

Tako-tsubo cardiomyopathy as initial presentation of pheochromocytoma

A clinical case



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Tako-tsubo cardiomyopathy as initial presentation of pheochromocytoma. A clinical case.

INTRODUCTION: *Tako-tsubo cardiomyopathy is a rapidly reversible form of acute heart failure triggered by stressful events that occur more frequently in postmenopausal women. A central role is supposed to be played by catecholamines and the association with pheochromocytoma is rare.*

CASE PRESENTATION: *We describe a patient admitted for abdominal pain and suffering of hypertension pharmacologically treated. During hospitalization the patient presented cephalgia and precordial pain with nausea and profuse sweating. ECG showed ST elevation and deep negative T wave. Blood tests were moderately elevated. Echo-cardiography reported a left ventricular apex akynesia and hyperkynesia of the base while coronarography was negative. As hypertension persisted the suspicion of pheochromocytoma arose. Urinary and blood catecholamines were mildly elevated and echography and Magnetic Resonance revealed a left adrenal gland mass. The diagnosis of pheochromocytoma was thus confirmed. Left laparoscopic adrenalectomy was performed after adequate stabilization and preoperative pharmacological preparation by hydration, α - and β -blockers. Intraoperatively blood pressure was controlled by nitroprussiate, rapid half life β -blockers (esmolol cloridrato). Post-operative course was uneventful and arterial pressure returned to normal as well as catecholamines values. Patient was discharged on the 5th post-operative day. Five months afterwards the patient had normal arterial pressure without anti-hypertensive therapy and symptom free.*

CONCLUSION: *The case confirmed that tako-tsubo cardiomyopathy could be the first manifestation of tumors secreting catecholamines and that pheochromocytoma should be considered in patients with hypertension and acute stress-induced cardiomyopathy without evidence of acute coronary disease and with negative coronarography.*

KEY WORDS: Adrenalectomy, Heart failure, Pheochromocytoma.

Introduction

Tako-tsubo cardiomyopathy also known as broken heart syndrome or stress-induced cardiomyopathy or transient left ventricular apical ballooning is a rapidly reversible form of acute heart failure reported to be triggered by stressful events and associated with a distinctive left ven-

tricular contraction pattern ¹. The name of this syndrome has oriental origin, in fact *tako-tsubo* is the Japanese name for traps that fishermen still use to catch octopus. In this syndrome, the left ventricle takes the shape of an octopus trap. This shape is due to a state of complete exhaustion of the heart muscle in the mid-section and tip of the heart. Ecocardiography frequently reports an hypo-akinesia of the left ventricular apex, like an aneurysm (apical ballooning) with hyperkinesia of the bases. However, after the first description in 1991 some variants have been described ² in particular the so called inverted tako-tsubo ³.

Diagnosis of tako-tsubo syndrome can only be made after excluding other heart disease such as: coronary artery

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disease (particularly proximal left main artery stenosis), acute coronary syndrome, myocardial stroke, myocarditis, pericarditis and aortic dissection⁴. A combination of patient's history, pathognomic wall motion abnormalities accompanied by the lack of significant coronary artery stenosis and the apical ballooning would suggest the diagnosis of tako-tsubo syndrome.

Literature reports various etiologies for this cardiomyopathy⁵⁻⁸. The most plausible is an abnormal response to catecholamines released in response to stress producing a sort of "myocardial stupor"⁹. The central role played by catecholamines explains why tako-tsubo syndrome could be the first clinical manifestation of a pheochromocytoma as described in the present case.

Case report

A 74-year old man was admitted to our Unit, sent by the Emergency, for evaluation of abdominal pain in December 2009. Past history of the patient was positive for mild arterial hypertension pharmacologically treated. There was no previous history of surgical operation. He presented generalized abdominal pain not associated with nausea, vomiting, diarrhoea or constipation. An initial FAST (Focused Assessment with Sonography for Trauma) abdominal echotomography in the Emergency room was negative for intra-abdominal diseases.

