ARC Journal of Diabetes and Endocrinology
Volume 2, Issue 1, 2016, PP 19-23
ISSN 2455-5983 (Online)
http://dx.doi.org/10.20431/2455-5983.0201003
www.arcjournals.org

Tako-Tsubo Syndrome and Diabetic Mellitus Review of Literature and a Case Report

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Abstract: *The entity of Takotsubo syndrome or cardiomyopathy also referred to as transient apical ballooning syndrome, stress cardiomyopathy or broken heart syndrome is a recently recognized syndrome typically characterized by transient and reversible left ventricular dysfunction that develops in the setting of acute severe emotional or physical stress. Increased catecholamine levels have been proposed to play a central role in the pathogenesis of the disease, although the specific pathophysiology of this condition remains to be fully determined. At present, there have been few reports of Takotsubo cardiomyopathy associated with diabetes mellitus. In this case report, we present a patient with multiple recurrences of Takotsubo triggered by diabetic ketoacidosis.*

Keywords: *Takotsubo, Recurrence, Diabetes, Ketoacidosis.*

1. INTRODUCTION

Tako-tsubo syndrome (TTS) or Cardiomyopathy (TC) is an increasingly recognized entity characterized by transient (reversible) apical and mid left ventricular (LV) dysfunction in the absence of significant coronary artery disease that is potentially triggered by severe emotional, physical stress, medical illness (acute exacerbations of multiple medical conditions such as asthma, sepsis, gastrointestinal bleeding or hypoglycemia) procedures or surgeries [1,2,3]. Increased catecholamine levels have been proposed to play a central role in the pathogenesis of this condition [4].

The Takotsubo phenomenon was first described in 1991 by Dote et al [1], who named the syndrome "Takotsubo like cardiomyopathy" because the appearance resembles a pot historically used in Japan to catch octopi. Other names of this syndrome are Stress-induced Cardiomyopathy, apical ballooning syndrome, broken heart syndrome, ampulla cardiomyopathy [1,2,3].

Typically, it recovers to normal LV function in 1-4 weeks. It may account for up to 2% of suspected acute coronary syndrome (ACS), TTS or TC is much more common in women than men, particularly post-menopausal women [1,2,3,5]. In a review of six prospective and four retrospective studies women accounted for 80 to 100 percent of cases, with a mean age of 61 to 76 years [5].

Tako-tsubo cardiomyopathy is a diagnosis of exclusion [6]. Researchers at the Mayo Clinic proposed diagnostic criteria in 2004, which include; (1) transient hypokinesis, akinesis, or dyskinesis in the left ventricular mid segments with or without apical involvement; regional wall motion abnormalities that extend beyond a single epicardial vascular distribution and frequently, but not always, a stressful trigger; (2) the absence of obstructive coronary disease or angiographic evidence of acute plaque rupture; (3) new ECG abnormalities (ST-segment elevation and/or T-wave inversion) or modest elevation in cardiac troponin; and (4) the absence of pheochromocytoma and myocarditis [2].

Numerous etiologies have been described, including catecholamine release during stress [2, 7, 8], and microvascular spasm or ischemia [9, 10].

Acute complications of TC include arrhythmias, pulmonary edema, cardiogenic shock, transient LV outflow tract obstruction, mitral valve dysfunction, acute thrombus formation, stroke and Death [11].

There are no established treatment algorithms for TC at present, but as most patients present with an ACS or heart failure (HF), they are treated according to ACS/HF guidelines. Tako-tsubo cardiomyopathy is generally a benign condition; in-hospital mortality is 0-8% [11-16].

Recurrent TC disease is rare and only few cases have been previously reported [14, 15].

Diabetes has been reported to be protective against TC and a few reported TC in diabetic patient indicating low prevalence (10-20%) [17, 18, 19], in contrast to the high prevalence of diabetes in ACS (52%) in our previous study [20].

We present in this report a rare case of recurrent apical ballooning syndrome in a woman with several hospitalizations for chest pain, dyspnea, and electrocardiographic (ECG) changes triggered by diabetic ketoacidosis (DKA).

2. THE CASE

A 53 year old female with poorly controlled type 2 diabetes due to medication non compliance who had 4 hospital admissions over the last 3 years for chest pain, dyspnea, acute ST-T elevation, cardiac biomarkers elevation, left ventricular apical severe hypokinesis and ballooning diagnosed by echocardiography. She always received acute coronary syndrome (ACS) management at presentation and had urgent coronary angiogram during the initial three presentations and all revealed normal coronary arteries. The common associated factor in all admissions was the presence of DKA at all presentations. After DKA treatment, she was kept on anti failure medications in the form of angiotensin converting enzyme inhibitor (ACEI), beta blocker (β-blocker), diuretic and aspirin. She always recovered fully in few weeks time with normalization of LV function and wall motion in follow up echocardiography and usually she stopped all her cardiac medications. Currently, she is stable with much better compliance with treatment, glycemic control, HbA1c and last echocardiography 6 months after the last TC event showed completely normal LV systolic function.

