Recurrent, severe, and rapidly reversible apical ballooning syndrome in status asthmaticus

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Apical ballooning syndrome, or Tako-tsubo cardiomyopathy, is a peculiar form of transient left-ventricular dysfunction originally described as triggered by emotional stress. Subsequent reports indicated that physical stressors can also induce this clinical syndrome. We describe for the first time, to the best of our knowledge, a case of recurrent, severe, and quickly reversible apical ballooning syndrome provoked by the use of high-dose inhaled β-adrenergic agonists in status asthmaticus. (Heart Lung® 2010;39:537–539.)

Apical ballooning syndrome, or Tako-tsubo cardiomyopathy, is a reversible form of left-ventricular dysfunction triggered by acute emotional or physical stress. The clinical presentation is usually that of an acute coronary syndrome characterized by chest pain, shortness of breath, electrocardiographic ST-segment elevation or ST-segment depression, and elevated cardiac serum markers.[1,2] The coronary angiogram is generally normal. Imaging studies typically reveal severe regional wall-motion abnormalities, most often with a characteristic anteroseptal and apical akinesis or dyskinesis, with systolic ballooning of the left-ventricular apex. Despite the sometimes dramatic acute clinical presentation, hospital mortality is low, and the long-term prognosis is excellent.

We describe a patient who presented with 2 separate episodes of apical ballooning syndrome within a 6-month period, both triggered by status asthmaticus treated with continuous nebulized adrenergic agonists. On each occasion, the clinical picture suggested ST-segment elevation myocardial infarction with pulmonary edema, but the coronary angiograms were normal, and the severe left-ventricular dysfunction and apical ballooning completely resolved within days.

CASE REPORT

A 66-year-old African-American woman with a long history of poorly controlled chronic obstructive pulmonary disease (COPD) presented with an acute onset of shortness of breath. Her medical history included hypertension, breast cancer, and pulmonary embolism. She also had a long history of heavy tobacco abuse. Pulmonary-function testing had been attempted twice, but because of poor patient cooperation, these tests were not successful. The severity of her COPD, however, was evident, based on her need for 11 hospitalizations because of COPD exacerbations over a 2-year period. On previous admissions, she was treated with nebulizers, intravenous corticosteroids, and antibiotics. On most occasions, she required noninvasive or invasive ventilation support.

During the present hospitalization, she reported a repeated, almost continuous use of β-agonist inhalers at home, without relief. Upon arrival, she was in severe respiratory distress, characterized by tachypnea with increased work of breathing, poor air movement, and an arterial oxygen saturation of 78%. A chest x-ray showed hyperexpanded, hyperinflated lungs, with no focal infiltrate. Treatment was initiated with continuous nebulized β-adrenergic agonists, intravenous steroids, and noninvasive ventilation. Later, while still in the emergency department, she complained of severe substernal

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chest pain, and developed symptoms consistent with cardiogenic shock. An electrocardiogram (ECG) revealed abnormal Q-waves and ST-segment elevation in leads V_1 to V_4 (Fig 1A). Her initial troponin level was normal, but subsequent troponin and creatine kinase MB fraction (CK-MB) levels were mildly elevated. Emergent cardiac catheterization indicated patent coronary arteries, a large area of apical dyskinesis, and severely depressed left-ventricular function, with an estimated ejection fraction of 15% (Fig 1B). The patient was treated supportively. A second ECG the next day demonstrated a resolution of the Q-waves in leads V_3 and V_4 and a new, giant, near-global T-wave inversion, with marked prolongation of the QT interval (Fig 1C). All symptoms of acute coronary syndrome and cardiogenic shock resolved within 36 hours. An echocardiogram performed 2 days after the initial presentation was completely normal, with an estimated ejection fraction of 60% to 65%.

Almost exactly 6 months after the first episode, the patient again presented with status asthmaticus. After treatment with continuous nebulized β-adrenergic agonists, she again developed acute chest pain, pulmonary edema, and ST-segment elevation in the anteroseptal leads. Once more, she underwent emergent cardiac catheterization, which revealed patent coronary arteries and severe apical ballooning. The clinical symptoms resolved within 2 days, and another echocardiogram 5 days later was normal.

DISCUSSION

Beta-adrenergic agonists are the mainstay of treatment in patients with obstructive lung disease who present with an acute exacerbation. The desired potent bronchodilatory effects, however, may be associated with adverse events in the cardiovascular system. In the short term, an increased heart rate and decreased serum potassium concentrations are well-documented.[3] The long-term use of β-adrenergic agonists is also associated with cardiac arrhythmias, congestive heart failure, myocardial ischemia, and even sudden cardiac death.[3] These cardiovascular risks appear to be dose-dependent.[4] Cardiovascular events are more prevalent in patients with a previous cardiac history.[5]

Apical ballooning syndrome, or Tako-tsubo cardiomyopathy, is a unique form of stress-induced cardiomyopathy originally described in postmenopausal Asian women after severe emotional stress. These patients usually present with symptoms consistent with an acute coronary syndrome, sometimes associated with pulmonary edema and even overt cardiogenic shock.[1,2] The left ventricle's appearance in an echocardiogram or contrast ventriculogram is characterized by midventricular and distal ventricular akinesis-dyskinesis with preserved basal function, and end-systolic images present a characteristic apical ballooning pattern (Fig 1B). The initial ECG frequently mimics an acute ST-elevation myocardial infarction (STEMI), with or without abnormal Q-waves (Fig 1A).[1,2,6] Levels of cardiac serum markers are elevated, but to a lesser degree than typically observed with a STEMI. Although major complications, including ventricular rupture and death, have been reported,[7] in the majority of cases, rapid clinical recovery and a normalization of ventricular function occur. In ECGs, the STEMI pattern progresses to a pattern of large, global T-wave inversion, with marked prolongation of the QT interval (Fig 1C), and slow and gradual normalization.

