Case of takotsubo cardiomyopathy in a patient with COPD

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Takotsubo cardiomyopathy (TCM) is a transient, reversible form of acute left ventricular (LV) dysfunction often presenting as acute myocardial infarction (AMI). It accounts for approximately 1.7 to 2.2% of all suspected cases of AMI more frequently seen in females between 59–72 years of age.1,2 It is believed that the LV dysfunction is caused by a surge in catecholamine levels, precipitated by one, or a combination of, acute emotional/physical stressors, iatrogenic stressors, neurologic triggers, or pre-existing cardiovascular factors and endothelial dysfunction.1 We describe a case where TCM developed acutely during hospitalisation for COPD exacerbation.

Case presentation
A 62-year-old woman with a history of long-standing COPD (on inhalers), hypertension, hypothyroidism, smoking, and essential tremor, presented with acute respiratory distress. On presentation, she was febrile, tachypneic and hypoxemic with an oxygen saturation of 91% on room air. Her blood pressure was 220/85 mmHg with a pulse rate was 126 beats per minute (bpm). She displayed bilateral expiratory wheezing, with decreased air movement. Cardiovascular examination was unremarkable.

Electrocardiogram (ECG) showed sinus tachycardia at 103 bpm (Figure 1), with no evidence of ischemia. Initial chest radiograph showed hyperinflation without consolidation. She was started on bilevel positive airway pressure (BiPAP) and 6 hourly nebulised albuterol sulfate and ipratropium bromide, as well as high dose oral corticosteroids. Troponin-I (TN-I) level of 0.279 ng/mL was obtained with a CK-MB of 5.6 ng/mL and N-terminal pro b-type Natriuretic Peptide (NT-proBNP) was 599 pg/mL. A two-dimensional (2D) transthoracic echocardiogram (TTE) (Figure 2) showed an ejection fraction (EF) of 65%, with no regional wall abnormalities.

ECG on day 2 showed atrial fibrillation with rapid ventricular response (160–180 bpm), converted back to normal sinus rhythm using amiodarone. She denied any palpitations, light-headedness, dizziness or chest pain during the episode. The TN-I peaked at 0.5 ng/mL on day 4, prompting cardiac catheterisation. No significant obstruction of epicardial coronary vessels was noted on selective coronary angiography (Figure 3); however, left ventriculogram (Figure 3C) revealed apical ballooning suggestive of TCM, with a mildly reduced EF of 45%. In view of her down trending cardiac biomarkers and improvement in her symptoms, she was discharged on aspirin, advised to be cognisant of her inhaler use, and close follow-up.

Discussion
Recent case reports have identified COPD exacerbation as a possible physical stressor triggering TCM. It has been hypothesised that excessive beta-2 adrenergic receptor (ADRB2) agonist use can trigger TCM in an already distressed patient with COPD exacerbation.3–6 Interestingly, Rajwani and Hall proposed a new subtype of TCM, ‘Bronchogenic Stress Cardiomyopathy’.4

Generally, the sympathetic nervous system works to have a positive inotropic effect on the myocardium mediated by norepinephrine and epinephrine predominantly via beta-1 adrenergic receptors. Epinephrine has a higher affinity for ADRB2s, and at physiological levels contribute to the positive inotropic effect on the heart. In experimental models, high
**Figure 1:** ECG on admission. Sinus tachycardia at 103 bpm, no evidence of ischemic changes.

**Figure 2:** 2D TTE on day 2 of hospital admission. Apical 4-chamber view showing normal LV function on diastole (A) and systole (B).

**Figure 3:** Cardiac catheterisation with selective angiography (A, B) and left ventriculogram (C) on day 4 of hospital admission. No significant obstruction in the right (A) and left (B) coronary systems. Left ventriculogram showing apical ballooning during systole and mildly reduced LV function.
levels of epinephrine can paradoxically have a negative inotropic effect on the myocardium mediated via ADRB2s. This epinephrine “biased agonism” is thought to be cardio-protective against the apoptotic effects on myocytes due to excessive simulation of ADRB2s. The apex of the heart has a higher concentration ADRB2s than the base, which might help to explain the unbalanced LV dysfunction in TCM, especially the apical ballooning. This is clinically important because ADRB2 agonists are part of the standard or care of COPD, and at high doses they might mimic the effect of high levels of epinephrine on the myocardial tissue contributing to LV dysfunction.

Our patient had not been using her albuterol inhaler at home for a year until 2 days prior to presentation. In the hospital, she received nebulised albuterol sulfate/ipratropium bromide solution every 4 hours on presentation with COPD exacerbation prior to cardiac catheterisation. She was also treated with a long-acting ADRB2 agonist, formoterol daily, along with tiotropium bromide and steroid therapy. High levels of ADRB2 agonists to treat COPD superimposed on the increased sympathetic nervous system activity secondary to hypercapnia and hypoxaemia contributed to the TCM in this patient.

TCM should be considered in patients presenting with COPD exacerbation, abnormal cardiac biomarkers, and continuing chest pain. Its recognition can alter a patient’s medical therapy and follow-up. Due to akinetic segments of the ventricles, up to 5% of TCM patients can develop ventricular thrombi, leaving them susceptible to embolic events, especially in the setting of poor ambulation and acutely sick state. Upon discharge, these patients require close follow-up, with repeat TTE and ECG evaluation. Beta-blockers and ACE inhibitors for LV systolic dysfunction may also be considered, however it is unclear what the cardio-protective effects in this subset are due to lack of data. In fact, there have been cases of recurrent TCM in patients on beta-blocker therapy. Additionally, a multidisciplinary approach may be required when addressing ARDB2 agonist inhaler and/or cardio-selective beta-blocker use in such patients as the pathogenesis of TCM is still not well understood.

**Competing interests:**
Nil

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