Am J Cardiovasc Dis 2013;3(3):175-179
www.AJCD.us /ISSN:2160-200X/AJCD1307001

Case Report

Subacute stent thrombosis and stress-induced cardiomyopathy: trigger or consequence?

Francesco Tota[1], Massimo Ruggiero[1], Marco Sassara[1], Nicola Locuratolo[1], Lucia Sublimi Saponetti[1], Giulia Frasso[2], Mariangela Carbone[2], Pietro Scicchitano[2], Francesca Cortese[2], Pasquale Caldarola[1], Marco Matteo Ciccone[2]

[1]Division of Cardiology, San Paolo Hospital, Bari, Italy; [2]Cardiovascular Diseases Section, Department of Emergency and Organ Transplantation (DETO), University of Bari, Bari, Italy

Received July 8, 2013; Accepted July 31, 2013; Epub August 16, 2013; Published August 30, 2013

Abstract: Stress-induced cardiomyopathy or Takotsubo cardiomyopathy (TCM) is a unique syndrome, characterized by transient left ventricular (LV) apical ballooning without significant coronary arteries stenosis, affecting mainly menopausal women. We present the case of a 70 year old woman with subacute stent thrombosis (ST) at the level of the right coronary artery and transient apical ballooning with normal flow of left and circumflex coronary arteries. TCM is frequently associated with emotional stress, but to date no case of ST triggering TCM have been reported.

Keywords: Stress-induced cardiomyopathy, Takotsubo cardiomyopathy, subacute stent thrombosis

Introduction

Takotsubo cardiomyopathy (TCM) occurs predominantly in postmenopausal women. Catecholamine excess in circulation has been identified as a possible cause of the acute cardiac dysfunction characteristic of this stress cardiomyopathy [1]. In fact, literature data show the association between stress cardiomyopathy and sudden emotional stress (in about 27%) and/or physical illness (in other 38% of cases), but to date no case of stent thrombosis (ST) able to trigger TCM have been reported [2].

Despite dual antiplatelet therapy, ST represents nowadays a catastrophic complication of approximately 0.5-2% of all percutaneous coronary interventions with a high mortality and non-fatal myocardial infarction rates [3]. In this paper we present a case of an elderly woman admitted to the cardiological emergency department of San Paolo Hospital for chest pain, with acute heart failure, echocardiographic aspect of cardiac apical ballooning, subacute ST at the level of the right coronary artery and absence of significant atherosclerotic disease of left and circumflex coronary arteries.

Case report

A 70 year old woman with history of hypertension and diabetes was admitted to our cardiology division for chest pain, dyspnea and ST-segment depression in leads V4-V6. On arrival, blood pressure and heart rate were respectively 170/100 mmHg and 115/min and she was afebrile. Physical examination showed tachycardic and lower intensity heart sounds and vesicular sounds heard over most of the lung fields. Transthoracic echocardiogram revealed a moderate global left ventricular (LV) systolic dysfunction with an ejection fraction (EF) of 40% (biplane Simpson method), hypokinesia of the inferior wall and normokinesia of the remaining regions (apex, anterior and lateral walls). The patient was immediately transferred to our catheter laboratory to undergo coronary angiography. The angiographic evaluation revealed a subtotal occlusion (99%) of the right coronary artery and absence of lesions obstructing blood flow at the level of left and circumflex coronary arteries (**Figures 1A** and **2A** respectively). We performed percutaneous coronary intervention (PCI) using a drug-eluting stent (DES) Nobori 3.0/28 with good angiographic (Thrombolysis In Myocardial Infarction