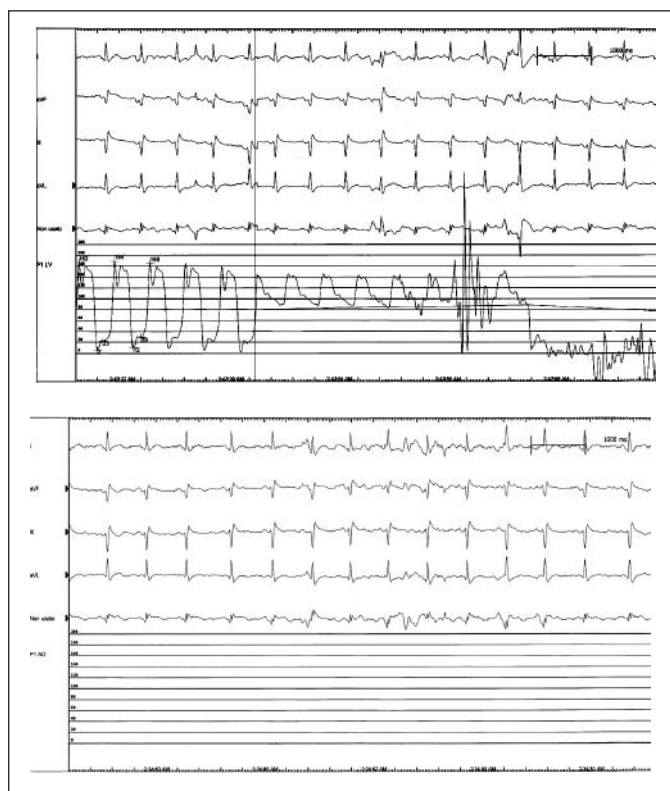


Fig. 1: ECG showing ST elevation and deep negative T wave.

During hospitalization, the patient presented a sudden onset of cephalgia and precordial pain with nausea and profuse sweating. Electrocardiography (ECG) showed ST elevation and deep negative T wave while blood tests for myocardial acute ischemia, such as troponin and creatin-phosphokinase, resulted elevated, consequently a diagnosis of anterior myocardial infarction was made (Fig. 1). Echocardiography reported a left ventricular apex akynesia and hyperkynesia of the bases (Fig. 2), while coronary angiography resulted negative for any coronary occlusion. The patient was stabilized with oxygen, diuretics (spironolactone and furosemide), and β -blockers (esmolol).

Faced with a persisting arterial hypertension and after having excluded other causes for this cardiomyopathy such as anatomical variant of the myocardial vessels, dysfunction of the coronary arteries and other stressing events, blood and urinary tests were performed in order to confirm or exclude the diagnosis of pheochromocytoma. Urinary catecholamines dosage resulted mildly elevated: epinephrine 2080,5 mcg/24 h (normal values 0-20 mgr/24 h); norepinephrine 1705,3 mcg/24 h (n.v.: 0-80 mcg/24 h). A second standard abdominal echotomography showed the presence of a left adrenal mass, and a magnetic resonance confirmed a 57x55x55 mm mass in the left adrenal gland showing a central necrosis (Fig. 3). The presence of adrenal gland mass and the elevation of urinary catecholamine values allowed the diagnosis of pheochromocytoma. These findings associated with the exclusion of other causes of elevated catecholamine such as cocaine use, hyperthyroidism, sub-arachnoid haemorrhage, supported the hypothesis that the excess of catecholamine could be the cause of tako-tsubo cardiomyopathy.

The patient underwent to a laparoscopic adrenalectomy, previously treated by hydration, α - and β -blockers and ACE-inhibitors therapy in order to stabilize the arterial blood pressure, avoiding intra and post-operative hypotension. The peri-operative treatment protocol of patients with pheochromocytoma has been already described¹⁰.

Surgical technique: the patient was placed in right lateral decubitus, secured at the waist, a cushion was placed under the contro-lateral lumbar fossa, which opens the operative field, thereby facilitating trocars placement. The optical trocar was introduced in the left sub-costal position, a second 10 mm trocar on the anterior axillary line, while two 10 mm trocars were inserted on either side of the first trocar under costal margin. The procedure began with dissection of the spleno-phrenic ligament until the gastric greater curvature and the left crus were exposed. This allowed for the entire mobilization of the spleen along with the pancreatic tail. The main adrenal vein was clipped at the origins from the renal vein, as well as the inferior phrenic vein, the middle adrenal artery, the superior adrenal artery and inferior adrenal artery. After ligation of the vessels, the gland could be completely mobilized and removed.

