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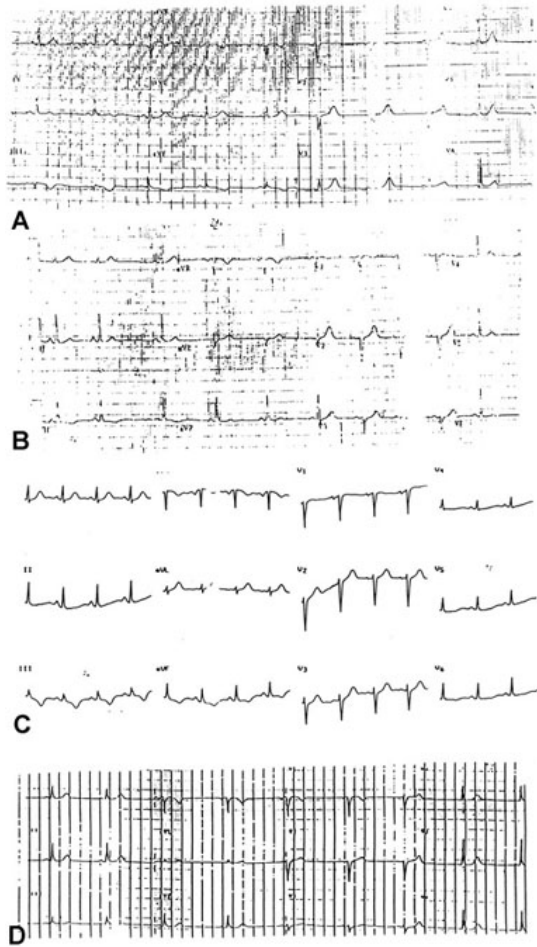
Coronary and laryngeal spasm provoked by methacholine inhalation

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To the Editor:

A 34-year-old flight attendant was referred for evaluation of possible allergy to bleaching powder. She described a 12-month history of symptoms of wheezing, light-headedness, nausea, and dysphonia and an anaphylactic reaction on smelling chlorine and other strong odors of cleaning solutions in the aircraft. For these symptoms, she had numerous admissions to hospital emergency departments and had received treatment for anaphylaxis and asthma with subcutaneous and intravenous adrenaline, corticosteroids, and bronchodilators. However, objective evidence of variable or reversible airflow limitation was never established. Two months earlier, she had had similar symptoms during a contrast-enhanced computed tomography scan of her abdomen to investigate a possible loin mass. On the basis of her previous history of anaphylaxis, she was given intravenous epinephrine and corticosteroids, shortly after which she experienced central chest tightness and nausea. Her electrocardiogram (ECG) (Fig 1, A) showed T-wave inversion in the inferior limb leads. Her troponin (15 ng/mL) and creatine kinase (284 IU; MB isoenzyme fraction, 42%) levels were raised. Findings of a coronary angiogram, a technetium Tc 99m sestamibi exercise perfusion scan, and an echocardiogram 5 days later were normal. Her chest radiograph and blood autoantibody profile findings were normal. She had regular symptoms of heartburn, acid regurgitation, and arthralgia and was taking levothyroxine for hypothyroidism. She had never smoked.

Fig. 1. A, ECG showing T-wave inversion in leads III and aVF following the administration of intravenous epinephrine, associated with central chest pain and raised troponin. **B,** Normal ECG 5 days after the episode of chest pain. **C,** ECG showing T-wave inversion in leads III and aVF following the inhalation of methacholine (16 mg/mL). **D,** Normal ECG 2 weeks after the methacholine inhalation test.

