A Midsystolic Ejection Click

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A patient of faintly marfanoid habitus with left ventricular failure, aortic regurgitation, and rate-related left bundle-branch block was found to have a midsystolic click and echocardiographic findings suggestive of mitral valve prolapse; however, the click did not move earlier in systole in response to head-up tilt or atrial pacing. Cardiac catheterization and angiocardiographic studies revealed severe left ventricular dysfunction out of proportion to the moderate amount of aortic regurgitation observed on aortographic study. Mitral valve prolapse was not confirmed by left ventriculographic study. Intracardiac phonocardiographic and catheter-tip manometric studies identified the click as being aortic in origin, ejection in timing, and midsystolic, rather than early systolic, because of delayed aortic valve opening related to left ventricular dysfunction and delay in conduction.

Midsystolic and late systolic clicks are most often caused by mitral valve prolapse.1-3 Early systolic clicks most commonly are associated with pathologic abnormalities in the semilunar valves or great vessels and are often termed "ejection clicks" because of their coincidence in time with aortic or pulmonic valve opening and the beginning of ventricular ejection.4-6 Although instance where mitral valve prolapse is associated with an early systolic click, rather than a midsystolic or late systolic click, are not uncommon, the ejection click is expected to be relatively close to the first sound in all cases where it is audible, since semilunar valve opening is separated from ativoventricular valve closure only by the time of isovolumetric contraction.7

The patient described herein had a murmur of aortic regurgitation and a midsystolic click originally thought to be of mitral valve origin; however, subsequent investigation revealed this transient to be a delayed aortic valve ejection click.

CASE REPORT

A 37-year-old woman with a history of left ventricular failure since 1967 was admitted to Cook County Hospital, Chicago, in April 1978, with recent worsening of symptoms. There was no history of acute rheumatic fever or chorea. The patient was known to have a murmur of aortic regurgitation since adolescence; cardiac catheterization in 1971 showed normal pressures and cardiac output at rest. Left ventricular end-systolic and end-diastolic volumes were 77 ml and 148 ml, respectively, with an ejection fraction of 0.5. Retrograde ascending aortograms and left ventriculograms confirmed

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PHOTOGRAPHS

Figure 1. Carotid pressure systemic arterial pressure. A: Control. B: Overload. LV = left ventricle; aortic root regurgitation at baseline.

Figure 2. Pressure gradients across the mitral valve in the midsystolic period. A: Control. B: Overload. LV = left ventricle; aortic root regurgitation at baseline.

Figure 3. Aortic regurgitation over time in the midsystolic period. A: Control. B: Overload. LV = left ventricle; aortic root regurgitation at baseline.

Figure 4. Right atrial pressure changes in the midsystolic period. A: Control. B: Overload. LV = left ventricle; aortic root regurgitation at baseline.

Figure 5. Left ventricular ejection fraction in the midsystolic period. A: Control. B: Overload. LV = left ventricle; aortic root regurgitation at baseline.

Figure 6. Left ventricular volume changes in the midsystolic period. A: Control. B: Overload. LV = left ventricle; aortic root regurgitation at baseline.

Figure 7. Left ventricular dimension changes in the midsystolic period. A: Control. B: Overload. LV = left ventricle; aortic root regurgitation at baseline.

Figure 8. Right ventricular dimension changes in the midsystolic period. A: Control. B: Overload. LV = left ventricle; aortic root regurgitation at baseline.

Figure 9. Right ventricular dimension changes in the midsystolic period. A: Control. B: Overload. LV = left ventricle; aortic root regurgitation at baseline.

Figure 10. Right ventricular dimension changes in the midsystolic period. A: Control. B: Overload. LV = left ventricle; aortic root regurgitation at baseline.

Figure 11. Right ventricular dimension changes in the midsystolic period. A: Control. B: Overload. LV = left ventricle; aortic root regurgitation at baseline.

Figure 12. Right ventricular dimension changes in the midsystolic period. A: Control. B: Overload. LV = left ventricle; aortic root regurgitation at baseline.

Figure 13. Right ventricular dimension changes in the midsystolic period. A: Control. B: Overload. LV = left ventricle; aortic root regurgitation at baseline.

Figure 14. Right ventricular dimension changes in the midsystolic period. A: Control. B: Overload. LV = left ventricle; aortic root regurgitation at baseline.