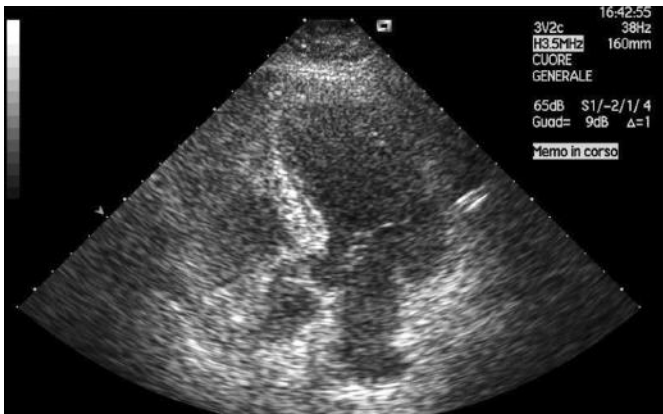


Fig. 2: Echocardiography reported a left ventricular apex akynesia and hyperkinesia of the base.



Fig. 3: Magnetic Resonance Imaging shows a 48x60 mm mass in the left adrenal gland.

During surgical procedure, the intra-operative arterial pressure was monitored and maintained stable with an infusion of rapid half-life β -blockers (esmolol chloridrate), sodium nitroprussiate and ephedrine chloridrate¹¹. Post operative course was uneventful and the arterial pressure returned to normal range as well as serum and urinary catecholamines values. The histopathological evaluation confirmed the cromaphin nature of the tumor without signs of malignancy. Patient was discharged on the 5th post-operative day with ventricular function improvement during hospitalization. Five months after surgical treatment, the patient was under regular follow-up with normal arterial pressure, without any anti-hypertensive therapy and symptom free.

Discussion

Tako-tsubo cardiomyopathy is a temporary left cardiac ventricular apical ballooning due to a transient dyskinesia of the left cardiac ventricle. Although the original tako-tsubo cardiomyopathy is by far the most common presentation other rare patterns such as mid-ventricular type, anterior left ventricular wall type and reverse (or inverted) apical ballooning type have been described^{2,3}. In most cases, the typical presentation of this cardiomyopathy is a sudden onset of angina pectoris symptoms, ECG changes (such as ST elevation and deep negative T wave), while coronary angiogram is usually negative for any significant stenosis and, occasionally, very slightly elevated cardiac markers of heart damage (troponin, creatine kinase)^{12,13}. The shape of ballooning is due to a state of complete exhaustion of the heart muscle in the mid section and tip of the heart. In these cases echo-cardiography frequently reports an hypo-akinesia of the left ventricular apex, like an aneurysm (apical ballooning) with hyperkinesia of the bases. Diagnosis of tako-tsubo syndrome can only be made after excluding other heart disease such as: coronary artery disease (especially proximal left main artery stenosis), acute coronary

syndrome, myocardial stroke, myocarditis, pericarditis and aortic dissection⁴. Patient's history, the typical wall motion abnormalities accompanied by the lack of significant coronary artery stenosis or disease and the apical ballooning would suggest the diagnosis of tako-tsubo syndrome. Despite the severe initial presentation most of the patients survive the initial acute event, with a low rate of in-hospital mortality but sometimes with severe complications that need major resuscitation¹⁴. Patients can expect a favourable outcome once they recover from the acute stage of the syndrome, and the long-term prognosis is excellent, in fact ventricular systolic function improves within the first few days and normalises within the first few months. Recurrence of the syndrome has been reported but it is infrequent¹⁵. It's a rare syndrome that in about 70-80% of cases occurs in post-menopausal women under some form of extreme, exceptional and prolonged mental stress. Seldom if ever, the phenomenon has been described also in young people³. In a minority of patients (<20%) the stress is physical, such as massive trauma, surgery, severe pain or other type of stress^{16,17,18}. In very rare cases, no "cause" can be found. This syndrome has also a geographical distribution, in fact the prevalence of this particular disease is higher in Japan than in Europe.

The etiology of this rare syndrome is not fully understood. Several mechanisms have been proposed to explain how catecholamines can favour the myocardial stunning. There is evidence that elevated levels of catecholamines can induce a direct myocyte injury by calcium overload mediated by AMP-cyclic or through the production of free radicals that interfere with sodium and calcium carriers¹⁹. A second mechanism proposed is microvascular spasm due to the increased sympathetic tone in absence of coronary obstruction. The demonstration of regional cardiac defects on cardiac scintigraphy suggests a microcirculatory dysfunction induced by catecholamines excess²⁰. Another mechanism to explain myocardial stunning is an abnormal fatty acid metabolism by myocardial tissue but the relationship with the increased release of catecholamines

remains unexplained²¹. Another mechanism proposed is a functional mid-cavity obstruction induced by the catecholamines excess.