The exact causes and mechanisms of Tako-tsubo cardiomyopathy are unknown. The prevailing hypothesis contends that exaggerated sympathetic stimulation is central to the cause of apical ballooning.[8] In addition to postmenopausal Asian women, the apical ballooning syndrome has been described in all age groups and ethnicities. Moreover, several case reports and case series demonstrated that not only emotional stress, but other adrenergic stressors, including subarachnoid hemorrhage,[9] intravenous administration of catecholamines and β-receptor agonists,[10] and even dobutamine stress testing,[10,11] may induce apical ballooning syndrome.

We are aware of 2 previous case reports describing stress-induced cardiomyopathy in status asthmaticus.[12,13] In both cases, the patients were treated with high-dose β-adrenergic agonists. Our case provides the first documentation of a recurrence of Tako-tsubo cardiomyopathy on 2 separate occasions in a patient with COPD exacerbations. We think that the use of continuous high-dose adrenergic agonists, rather than the emotional stress of status asthmaticus, was primarily responsible for the described dramatic cardiovascular presentation. On both occasions, the prehospital use of high-dose adrenergic inhalers was followed by the use of continuous nebulized β-adrenergic agonists upon hospital presentation, whereas the other 10 hospitalizations for similar COPD exacerbations were not associated with apical ballooning syndrome, and the use of a high-dose adrenergic agonist was not reported.

Our case report should raise awareness of the fact that some patients are uniquely sensitive to the cardiovascular effects of high-dose adrenergic agonists.

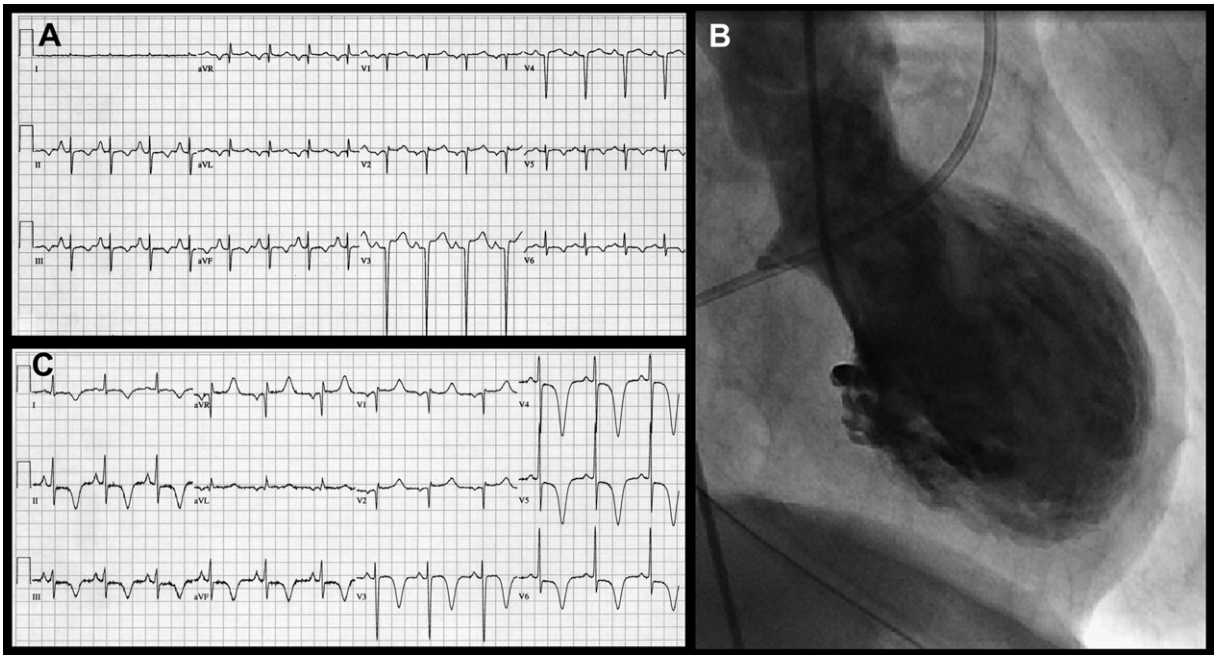

Fig 1 A, Electrocardiogram on presentation shows sinus tachycardia with QS complexes and ST-segment elevation in leads V_1 to V_4, consistent with acute anteroseptal myocardial infarction. **B,** Left-ventricular angiogram, with end-systolic image in right anterior oblique view, demonstrates appropriate systolic function of ''neck'' of left ventricle only, and a large area of apical ballooning. **C,** Electrocardiogram on hospital day 2 shows not only resolution of both QS complexes and ST-segment elevation, but the development of large, global T-wave inversion with markedly prolonged QT intervals.

Those patients who have already experienced an iatrogenic cardiovascular event may be at increased risk for a recurrence of such events. These patients require special clinical vigilance and extreme caution when dosing adrenergic agonists.

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