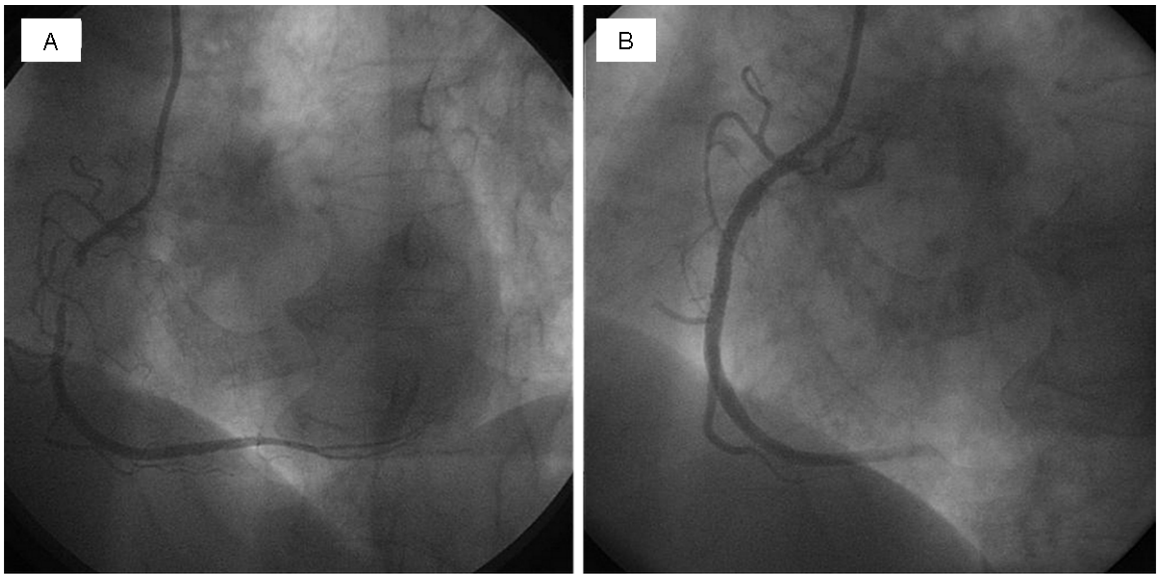

Figure 1. Coronary angiograms showing: A subtotal occlusion (99%) of the right coronary artery and B the good angiographic outcome after primary percutaneous coronary intervention with stent.

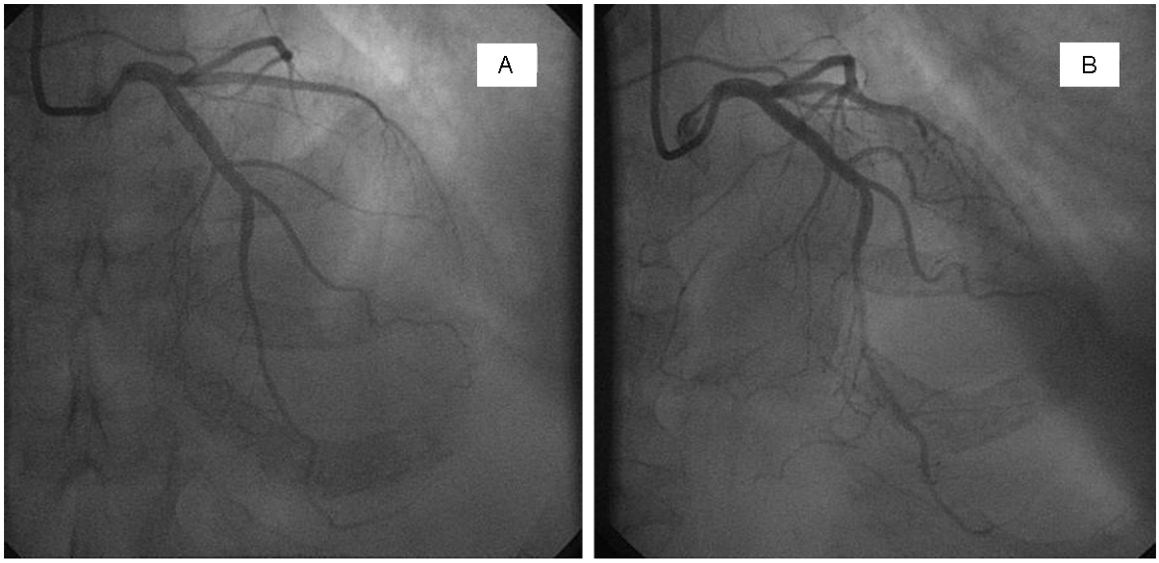

Figure 2. Coronary angiograms showing the absence of significant luminal obstructions of left and circumflex coronary arteries: A during the first and B the second coronary angiography.

