Cough Reflex by Ventricular Premature Contractions

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SUMMARY

A 72-year-old man was referred for further assessment of a chronic cough. He noticed an association between the episodes of coughing and palpitations. Electrocardiography (ECG) revealed normal sinus rhythm and sporadic unifocal ventricular premature contractions (VPCs). Each cough was preceded by a premature beat. Continuous wave Doppler echocardiography revealed a VPC-induced transient increase in the pulmonary artery blood flow. He was successfully treated for VPCs with oral disopyramide, resulting in subsidence of both the coughing and palpitations. We suspect that the VPC-induced hemodynamic changes in the pulmonary circulation might be responsible for coughing in our patient. Premature contractions should be considered as a possible cause of chronic dry cough in the clinical setting. (Int Heart J 2005; 46: 923-926)

Key words: Bowditch effect, Cough, Doppler echocardiography, Ventricular premature contraction

There are various causes of chronic coughing.1) Odeh and Oliven were the first to report an association between atrial premature contractions and coughs.2) However, the underlying mechanisms as to why premature contractions cause cough reflex have not been elucidated. We present a case with cough reflex associated with ventricular premature contractions along with a possible explanation for the relationship between the two pathophysiological phenomena.

CASE REPORT

A 72-year-old man was referred by his family physician in April 2004 to our outpatient clinic for further assessment of a cough that had continued for 3 months. The cough was dry and sporadic over a 24 hour period. He noticed that the cough was associated with palpitations and that the episodes of coughing and palpitations increased and decreased simultaneously. Physical examination was normal except for skipped heart beats. There were no other symptoms and signs

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related to causative diseases of the chronic cough such as bronchial asthma, gastroesophageal reflux, and postnasal drip. Data on blood chemistry were all within normal limits. A chest roentgenogram was normal. Electrocardiography (ECG) revealed sinus rhythm and infrequent unifocal ventricular premature contractions (VPCs). Each cough, evidenced by artifacts on ECG, was preceded by a
premature beat (Figure 1). Holter ECG monitor recording was conducted and the patient kept a diary. The frequent occurrence of VPCs was associated with repetitive coughing. The results of treadmill exercise testing were negative. Two-dimensional color echocardiography was normal except for a VPC-induced trivial regurgitant flow to the left atrium. Continuous wave Doppler echocardiography revealed a VPC-induced transient increase in the calculated pulmonary artery blood flow, from 65 mL/sec to 91 mL/sec (Figure 2). Initially, he was treated for VPCs with mexiletine at 100 mg three times daily. However, he continued to complain of coughing and palpitations. He was successfully treated for VPCs with disopyramide at 150 mg twice daily, resulting in subsidence of both the coughing and palpitations. He was ultimately diagnosed as having chronic cough due to VPCs.

**DISCUSSION**

Mexiletine was selected as the first line of treatment for the VPCs since it has been reported that a single oral dose of mexiletine can reduce tussive agent-induced cough reflex. However, mexiletine failed to reduce the frequency of VPCs, with no subsidence of the coughing. This suggests that the cough remedy may have been ineffective for suppressing the cough in our patient. Examination of the time sequence of the noise provoked by coughing revealed that the cough occurred immediately after a post-extrasystolic beat (Figure 1). Thus, it is probable that the cough was due not to VPC itself, but to a high stroke volume resulting from the post-extrasystolic potentiation (Bowditch effect), which might be the case also in atrial premature beats, as reported previously. Moreover, since the VPC-induced mitral regurgitant flow was trivial, it is unlikely that VPC-induced changes in the left atrium triggered the coughs. It is tempting to speculate on the underlying mechanisms associated with the premature beats and coughs. One possible mechanism of the cough, secondary to the premature atrial or ventricular beats, is stretching of the pulmonary arteries. Cough is considered to be exclusively mediated via the vagus nerves. It is well known that various organs such as the larynx, trachea, bronchi, and lower esophagus are responsible for a vagus-mediated cough reflex via cough receptors. Coleridge and Kidd have demonstrated that the vagus receptors exist in the vicinity of the main bifurcation of the pulmonary artery in anesthetized dogs. Furthermore, Moore, et al demonstrated that cervical vagal afferent fibers respond with an increase in discharge to a large step increase in pulmonary artery pressure in anesthetized dogs. Thus, stimulation of the pulmonary artery may provoke a cough reflex. Indeed, it has been reported that not low-osmolality but conventional contrast agents frequently produce coughing during pulmonary arteriography. In our patient, Doppler
echocardiography revealed a transient increase in the pulmonary artery flow velocity in a post-extrasystolic beat. Based on these observations, we suspect that the VPC-induced hemodynamic changes in the pulmonary circulation might have elicited coughing in our patient.

As coughing may be the presenting symptom of undiagnosed atrial or ventricular premature beats, a diagnosis should be followed by focusing on the timing of the occurrence of premature beats and coughing in the ECG recording.

REFERENCES