6. The tachycardia was terminated by the administration of adenosine (Figure 1D). Revising the whole electrocardiographic registry the episode was consistent with paroxysmal atrial tachycardia. In the next hours the clinical state of the patient progressively impaired, with development of acute dyspnea, hypotension and obtundation, suggesting heart failure and low cardiac output. Chest X-ray also demonstrated an impairment respect to the previous one on admission (Figure 2). Echocardiography showed dyskinesia of basal and mid-ventricular segments, with hyperkinesia of left ventricular apex (Figure 3). The ejection fraction was estimated at 25%. Serum troponins were mildly elevated with a peak of 4.2 ng/mL, with non-elevated creatine phosphokinase (CPK) levels (80 UI/L). The patient was treated with noninvasive positive pressure ventilation and inotropic drugs at the Intensive Care Unit. Along the next days her clinical situation progressively improved, and a echocardiogram performed one week later showed recovery of the wall motion abnormalities of the left ventricle, with hyperdynamic ejection fraction (Figure 4). Finally, as a complication she developed respiratory distress due to a Serratia marcescens-induced acute pneumonia, and she died. Subsequent necropsy revealed coronary arteries with non obstructive lesions.

DISCUSSION

Once other causes of weight loss had been excluded, all the evidence (clinical signs and findings, along with information provided by the family) pointed towards our patient in the present case suffered from anorexia nervosa (AN).

In patients with AN, cardiac complications can be present in up to 80% of cases and have been reported as cause of at least one-third of all deaths[4].
Main cardiovascular disorders include alterations in hemodynamics (mainly hypotension), in structure (radiographic evidence of decreased cardiac size associated with lower left ventricular mass) and in electrical activity, including sinus bradycardia (present in this patient), reduction in QRS voltage, alterations in ST segment, U waves and prolonged QT interval. QT prolongation may be influenced both by electrolyte abnormalities and psychotropic drugs, with subsequent higher risk of ventricular arrhythmias or torsades de pointes. However, left ventricle function generally remains normal, and Takotsubo’s cardiomyopathy has only been reported in AN in isolated cases, some of them with hypoglycaemic coma as the precipitating event.

Over a chronic severe malnutrition state, the patient had been urged to ingest a copious dinner just before admission. Clinical impairment that she developed within the next hours can be attributed to the appearance of a refeeding syndrome (RF).

RF describes a series of metabolic and biochemical changes that occur as consequence of reintroduction of feeding after a period of starvation or fasting. First reports of the syndrome appeared in the 1950s after observations of malnourished prisoners of war who developed cardiac and neurological symptoms soon after the recommencement of feeding. In 2001 Crook et al. referred to a syndrome of important electrolyte and fluid shifts associated with metabolic abnormalities in malnourished patients undergoing oral, enteral or parenteral refeeding.

This potentially lethal condition encompasses a severe electrolyte disturbance, mainly low serum concentrations of intracellular ions such as phosphate, magnesium, and potassium. Hypophosphataemia is the adopted surrogate marker for diagnosing RF, though low serum phosphate is not pathognomonic. It may produce clinical complications affecting
Figure 3 Two-dimensional echocardiogram, subcostal four chambers view, showing the anteroseptal and posterolateral walls of the left ventricle. End-diastolic (A) and mid-systolic (B) frames at the time of acute cardiac symptoms presentation showed dyskinesia of basal and medium segments, with hyperkinesia of the left ventricular apex. One week later, recovery of the wall motion abnormalities was demonstrated, with hyperdynamic ejection fraction (C and D). A previous echocardiogram performed two years before in this patient was similar to this last one. RA: Right atrium; LA: Left atrium; LV: Left ventricle.

Figure 4 Bull’s eye mapping of two-dimensional speckle tracking strain imaging longitudinal (A) and circumferential (B) showed decreased strain values of the basal and mid-ventricular segments, with normal or increased strain values of the apical segments.

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the cardiac, respiratory, haematological, hepatic and neuromuscular systems and leading even to death[10,11].

Atrophy of the heart during starvation renders the patient more vulnerable to fluid overload and heart failure, and electrolyte abnormalities may contribute to ventricular arrhythmias[12]. Nevertheless, our patient developed unusual cardiovascular complications associated with RF, as atrial tachycardia and stress-induced cardiomyopathy.

Automatic atrial tachycardias (caused by abnormal automaticity in cardiac cells) are catecholamine sensitive and the discharge of the abnormal pacemaker involved can be triggered by drugs, various forms of cardiac disease, reduction in extracellular potassium or alterations of autonomic nervous system tone. One or more of them could have influenced in the episode suffered by this patient in the context of RF[13].