(TIMI) 3, **Figure 1B** and clinic outcomes.

Her hospital stay was uneventful and she was discharged after a few days with the following home therapy: acetylsalicylic acid, clopidogrel, beta-blocker, ACE-inhibitor and statin.

After seven days of discharge, early in the morning (five o'clock) she was admitted again to our division for intense chest pain, dyspnea and palpitations. On arrival blood pressure, heart rate and temperature were 135/60 mmHg, 138/min and 36°C, respectively. Clinical examination revealed tachycardic heart sounds and a proto-meso-systolic murmur (2/6 Levine's scale) at the cardiac apex, with rales, rhonchi and wheezes in the lung fields, especially at the bases, bilaterally. Her initial 12-lead electrocardiogram (ECG) showed sinus tachycardia (138 b/m) and ST-elevation of 0.15 mV

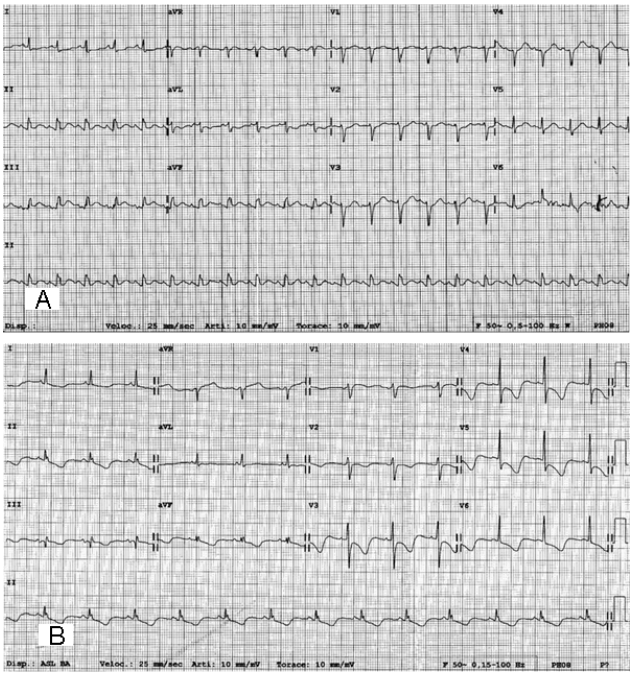

Figure 3. Electrocardiograms showing: A sinus tachycardia with ST-elevation in leads D2-D3-aVF and B diffuse T-inversion and QT prolongation.

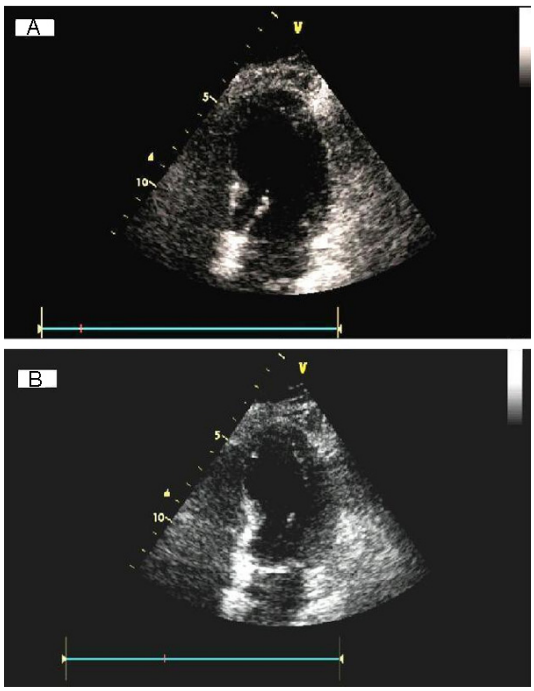

Figure 4. Bi-dimensional transthoracic echocardiogram apical four-chamber views in diastole A and systole B, showing apical ballooning with intra-cardiac thrombus.

in leads D2, D3, aVF, and ST depression of 0.10 mV in leads D1 e aVL (**Figure 3A**).