Figure 15. Right ventricular dimension changes in the midsystolic period. A: Control. B: Overload. LV = left ventricle; aortic root regurgitation at baseline.
mild to moderate aortic valvular insufficiency and were suggestive but not diagnostic of mitral valve prolapse. Three aortic sinuses of approximately equal size were identified, and the ascending aorta was not dilated.

Physical examination revealed a thin (height, 157 cm [5 ft 2 in]; weight, 44 kg [97 lb]) black woman with slight arachnodactyly but no features diagnostic of Marfan’s syndrome. Her blood pressure was 135/72 mm Hg, and her pulse rate was 86 beats per minute and regular. There was no clubbing, cyanosis, or venous distention in the neck. The venous pulsations were normal, while the arterial pulses were moderately hyperactive. The first heart sound was moderately diminished in intensity, while the second heart sound was somewhat increased and single. A prominent third heart sound was audible at the apex, and a medium to high frequency middiastolic click was heard throughout the precordium and was loudest at the left sternal border. A long grade 3/6 early diastolic blowing decrescendo murmur was heard at the left sternal border, as was a short grade 2/6 blowing ejection systolic murmur that followed the click. On one occasion, pulsat alternans was observed upon standing. The middiastolic click did not appreciably change its position on standing or squatting.

A resting electrocardiogram revealed sinus rhythm with rate-related left bundle-branch block. When conduction was normal, a pattern of left ventricular hypertrophy with strain was present. Roentgenograms of the chest revealed moderate cardiac enlargement (cardiothoracic ratio, 0.64).

Echocardiographic study showed diastolic flutter of the anterior mitral leaflet, as well as enlargement of the left ventricle, with diminished septal and posterior wall motion. The click coincided in timing with maximal aortic valve opening (Fig 1). The aortic root and left atrial diameters were within normal limits. Slight posterior bowing of the mitral valvular leaflets in systole was suggestive but by no means diagnostic of mitral valve prolapse.

At cardiac catheterization, the right and left-sided pressures were normal at rest; exercise could not be carried out. There was no gradient across the aortic valve, and the aortic pulse pressure was only slightly widened (110/64 mm Hg). The cardiac index by thermodilution was 2.7 L/min/sq m. Selective left ventriculograms in two projections revealed left ventricular enlargement with poor contractility (ejection fraction, 0.27) but failed to confirm mitral valve prolapse; however, mild mitral regurgitation was noted. An ascending aortogram showed no change from the previous study. The amount of aortic regurgitation was considered inadequate to account for the observed left ventricular enlargement and dysfunction.

At the conclusion of angiographic study, intracardiac phonocardiographic study was carried out using a catheter-tip manometer (Millar 8F NIH) and recorder (Electronics for Medicine DR 16). The click could not be recorded from any position in the left ventricle but was easily recorded in the ascending aorta, diminishing in intensity as the catheter-tip manometer was withdrawn from the vicinity of the aortic valve (Fig 2). Both in a control state (Fig 2A) and during right atrial pacing, the click coincided on all cycles with a small notch in the ascending aortic pressure tracing, occurring just subsequent to delayed aortic valve opening. Catheter-tip manometric study also confirmed a grossly diminished rate of increase in the pressure in the left ventricle (Fig 2B). The combination of a delayed rise in left ventricular pressure and delayed electrical activation of the ventricle secondary to left bundle-branch block during right atrial pacing led to the positioning of the click in the latter half of systole at a

![Figure 1. Simultaneous recording of surface electrocardiogram (EKG) (no left bundle-branch block), phonocardiogram (PHONO 2 Rt) recorded at the second right intercostal space, and echocardiogram of aortic root (AO), showing exact coincidence of click (C) with maximum aortic valvular opening. S1, First heart sound; and S2, second heart sound.](http://journal.publications.chestnet.org/pdaccess.ashx?url=/data/journals/chest/21105/)

![Figure 2. Simultaneous recording of standard ECG from lead-3 (L3) (no left bundle-branch block), external phonocardiogram (EXT), and pressure tracing obtained by tip manometric study (TIP MAN) from aortic root (AO) and left ventricle (LV). A (top), Click (X) is recorded in ascending aorta and closely follows initial rise in pressure in aorta. B (bottom), Click (X) is not recorded in left ventricle, and rate of increase in left ventricular pressure is severely reduced. 1, First heart sound; and 2, second heart sound.](http://journal.publications.chestnet.org/pdaccess.ashx?url=/data/journals/chest/21105/)
FIGURE 3. Simultaneous recording of ECG from surface lead 1 (L1), phonocardiogram recorded at medium frequency from apex (APEX MF), and fluid-filled catheter pressure tracing from ascending aorta (AO): A (left), With sinus rhythm and normal conduction, click (X) is closer to first heart sound (1). B (right), When left bundle-branch block (LBBB) was induced by atrial pacing at rate of 114 impulses per minute, click (X) is midsystolic and actually slightly closer to second heart sound (2) than to first heart sound (1). Increase in interval from first heart sound to click (S1-X) from 109 to 147 msec is presumed to be due to delay in left ventricular activation secondary to left bundle-branch block. HR, Heart rate.

relatively low rate (Fig 3), thus documenting the occurrence of a late systolic ejection click.

