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Iatrogenic corticosteroids induced Takotsubo cardiomyopathy

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A 65-year-old female was admitted with a suspected ST-segment elevation myocardial infarction (STEMI) following an acute onset of chest pain and dyspnea, and evidence of antero-lateral ST-segment elevation on ECG **(Figure 1)**. She was clinically in cardiogenic shock and bedside trans-thoracic echocardiogram (TTE) demonstrated a dilated left ventricle (LV) with apical ballooning, overall moderate to severe LV systolic dysfunction (LVSD), systolic anterior motion of the mitral valve (SAM) and LV outflow tract obstruction (LVOT, **Videos 1-2**).

She had a past medical history of hypertension, 5-pack year smoking history and a recent diagnosis of hypersensitivity pneumonitis, for which she had received a 3-day regime of high-dose pulsed methylprednisolone five days prior to admission as part of a clinical trial. She denied any history of physical or psychological stressor. She had a previously documented normal LV function on a TTE performed prior to the start of intravenous corticosteroids. Emergency cardiac catheterization demonstrated a wrap-around left anterior descending artery but no obvious occlusion in the coronary tree **(Figure 2)**. It also confirmed severe LVSD with apical ballooning. An intra-aortic balloon pump (IABP) was inserted and the patient was transferred to coronary care unit for supportive management, with furosemide infusion but not inotropic support as this was thought to be detrimental in view of the presence of SAM and LVOT on TTE. Routine blood tests indicated an inflammatory response and peak troponin was significantly elevated at 7992 ng/L (normal range: <16 ng/L).

Autoimmune and virology screens were normal. She subsequently experienced recurrent haemoptysis and computed tomography of the thorax showed evidence of pulmonary oedema and haemorrhage with underlying pneumonitis **(Figure 3)**. Following reviews by the Respiratory and Rheumatology teams and with cautious consideration of both risks and benefits, she was commenced on a weaning dose of oral prednisolone and over the following days, she made a gradual recovery and both frusemide infusion and IABP were discontinued. Sequential TTEs demonstrated gradually improving LV function **(Videos 3-4)** and a cardiac magnetic resonance imaging (MRI) scan showed a normal LV cavity size with severe hypokinesis of the mid anterior, anteroseptal and lateral walls and all of the apical segments with the exception of the apical inferoseptum. The apical inferoseptum and other segments retained good function resulting in an overall normal ejection fraction **(Figure 4)**.

Therefore, a diagnosis of methylprednisolone induced Takotsubo cardiomyopathy (TCM) was made, based on the very close temporal relationship between the initiation of steroid treatment and patient's acute illness, the exclusion of any other potential triggering factor, normal autoimmune and virology screens, the characteristic regional wall motion abnormalities (RWMA) on both TTE and cardiac MRI and the dramatic improvement in LV function during the admission following supportive management. She was discharged home on beta-blockers and angiotensin converting enzyme-inhibitors and remained clinically well on a subsequent follow-up appointment, when a repeat TTE confirmed normal LV function and resolution of RWMA.

TCM[1], also known as stress cardiomyopathy, apical ballooning syndrome or broken heart syndrome, most commonly occurs in post-menopausal women (1) and presents with symptoms suggestive of an acute coronary syndrome (2). Other potential presentations include Other potential complications include tachy or bradyarrhythmias, mitral regurgitation and decompensated heart failure even resulting in cardiogenic shock