Transthoracic echocardiogram revealed a severe global LV systolic dysfunction, with an EF of 30% (biplane Simpson method), the typical apical-mid-ventricular ballooning and akinesia of the basal inferior segment. Moreover the ultrasound method showed a restrictive diastolic pattern, a moderate mitral regurgitation and a small spherical protruding thrombus in the cardiac apex with spontaneous echo-contrast (**Figure 4A** and **4B**).

Chest radiograph showed vascular redistribution, bilaterally engorged hila and the presence of interstitial and alveolar fluid with typical pattern of pulmonary oedema. The immediately performed coronary angiography revealed subacute ST at the level of the right coronary artery (**Figure 5A**) and absence of blood flow obstructive lesions of left and circumflex coronary arteries (**Figure 2B**). We performed primary PCI with DES XIENCE PRIME 3.0/33 with a good angiographic outcome (TIMI 3) (**Figure 5B**).

After eight days of hospitalization, for an acute right leg ischemia as a result of an embolic arterial occlusion, the patient was transferred to the surgical vascular department and arterial flow restored.

Serial echocardiograms, during hospital stay, revealed a final complete recovery of systolic function of apical and mid ventricular segments, persisting only the basal-inferior segment akinesia. The small spherical protruding thrombus in the apex was ultimately not found.

ECG performed on day 8 showed a sinus rhythm and T inversion in leads D1, D2, D3, aVF and V2-V6 and QT prolongation (**Figure 3B**). The patient was discharged on the fifteenth day event.

Discussion

Our case showed some interesting clinical features. First of all, to the best of our knowledge, it was the first case of TCM associated with subacute ST. Secondly, TCM in this case was complicated by apical thrombus and embolic arterial occlusion in concomitance with the progressive and complete recovery of cardiac systolic function. Thirdly, in the present case, the