Moreover, increased serum concentration of catecholamines has been shown to induce damage for myocardial tissue and the pattern of histologic changes induced by catecholamines on myocytes have also been reported in patients with tako-tsubo syndrome²².

The central role played by the catecholamines can explain why tako-tsubo syndrome is not infrequently the first clinical finding of a pheochromocytoma. On the other hand tako-tsubo cardiomyopathy has been described associated with elevated concentration of catecholamines, notably norepinephrine, even in absence of pheochromocytoma.

Since first description by Iga et al. in 1989²³, the association of transient cardiomyopathy and pheochromocytoma has been described in literature in other few cases including case of extra-adrenal tumor²⁴.

Despite the initial description of tako-tsubo syndrome as idiopathic, in the recent years there is general agreement⁴ that tako-tsubo-like myocardial dysfunction might occur in association with increased secretion of catecholamines such as pheochromocytoma or cerebrovascular disease.

In recent years there is evidence that the pattern called reverse or inverted tako-tsubo syndrome characterized by an adynamic cardiac base and an hyper-kynetic apex, seems to correlate more frequently than other pattern of tako-tsubo to pheochromocytoma³.

This report emphasizes the importance of taking into consideration pheochromocytoma in the differential diagnosis of patients with hypertension affected by acute stress-related cardiomyopathy.

Moreover, the diagnosis of pheochromocytoma should be considered in patients with acute coronary syndrome with coronarography negative and signs of adrenergic stimulation in order to avoid the use of β -blockers without adequate, contemporary, α -blockage. More precocious and accurate is the diagnosis more adapted are the pharmacological and surgical treatments.

Conclusions

Tako-tsubo, a stress-induced acute cardiomyopathy, could be the first manifestation of tumor secreting catecholamines. These tumors should be searched for in case of acute heart failure with typical echocardiographic findings of apical ballooning associated with hyperkinesis of cardiac base and in absence of acute coronary disease and with negative coronarography.

Riassunto

INTRODUZIONE: La sindrome di tako-tsubo è una forma rapidamente reversibile di insufficienza cardiaca scatenata

da eventi stressanti ed è più comune nel sesso femminile in età post-menopausale. Si ipotizza che un ruolo centrale sia giocato dalle catecolamine, nonostante l'associazione con il feocromocitoma sia rara.

CASO CLINICO: In questo lavoro descriviamo il caso di un paziente con ipertensione controllata farmacologicamente, giunto alla nostra osservazione per dolore addominale. Durante l'ospedalizzazione ha presentato cefalea e precordialgie associate a nausea e sudorazione profusa. L'ecocardiogramma ha dimostrato un'acinesia dell'apice ventricolare sinistro ed un'ipercinesia della base, a fronte di una coronarografia negativa mentre l'ECG ha rilevato un'elevazione del tratto ST ed una profonda onda T negativa con enzimi cardiaci moderatamente elevati. Vista la persistenza dell'ipertensione, sono stati eseguiti i dosaggi delle catecolamine urinarie, una ecografia addominale ed una risonanza magnetica che confermano la presenza di un feocromocitoma a carico del surrene sinistro. La risonanza magnetica ha permesso una migliore definizione della sede della neoplasia.

È stata eseguita una surrenectomia sinistra laparoscopica dopo adeguata stabilizzazione pre-operatoria mediante idratazione, α e β bloccanti ed intra-operatoria mediante nitroprussiato e β bloccanti ad emivita breve (esmololo cloridrato).

Il decorso post-operatorio è stato privo di complicanze, la pressione arteriosa è ritornata a valori normali, così come i livelli di catecolamine e il paziente è stato dimesso in quinta giornata postoperatoria.

Durante il follow-up, a cinque mesi, non si è ripresentata la sintomatologia e i valori pressori si sono normalizzati in assenza di terapia medica.

CONCLUSIONI: Tale caso conferma quindi che la sindrome di tako-tsubo può essere la prima manifestazione di un feocromocitoma e che quest'ultimo deve essere preso in considerazione in pazienti con ipertensione e cardiomiopatia stress-indotta senza l'evidenza di patologia coronarica, ovvero con coronarografia negativa.

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