3. DISCUSSION

Tako-tsubo syndrome or cardiomyopathy is a recently recognized entity. Many theories have been presented for the possible pathophysiology of TC. Studies have proposed the mechanism as an association with excessive sympathetic stimulation, microvascular dysfunction, spasm and metabolic abnormalities [1-5, 16, 21].

Emotional and physical stresses often precipitate the clinical presentation. This suggests a relationship between cortical brain activity (a central catecholamine surge) and myocardial stunning [1,2,22,23].

Studies have found that patients with TC have statistically significant higher levels of serum catecholamines (norepinephrine, epinephrine, and dopamine) than patients with myocardial infarctions [23-26]. Increase beta-2-adrenoceptor activity in the setting of a high catecholaminergic state has been proposed as possible reproducible model for this entity, inducing cardiac dysfunction and myocyte injury though calcium leakage due to hyperphosphorylation of the ryanodine receptor 2 [27]. The apical portions of the left ventricle have the highest concentration of sympathetic innervations found in the heart and increased beta-2 concentration gradient from apex to base could play an important role in the apical myocardial dysfunction and ballooning commonly found in TC cases [19-23]. Combining the results from multiple studies plasma norepinephrine levels were elevated in 74% of cases [12].

The pathogenesis of TC may be multifactorial, similar to catecholamine induced cardiomyopathy [25], pheochromocytoma [26] and subarachnoid hemorrhage [27].

Catecholamine excess has reversible toxic effects on myocardium that have been documented in cases of pheochromocytoma [26-30]. Histological examination of biopsy samples from the affected left ventricle of patients with TC has shown intracellular accumulation of glycogen, many vacuoles, disorganized cytoskeleton and contractile structure, contraction band necrosis and increased extracellular matrix proteins, which is associated with clinical states of catecholamine excess [31,32,33]. These alterations resolved nearly completely after functional recovery.

Takotsubo cardiomyopathy is associated with minor release of cardiac enzymes so suggests some microscopic damage to the myocytes. The absence of causative coronary artery disease on angiography and the wall motion abnormalities point to an insult that is microscopic in nature.

Recurrent TC disease is rare and only few cases have been previously reported [14, 15].

Data on diabetes as a trigger for TC is scarce and previous reports suggest even a protective role of diabetes against TC [17, 18, 19, and 34] as compared to the higher prevalence of diabetes in ACS as shown in our previous study [20].

No previous documentation regarding recurrent TC triggered by DKA as in our case. We strongly believe that the above mentioned catecholamine and neuro-hormonal axis is probably the underlying mechanism that is stressed and over stimulated during DKA as in our patient, overwhelming and counteracting the baseline autonomic neuropathy known in diabetic patient.

There is no controlled data to define the optimal medical regimen to treat TC during DKA, but it has been postulated that it is reasonable to treat the underlying cause and with the standard medications for LV systolic dysfunction. These include ACE I, β-blocker (or combined α- and β-blocker), and diuretics, which may be necessary for volume overload states [2]. Aspirin and statin are also reasonable treatment [6, 35, 36].

It was reported that thrombosis occurs in takotsubo cardiomyopathy cases, which might reflect vasoconstriction, platelet activation, or prothrombotic effects of extremely high epinephrine levels that of course will be more exaggerated in diabetic patients [37-41]. In one study, 5% of patients with TC developed LV thrombus, and all patients with LV thrombus, were started on anticoagulation and one patient developed stroke [41]. It is reasonable to continue anti-coagulation until the thrombus resolve and left ventricular function improves [42].

4. CONCLUSION

To the best of our knowledge, we report a unique first case of multiple recurrences of TC triggered by diabetic ketoacidosis. Our patient was diagnosed 4 times with TC based on the widely accepted Mayo guidelines for TC Prevention with good glycemic control, medications compliance, and avoidance of other triggers have been the key to prevent further cardiac events.

Chronic management of TC is primarily empirical, but there is emerging data supporting the role for alpha and beta blockade. In diabetic patients who are stable, it appears advantageous to prevent excessive sympathetic activation by combining alpha and beta blockade during episodes of ketoacidosis.

We hope our case contribute to the understanding of this interesting rare condition and will further help in the management of patients with similar conditions.

Lastly, a more complete understanding of the pathophysiology of this syndrome in diabetics awaits further research.

REFERENCES

[1] Dote K, Sato H, Tateishi H, et al. Myocardial stunning due to simultaneous multivessel coronary spasm: a review of 5 cases. J Cardiol. 1991; 21 (2):203-214.