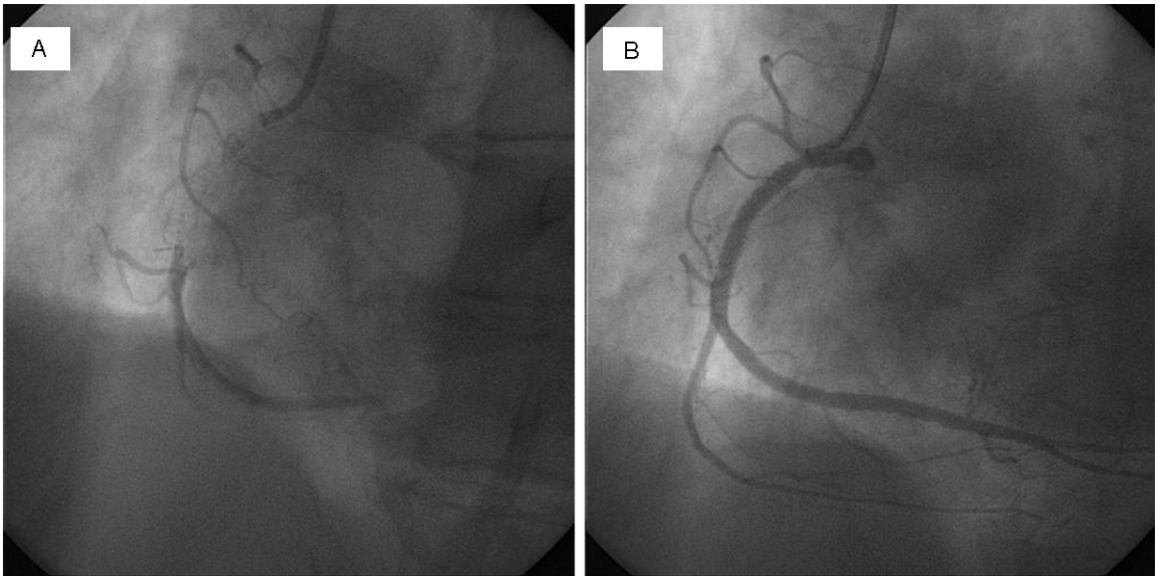

Figure 5. Coronary angiogram showing: A subacute stent thrombosis at the level of the right coronary artery and B flow restoring after revascularization with stent.

patient did not refer any emotional stress preceding chest pain.

TCM pathogenesis is still obscure. Catecholamine mediated cardio-toxicity provoked by emotional or physical illness, multivessel coronary vasospasm and abnormalities in coronary microvascular function have been proposed as possible explanations [1-3].

Higher admission level of plasma catecholamine in patient with TCM compared to patients with Killip class III myocardial infarction, as described by Wittstein at al., supported the theory of an exaggeration of sympathetic stimulation as the cause of this syndrome [4]. Takotsubo like LV dysfunction was also seen in patients with pheochromocytoma [5].

The available pathophysiological information indicates that apical ballooning characterizing TCM reflects toxic high local concentration of catecholamine, not coronary arteries or microvascular diseases. Exposure to sudden emotional stresses (in approximately 27% of cases) or physical illnesses (in other 38% of cases) such as sepsis, head trauma and cerebrovascular accidents, may precipitate stress cardiomyopathy in about two-thirds of the instances, but, to date, no case of ST triggering TCM have been reported [2].

Furthermore, a stress event triggering TCM is not always present ad is not a distinctive feature of this syndrome [6]. Admission in intensive care units for medical illness, surgical procedure, or traumatic injure could typically be the sufficient stress causing TCM. By performing serial echocardiograms in intensive care unit consecutive patients, Park at al. demonstrated the presence of stress cardiomyopathy in 28% of patients admitted for non cardiac physical illnesses [7].

More recently, Marcelino at al., performing transthoracic echocardiograms to 704 consecutive patients admitted to the intensive care unit during a 18-month period, detected LV systolic dysfunction in even 132 (18%) subjects [8]. Although cardiac impairment characterizing heart failure is associated with an increased blood concentration of catecholamine, as a compensatory mechanism to diminished contractile performance, epinephrine and norepinephrine circulating levels are not as high as those in TCM [9, 10].

On the base of available evidences showing that circulating epinephrine exerts more potent hormonal effects on the heart than norepinephrine, its excessive release has been proposed as the pathogenetic mechanism underlying TCM; linked to an increased susceptibility of the apex to the direct toxic effect of catechola-

mines due to an increased density of beta-adrenoreceptors [11].

In this context intravascular thrombosis, as the pathogenetic basis of ST, could be explained by multivessel epicardial coronary spasm, platelets activation, or by the pro-thrombotic effects of the extremely high epinephrine levels [11-13]. Epinephrine, in fact, is also able to promote platelets activation by stimulating platelet a2 adrenoceptor, providing, in this way, a valid reason for the combined use of alpha and beta-blockers in TCM treatment [14].

Innovatively, as in the examined case the patient did not report any stressful situation before chest pain, but ST was the only associated condition, we can consider this latter the triggering event able to unleash the catecholamine storm responsible for the intra vascular thrombosis, the reduced coronary flow and the consequent severe ventricular dysfunction. Reduced coronary flow velocity, measured by TIMI frame count, in the absence of relevant coronary arteries stenosis, was in fact observed immediately after TCM onset [15].

In conclusion, the current state of knowledge about the pathophysiological mechanisms involved in TCM, does not allow us to clearly identify ST as the cause or the consequence of this stress cardiomyopathy.