Stress-induced (Takotsubo) cardiomyopathy is characterized by the development of transient wall-motion abnormalities in the absence of obstructive coronary artery disease. It was initially described in the Japanese population in 1991 as a syndrome of reversible left ventricular dysfunction with wall-motion abnormalities that involved the apical segments[14]. This condition is typically triggered by severe emotional or physical stress, and it is thought to be caused by a catecholamine-mediated injury. Subarachnoid hemorrhage and pheochromocytoma have been described as common triggers of Takotsubo’s cardiomyopathy, which supports this hypothesis, with the exact mechanism of damage caused by catecholamines being less well understood[15].

Various patterns of stress-induced cardiomyopathy have been recently recognized and classified into 4 types based on the involvement of the left ventricle: (1) classic or apical type; (2) reverse or inverted type; (3) mid-ventricular type; and (4) localized type[16]. We report a case consistent with the inverted type, with dyskinesia of basal and mid-ventricular segments and hyperdynamic contractility of the apex.

Clinical differences affecting inverted type in comparison to common apical and mid-ventricular type have been evaluated by several studies. They conclude that patients with reverse Takotsubo are significantly younger compared with those with other types. It might be due to an asymmetric distribution of adrenergic receptors, which seem to play an important role to determine the area of hypokinesis[17]. The hypothesis is that adrenoceptor density is highest in the apex compared with the base in postmenopausal women, explaining the occurrence of apical variant in older women. The presentation of the inverted type at an early age could be explained by the abundance of adrenoreceptors at the base of the heart, compared with the apex, in younger patients[18].

Release of troponin is higher in inverted Takotsubo compared to other patterns, which might be the consequence of the larger muscle region involved compared to apical type. Nevertheless, in apical and midventricular patterns natriuretic peptides are more elevated and a higher prevalence of significant reversible mitral regurgitation is present, which is clinically translated by more severe heart failure symptoms and higher NYHA functional class[19].

Inverted Takotsubo also seems to be more often associated with either mental or physical stress than other types. Different authors have described cases of inverted type associated with varied physical triggers (pheochromocytoma, pulmonary embolism, cerebellar hemorrhage, pneumomediastinum, etc.)[20-22]. Nevertheless to our best knowledge, this is the first report of a case of stress cardiomyopathy presenting with an inverted pattern following a refeeding syndrome.

Regarding to malnourished patients, there are reported cases of classical Takotsubo associated with starvation states of different etiologies, but usually with refractory hypoglycemia as characteristic feature, and none of them presenting with the inverted variant[23].

A particular group would be patients with anorexia nervosa, with some reported cases of development of stress cardiomyopathy maintaining euglycemia; in these cases the syndrome might be triggered by emotional stress or electrolyte disturbances, and neither any of them presenting with the inverted Takotsubo type in the published cases.

In our case, we hypothesize that this particularly unique cardiac manifestations of refeeding syndrome (atrial tachycardia and inverted Takotsubo) might be influenced by hypoglycemia, electrolyte abnormalities, metabolic disturbances, emotional stress,...as isolated factors or by a contribution of all of them[24].

COMMENTS

Case characteristics
A 54-year-old woman with chronic malnutrition who experienced a rapid oral nutrition repletion.

Clinical diagnosis
Impaired consciousness, emaciation with a body mass index of 10.66 kg/m², bradycardia and edema in her lower limbs.

Laboratory diagnosis
Severe hypoglycemia (19 mg/dL), low levels of albumin (1.5 g/dL), phosphate (2.2 mg/dL), magnesium (1.6 mg/dL) and potassium (2.7 mmol/L), liver dysfunctions (AST: 122 IU/L; ALT: 72 IU/L) and coagulation disorders (PT: 55.9%; APTT: 43 s).

 Imaging diagnosis
Chest X-ray demonstrated marked heart failure signs and echocardiography showed dyskinesia of basal and mid-ventricular segments with hyperkinesia of left ventricular apex, consistent with inverted Takotsubo, with decreased ejection fraction (estimated at 25%).

Pathological diagnosis
Necropsy revealed coronary arteries with non obstructive lesions.

Treatment
The patient was treated with noninvasive positive pressure ventilation and inotropic drugs, but she finally died due to a Serratia marcescens-induced acute pneumonia.
Inverted apical ballooning syndrome in refeeding syndrome

Related reports
Takotsubo cardiomyopathy is a syndrome frequently triggered by intense emotional or physical stress, and although it is thought to be catecholamine mediated, the pathophysiology remains unknown.

Term explanation
Refeeding syndrome describes a series of metabolic and biochemical changes that occur as consequence of reintroduction of feeding after a period of starvation or fasting.

Experiences and lessons
In this report the authors describe the first case of inverted Takotsubo following a refeeding syndrome.

Peers-review
There are reported cases of classical apical Takotsubo associated with nutrition disorders, but none of them presenting with the inverted variant.

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