(3). TCM is more often characterized by transient left apical wall abnormalities both on echocardiogram and left ventriculography (4) and is classically preceded by an emotional (bereavement, divorce) (5) or physiological (surgery, chemotherapy) (6) stressor, although no specific trigger can be identified in up to one-third of cases (7). Different theories have been proposed regarding potential underlying etiology and mechanisms of TCM and one of the most accredited of these postulates the critical role of increased levels of catecholamines secondary to physical or psychological stressors and causing acute and transient myocardial toxicity in TCM patients (8,9). However, normal catecholamine concentrations were found in a small cohort of patients in a more recent study. More recently, the relatively high incidence of TCM in patients with subarachnoid hemorrage, epilepsy, electroconvulsive therapy, head injury, stroke, anxiety and depression has led to the concept of a neurogenic origin of the coronary microcirculation dysfunction responsible for myocardial stunning in TCM (1). Overall, such etiological factors result in increased sympathoneural activity, catecholamine-mediated coronary spasm, direct catecholamine-mediated cardiomyocite dysfunction, microvascular dysfunction and myocardial stunning (8), ultimately leading to depressed contractile function of the mid and apical walls of the LV with sparing of the basal segments, thereby producing the characteristic appearance of the LV. Crucially, regional wall motions abnormalities are typically not in a single coronary distribution. Other variants have been described, for example with involvement of the base and sparing of the apex (inverted or reverse TCM) or with global hypokinesis (10).

Treatment of TCM is conservative and involves supportive measure including heart failure management with beta-blockers and/or ACE-I, inotropes if cardiogenic shock is present, more rarely LV mechanical support, anticoagulation when LV thrombus is identified, and treatment of arrhythmias (11). The prognosis is favourable with full resolution of apical wall motion abnormalities in the majority of patients although mortality has been reported in up to 8% of patients (12). Recurrence rate is approximately 2-10%. Recurrence has been seen in 2-10% of subjects (12).

To our knowledge, this is the first documented case of corticosteroid induced TCM: it is possible that, in the absence of any other precipitating factor, the recent administration of high-dose intravenous methylprednisolone might have mimicked a stress response with subsequent acute LV failure and reversible apical cardiomyopathy. Additionally, while STEMI is a relatively common clinical presentation, it is also crucial to remain mindful of other potential causes of acute chest pain and dyspnea associated with ST-elevation, troponin level rise and clinical evidence of LV failure. Furthermore, this case illustrates the importance of a multi-disciplinary approach in similarly complex case, leading to successful management of an acutely ill patient.

Figure Legends

Figure 1. ECG: evidence of antero-lateral ST-segment elevation

Figure 2. Coronary angiogram: wrap-around left anterior descending artery but no obvious occlusion in the coronary tree

Figure 3. Computed tomography of the thorax: evidence of pulmonary oedema and haemorrhage with underlying pneumonitis

Figure 4. Cardiac MRI: severe hypokinesis/akinesis of the mid anterior, anteroseptal and lateral walls and all of the apical segments, with the exception of the apical inferoseptum

References

1. Templin C, Ghadri JR, Diekmann J et al. Clinical Features and Outcomes of Takotsubo (Stress) Cardiomyopathy. N Engl J Med 2015;373:929-38.
2. Syed IS, Prasad A, Oh JK et al. Apical ballooning syndrome or aborted acute myocardial infarction? Insights from cardiovascular magnetic resonance imaging. Int J Cardiovasc Imaging 2008;24:875-82.
3. Sharkey SW, Lesser JR, Zenovich AG et al. Acute and reversible cardiomyopathy provoked by stress in women from the United States. Circulation 2005;111:472-9.
4. Medeiros K, O'Connor MJ, Baicu CF et al. Systolic and diastolic mechanics in stress cardiomyopathy. Circulation 2014;129:1659-67.
5. Brandspiegel HZ, Marinchak RA, Rials SJ, Kowey PR. A broken heart. Circulation 1998;98:1349.
6. Sharkey SW, Windenburg DC, Lesser JR et al. Natural history and expansive clinical profile of stress (tako-tsubo) cardiomyopathy. J Am Coll Cardiol 2010;55:333-41.
7. Tsuchihashi K, Ueshima K, Uchida T et al. Transient left ventricular 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;38:11-8.
8. Wittstein IS, Thiemann DR, Lima JA et al. Neurohumoral features of myocardial stunning due to sudden emotional stress. N Engl J Med 2005;352:539-48.
9. Kyuma M, Tsuchihashi K, Shinshi Y et al. Effect of intravenous propranolol on left ventricular apical ballooning without coronary artery stenosis (ampulla cardiomyopathy): three cases. Circ J 2002;66:1181-4.
10. Eitel I, von Knobelsdorff-Brenkenhoff F, Bernhardt P et al. Clinical characteristics and cardiovascular magnetic resonance findings in stress (takotsubo) cardiomyopathy. JAMA 2011;306:277-86.
11. Villareal RP, Achari A, Wilansky S, Wilson JM. Anteroapical stunning and left ventricular outflow tract obstruction. Mayo Clin Proc 2001;76:79-83.
12. 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;50:448-52.