Disclosure of conflict of interest

None to declare.

Address correspondence to: Prof. Marco Matteo Ciccone, Cardiovascular Diseases Section, Department of Emergency and Organ Transplantation (DETO), University of Bari, Piazza G. Cesare 11 -70124 Bari, Italy. Tel: +39-080-5478791; Fax: +39-080-5478796; E-mail: marcomatteo.ciccone@uniba.it

References

[1] Akashi YJ, Goldstein DS, Barbaro G, Ueyama T. Takotsubo Cardiomyopathy: A New Form of Acute Reversible Heart Failure. Circulation 2008; 118: 2754-62.

[2] Gianni M, Dentali F, Grandi AM, Sumner G, Hiralal R, Lonn E. Apical ballooning sindrome or takotsubo cardiomyopathy: a systematic review. Eur heart J 2006; 27: 1523-9.

[3] Balaguer-Malfagón JR, Pomar-Domingo F, Vilar-Herrero JV, Planas-del Viejo AM, Pérez-Fernández E. Stent thrombosis in the modern era: incidence, outcome and predictive factors. Rev Esp Cardiol 2006; 59: 842-5.

[4] Wittstein IS, Thiemann DR, Lima JA, Baughman KL, Schulman SP, Gerstenblith G, Wu KC, Rade JJ, Bivalacqua TJ, Champion HC. Neurohumoral features of myordial stunning due to sudden emotional stress. N Engl J Med 2005; 352: 539-48.

[5] Spes C, Knape A, Mudra H. Recurrent takotsubo-like left ventricular dysfunction (apical ballooning) in a patient with pheochromocytoma - a case report. Clin Res Cardiol 2006; 95: 307-11.

[6] Maseri A. The tako-tsubo cardiomyopathy syndrome: lumpers or splitters? J Cardiovasc Med 2010; 11: 402-3.

[7] Park JH, Kang SJ, Song JK, Kim HK, Lim CM, Kang DH, Koh Y. Left ventricular apical ballooning due to severe physical stress in patients admitted to the medical ICU. Chest 2005; 128: 296-302.

[8] Marcelino PA, Marum SM, Fernandes AP, Germano N, Lopes MG. Routine transthoracic echocardiography in a general Intensive Care Unit: an 18 month survey in 704 patients. Eur J Intern Med 2009; 20: e37-42.

[9] Brinks H, Koch WJ. Targeting G protein-coupled receptor kinases (GRKs) in Heart Failure. Drug Discov Today Dis Mech 2010; 7: e129-e134.

[10] Wittstein IS. Stress cardiomyopathy: a syndrome of catecholamine-mediated myocardial stunning? Cell Mol Neurobiol 2012; 32: 847-57.

[11] Bounhoure JP. Takotsubo or stress cardiomyopathy. Cardiovasc Psychiatry Neurol 2012; 2012: 637672.

[12] Barrera-Ramirez CF, Jimenez-Mazuecos JM, Alfonso F. Apical thrombus associated with left ventricular apical ballooning. Heart 2003; 89: 927.

[13] Sasaki N, Kinugawa T, Yamawaki M, Furuse Y, Shimoyama M, Ogino K, Igawa O, Hisatome I, Shigemasa C. Transient left ventricular apical ballooning in a patient with bicuspid aortic valve created a left ventricular thrombus leading to acute renal infarction. Circ J 2004; 68: 1081-3.

[14] Ueno M, Kodali M, Tello-Montoliu A, Angiolillo DJ. Role of platelets and antiplatelet therapy in cardiovascular disease. J Atheroscler Thromb 2011; 18: 431-42.

[15] Bybee KA, Prasad A, Barsness GW, Lerman A, Jaffe AS, Murphy JG, Wright RS, Rihal CS. Clinical characteristics and thrombolysis in myocardial infarction frame counts in women with transient left ventricular apical ballooning syndrome. Am J Cardiol 2004; 94: 343-6.