[2] Bybee, KA, Kara, T, Prasad A, Lerman A, Barsness GW, Wright RS, et al. Systematic review: transient LV apical ballooning: a syndrome that mimics ST-segment elevation myocardial infarction. Ann Intern Med 2004; 141 (11):858-65.

[3] Tsuchihashi K, Ueshima K, Uchida T, Oh-mura N, Kimura K, Owa M, et al. Transient LV apical ballooning without coronary artery stenosis: a novel heart syndrome mimicking acute myocardial infarction. Angina Pectoris-Myocardial Infarction Investigations in Japan. J Am Coll Cardiol 2001; 38 (1):11-8.

[4] Abraham J, Mudd JO, Kapur NK, Klein K, Champion HC, Wittstein IS. Stress cardiomyopathy after intravenous administration of catecholamines and beta-receptor agonists. J Am Coll Cardiol. 2009; 53:1320–1325.

[5] Sharkey SW, Lesser JR, Zenovich AG, Maron MS, Lindberg J, Longe TF, et al. Acute and reversible cardiomyopathy provoked by stress in women from the United States. Circ 2005; 111 (4): 472-9.

[6] Wachsman Daniel. Takotsubo Cardiomyopathy: A Little-Known Cardiomyopathy Makes its Debut. Cardiology 2004; 102: 119-121.

[7] Prasad A, Lerman A, Rihal CS. Apical ballooning syndrome (Tako-Tsubo or stress cardiomyopathy): a mimic of acute myocardial infarction. Am Heart J 2008; 155 (3):408–17.

[8] Hanna M, Finkelhor RS, Shaw WF, Bahler RC. Extent of right and leftventricular focal wall-motion abnormalities in differentiating transient apical ballooning syndrome from apical dysfunction as a result of coronary artery disease. J Am Soc Echocardiogr 2007; 20:144–50.

[9] Parsad S. Apical ballooning syndrome: an important differential diagnosis of acute myocardial infarction. Circulation 2007; 115: e56–e59.

[10] Meimoun P, Malaquin D, Sayah S, Benali T, Luycx-Bore A, Levy F, et al. The coronary flow reserve is transiently impaired in tako-tsubo tako-tsubo cardiomyopathy: a prospective study using serial Doppler transthoracic echocardiography. J Am Soc Echocardiogr 2008; 21 (1): 72-7.

[11] Sharkey SW, Windenburg DC, Lesser JR, Maron MS, Hauser RG, Lesser JN, et al. Natural history and expansive clinical profile of stress (tako-tsubo) cardiomyopathy. J Am Coll Cardiol 2010; 55:333.

[12] Gianni M, Dentali F, Grandi AM, Sumner G, Hiralal R, Lonn E. Apical ballooning syndrome or takotsubo cardiomyopathy: A systematic review. Eur Heart J 2006; 27 (13): 1523-9.

[13] Dorfman TA, Iskandrian AE, Aqel R. An unusual manifestation of Tako-tsubo cardiomyopathy. Clin Cardiol 2008; 31: 194-200.

[14] Maroules CD, Linz NA, Boswell GE. Recurrent Takotsubo cardiomyopathy. J Cardiovasc Comput Tomogr.2009; 3: 187–189.

[15] Elesber AA, Prasad A, Lennon RJ, Wright RS, Lerman A, Rihal CS. Four-year recurrence rate and prognosis of the apical ballooning syndrome. J Am Coll Cardiol.2007;50:448–452 .

[16] Bybee KA, Murphy J, Prasad A, Wright RS, Lerman A, Rihal CS, et al. Acute impairment of regional myocardial glucose uptake in the apical ballooning (takotsubo) syndrome. J Nucl Cardiol 2006; 13: 244-50.

[17] Madias JE. Low prevalence of diabetes mellitus in patients with Takotsubo syndrome: A plausible 'protective' effect with pathophysiologic connotations. Eur H J: Acute Cardiovascular Care 2016 5: 164-170.

[18] Auzel O, Duboung O, Mansencal N. Protective Effect of Diabetes Mellitus in Takotsubo Cardiomyopathy?. Am J Cardiol 2016 (16); 30443

[19] Madias JE. What Is the Prevalence of Diabetes Mellitus in Patients With Principal and Secondary Takotsubo Syndrome? JACC Heart Fail. 2016 ; 4 (5): 417.

[20] Hassan W**,** Al-Sergani H, Al Buraiki J, Dunn B, Al Turki F, Akhras N, et al. Immediate and intermediate results of intracoronary stand-alone bolus administration of eptifibatide during coronary intervention (ICE) study. Am Heart J 2007; 154 (2): 345-51.

[21] Wittstein IS, Thiemann DR, Lima JA, Baughman KL, Schulman SP, Gerstenblith G, et al. Neurohumoral features of myocardial stunning due to sudden emotional stress. N Engl J Med. 2005; 352 (6): 359-48.