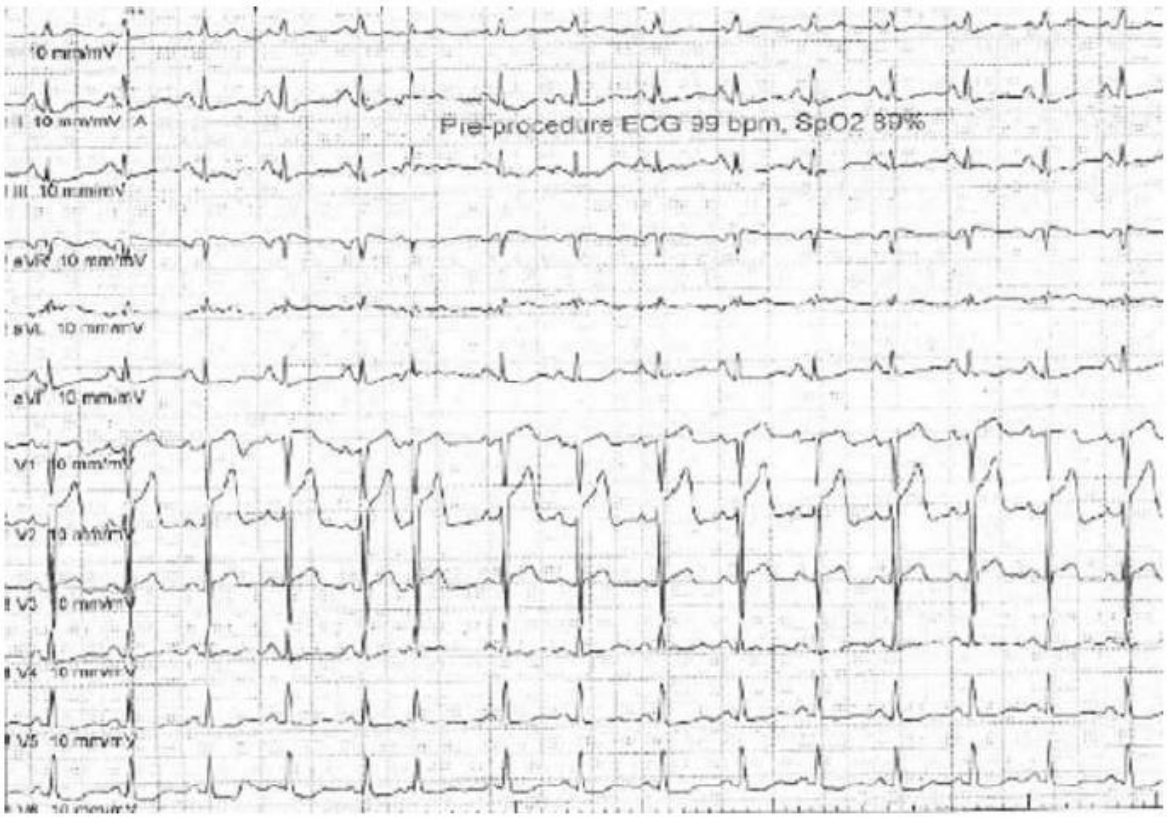

Figure 1

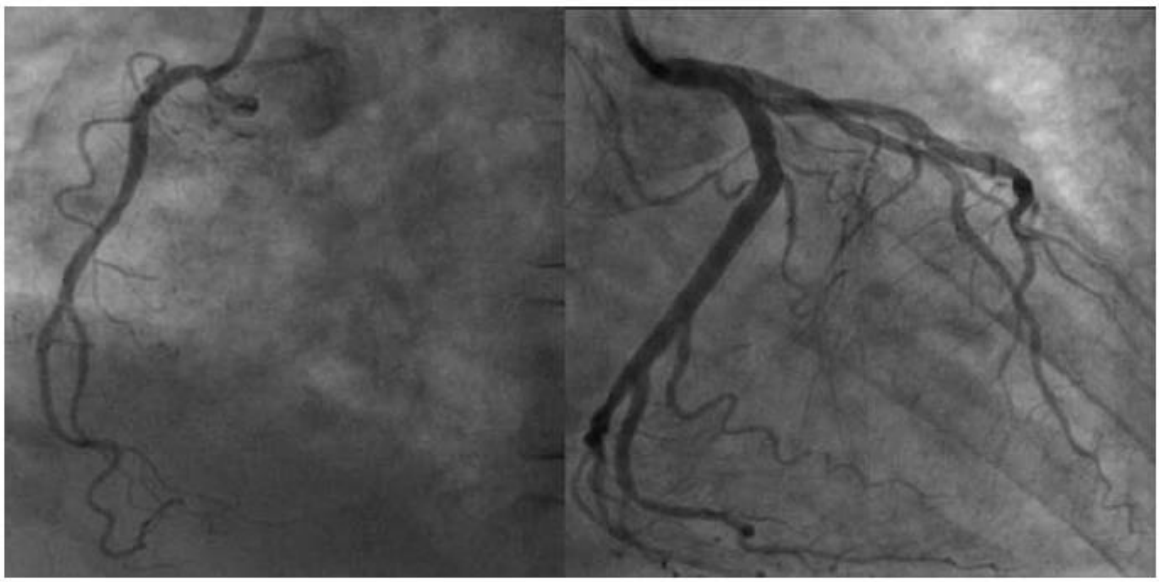

Figure 2

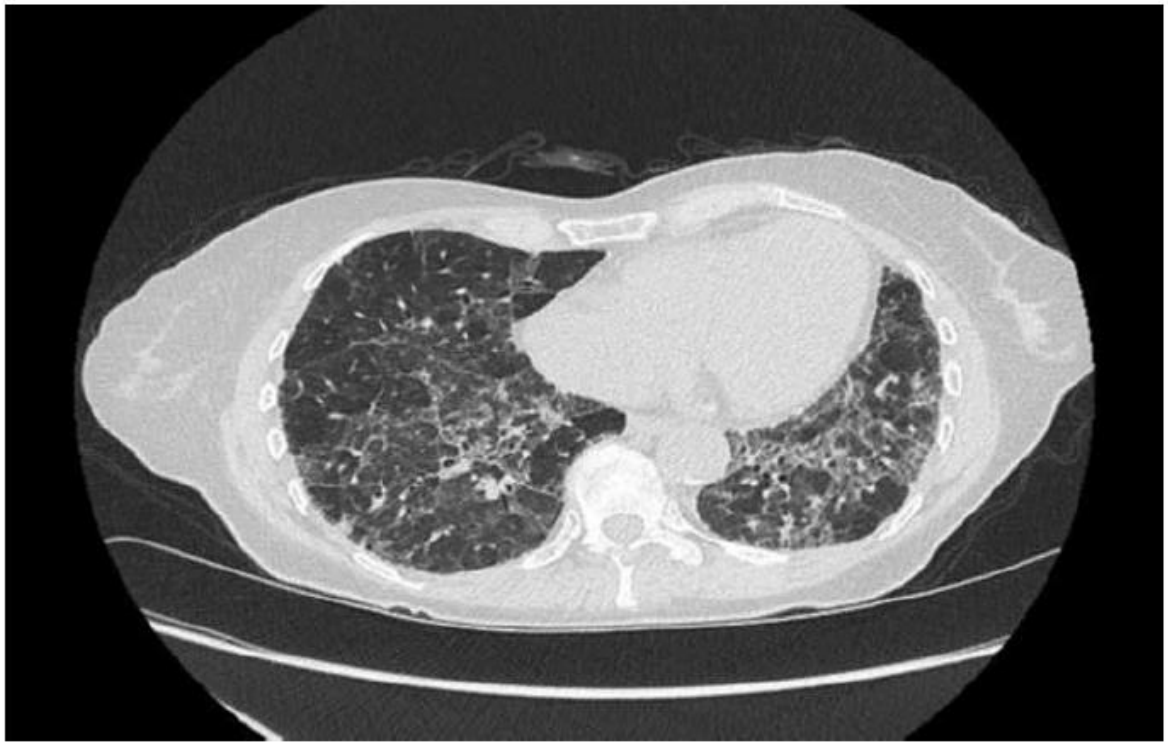

Figure 3

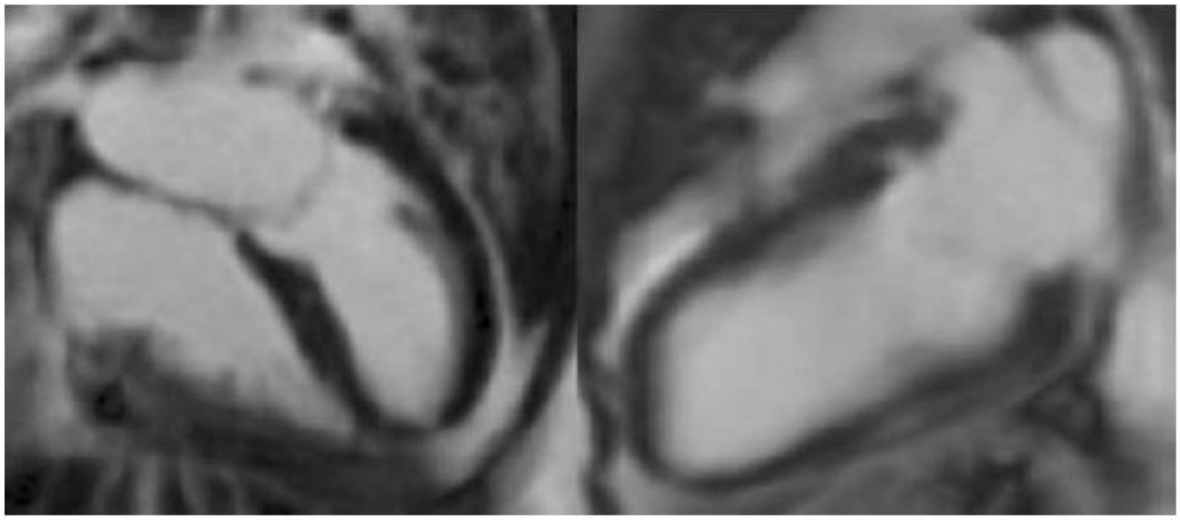

Figure 4

Highlights

- A case of Iatrogenic corticosteroids induced Takotsubo cardiomyopathy is proposed
- Takotsubo cardiomyopathy is characterized in the vast majority of cases by transient left apical wall abnormalities and is classically preceded by an emotional or physiological stressor
- No specific trigger can be identified in up to one-third of cases of Takotsubo cardiomyopathy
- The role of a multi-disciplinary approach is crucial in the successful management of complex cases in which no clear precipitating factor can be promptly identified and a careful evaluation of potential risks and benefits of intended treatment is required.