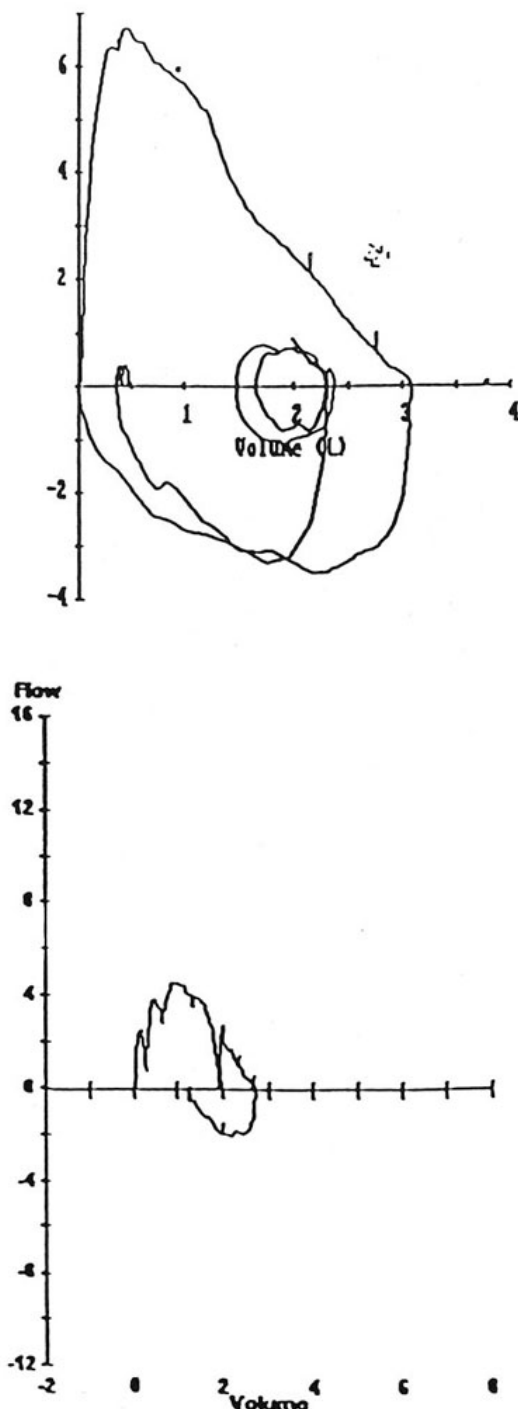


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We considered her symptoms to be consistent with laryngeal dysfunction (confirmed by direct laryngoscopy), hyperventilation, and gastroesophageal reflux. She was nonatopic (negative allergy skin prick test result and normal total serum IgE level) and had normal spirometry findings, ECG (Fig 1, B) findings, and cell counts in induced sputum. A methacholine inhalation test was performed by the tidal breathing method.¹ Immediately after inhalation of methacholine 16 mg/mL, she lost her voice and had central chest pain and sweating. The maximal inspiratory flow-volume curve (Fig 2) showed a variable extrathoracic obstructive pattern consistent with laryngeal dysfunction. Her ECG showed T-wave inversion in the inferior leads (Fig 1, C). Her end-tidal P_{CO_2} was 39 mm Hg. Cardiac

enzyme levels were not raised, and the pain was relieved with sublingual nitroglycerine. The PC₂₀ (provocative concentration of agonist producing a 20% fall in FEV₁) methacholine was 12 mg/mL, indicating borderline normal airway responsiveness. She was later assessed by a cardiologist, who confirmed the diagnosis of syndrome X and prescribed diltiazem, aspirin, and omeprazole. She has been told that she does not have asthma or allergies and is currently undergoing voice therapy and psychiatric counseling. An ECG repeated 2 weeks later showed normal findings (Fig 1, D).

Fig. 2. Flow volume curves before and after inhalation of 16 mg/mL concentration of methacholine showing flow limitation during maximal inspiratory effort.



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This is the first report of angina and coronary spasm after methacholine inhalation. The case also illustrates the use of the methacholine inhalation test to identify laryngeal dysfunction as a cause of asthmalike symptoms. The methacholine inhalation test is generally a safe procedure without any serious adverse effects.² Although subcutaneous administration of methacholine has been reported to cause angina in patients with Prinzmetal's variant angina pectoris,³ this has not been reported after a bronchial provocation test. We can only speculate on the mechanism of angina in our patient, who had a coronary-prone behavior pattern, possible syndrome X, epinephrine-induced myocardial necrosis,⁴ and gastroesophageal reflux.⁵ Chest pain relieved with nitroglycerine and associated with reversible ischemic changes in the ECG and normal coronary artery anatomy suggests coronary vasospasm as the cause of chest pain.

The role of laryngeal dysfunction in provoking angina is less clear. However, in this patient the recognition of the disorder during a methacholine inhalation test was important in counseling the patient that she did not have asthma. A proper evaluation of her spirometry on her numerous previous admissions may have detected this, and an earlier diagnosis may have prevented her from getting multiple injections of epinephrine and experiencing myocardial necrosis. Laryngeal dysfunction is a common cause of pseudoasthma⁶; however, the prevalence of the condition in suspected occupational asthma is not known.

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