[22] Singh NK. Apical ballooning syndrome: the emerging evidence of aneurocardiogenic basis. Am Heart J 2008; 156(3): e33.

[23] Buchholz S, Rudan G. Tako-tsubo syndrome on the rise: a review of the current literature. Postgrad Med J. 2007; 83(978):261-4.

[24] Dorfman TA, Iskandrian AE. Takotsubo cardiomyopathy: State-of-the-art review. J Nucl Cardiol 2009; 16 (1): 122-34.

[25] Ostadal B, Pelouch V, Ostadalova I, Novakova O. Structural and biochemical remodelling in catecholamine-induced cardiomyopathy: comparative and ontogenetic aspects. Mol Cell Biochem 1995; 147: 83–88.

[26] Nanda AS, Feldman A, Liang CS. Acute reversal of pheochromocytoma-induced catecholamine cardiomyopathy. Clin Cardiol 1995; 18:421–423.

[27] Neil-Dwyer G, Walter P, Cruickshank JM, Doshi B, O'Gorman P. Effect of propranolol and phentolamine on myocardial necrosis after subarachnoid haemorrhage. Br Med J 1978; 2: 990–992.

[28] Ellison GM, Torella D, Karakikes I, Purushothaman S, Curcio A, Gasparri C, Indolfi C, Cable NT, Goldspink DF, Nadal-Ginard B. Acute beta-adrenergic overload produces myocyte damage through calcium leakage from the ryanodine receptor 2 but spares cardiac stem cells. J Biol Chem 2007; 282:11397–11409.

[29] Mori H, Ishikawa S, Kojima S, Hayashi J, Watanabe Y, Hoffman JI, Okino H. Increased responsiveness of left ventricular apical myocardium to adrenergic stimuli.Cardiovasc Res. 1993;27:192–198.

[30] Kassim, TA, Clarke, DD, Mai, VQ, Shakir M KM. Catecholamine-induced cardiomyopathy. Endocr Pract 2008; 14 (9):1137-49.

[31] Lenders JW, Eisenhofer G, Mannelli M, Pacak K. Phaeochromocytoma. Lancet 2005; 366 (9486): 665-75.

[32] Nef HM, Möllmann H, Kostin S, Troidl C, Voss S, Weber M, et al. Tako-Tsubo cardiomyopathy: intraindividual structural analysis in the acute phase and after functional recovery. Eur Heart J 2007; 28 (20): 2456-.64.

[33] Abe, Y, Kondo, M, Matsuoka, R, Araki M, Dohyama K, Tanio H. Assessment of clinical features in transient LV apical ballooning. J Am Coll Cardiol 2003; 41:737-42.

[34] Murugiah K, Wang Y, Desai NR, Spatz ES, Nuti SV, Dreyer RP, et al. Trends in Short- and Long-Term Outcomes for Takotsubo Cardiomyopathy Among Medicare Fee-for-Service Beneficiaries, 2007 to 2012. JCHF. 2016; 4(3): 197-205.

[35] Yoshida T, Hibino T, Kako N, Murai S, Oguri M, Kato K, et al. A pathophysiologic study of tako-tsubo cardiomyopathy with F-18 fluorodeoxyglucose positron emission tomography. Eur Heart J 2007; 28: 2598–2604.

[36] Akashi Y.J, Goldstein D.S, Barbaro G, Ueyama T. Takotsubo Cardiomyopathy. A New Form of Acute Reversible Heart Failure. Circ 2008; 118: 2754-2762.

[37] 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: 1081–1083.

[38] Kurowski, V, Kaiser, A, von Hof, K, et al. Apical and midventricular transient LV dysfunction syndrome (tako-tsubo cardiomyopathy): frequency, mechanisms, and prognosis. Chest 2007; 132: 809.

[39] Kurisu S, Inoue I, Kawagoe T, Ishihara M, Shimatani Y, Nakama Y, et al. Incidence and treatment of LV apical thrombosis in Tako-tsubo cardiomyopathy. Int J Cardiol 2011; 146(3): e58-60.

[40] Tobar R, Rotzak R, Rozenman Y. Apical thrombus associated with Takotsubo cardiomyopathy in a young woman. Echocardiography 2009; 26(5): 575-80.

[41] Yoshioka T, Hashimoto A, Tsuchihashi K, Nagao K, Kyuma M, Ooiwa H, et al. Clinical implications of midventricular obstruction and intravenous propranolol use in transient LV apical ballooning (Tako-tsubo cardiomyopathy). Am Heart J 2008; 155: 526.e1-7.

[42] Palecek T, Kuchynka P, Linhart A. Treatment of Takotsubo cardiomyopathy. Curr Pharm Des 2010; 16 (26): 2905-9.