**Discussion**

In the case described, the midsystolic timing of the click and the patient's faintly marfanoid habitus, in combination with echocardiographic findings at least suggestive of mitral valve prolapse, led us to the initial erroneous conclusion that the sound was of mitral origin; however, suspicion that the midsystolic click might not be of mitral origin was raised by the clinical findings of aortic valve disease and delay in left ventricular conduction. In general, absence of a late or holosystolic mitral regurgitation murmur and absence of echocardiographic evidence of mitral valve prolapse would support an aortic origin for a systolic click; however, ascending aortic disease often coexists with mitral valve prolapse, and a click may be the sole sign of such prolapse, with both murmur and echocardiographic manifestations being absent. Noninvasive evidence that a midsystolic click is not due to mitral valve prolapse might be obtained by the use of echophonocardiographic studies to document coincidence of the click with aortic valve opening both in the control (supine) state and after interventions expected to cause the click associated with mitral valve prolapse to move earlier in systole, such as head-up tilt or inhalation of amyl nitrate. In that considerable proportion of patients in whom adequate aortic valve echoes cannot be recorded, failure to significantly change the position of the click relative to the first heart sound by similar maneuvers would constitute evidence against a mitral origin.

The midsystolic click observed in our patient was shown to be aortic in origin by the fact that it was recorded only in the ascending aorta by the catheter-tip transducer. Its occurrence after the onset of the rise in pressure in the central aorta in the control state and during (right atrial) pacing-induced left bundle-branch block is in concert with the thesis that the click is of valvular, rather than vascular, origin, as are the facts that the patient had no dilatation of the ascending aorta and did have aortic valvular incompetence.

We conclude that aortic valve disease associated with significant left ventricular dysfunction (congestive failure) and/or left ventricular conduction delay (left bundle-branch block), combined with failure of a midsystolic click to move earlier on standing, as in the case of our patient, should suggest the possibility of a delayed aortic ejection click even when the suspicion of mitral valve prolapse coexists.

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Prolonged Survival in an Adult with Cystic Fibrosis*

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Cystic fibrosis in patients over 40 is rare. We report a 52-year-old woman in whom cystic fibrosis was confirmed by sweat analysis. This patient represents the oldest cystic fibrosis patient (with confirmatory sweat chlorides) ever described. We conclude that any patient with the appropriate clinical presentation, regardless of age, should be investigated for cystic fibrosis.

An increasing number of children with cystic fibrosis are living into adolescence and adulthood.1-3 Patients with mild symptoms of cystic fibrosis may not be diagnosed until adolescence or even later in life.4 The diagnosis of cystic fibrosis should be considered in any adult patient with the appropriate clinical presentation, regardless of age, as shown by the following report.

CASE REPORT

A 51-year-old white woman was referred for evaluation of bronchiectasis. Her first significant illness was pneumonia at age eight from which she recovered promptly. Growth and development were normal during adolescence although she was told, when a teenager, that her chest roentgenogram was abnormal but "not TB." Her first chronic symptom was a persistent cough with mucoid sputum production which developed in her late teens. She had five successful uncomplicated pregnancies while in her 20's. None of her children has had chronic pulmonary or gastrointestinal disease. Recurrent bronchitis and pneumonia, complicated by pneumothorax on three occasions, have led to more than 20 hospitalizations over the past 25 years. Bronchography confirmed the presence of bronchiectasis in her late 20's. Dyspnea has limited her activities as a housewife for the past 15 years and she has required supplemental oxygen during exertion for the past year. She reports three to four, soft greasy stools a day.

Physical examination revealed a dyspneic woman with a respiratory rate of 36. Her oral temperature was 37.7° C; weight, 56.7 kg; and height, 163 cm. Coarse inspiratory and expiratory rhonchi were heard throughout the chest. Marked clubbing was present. Complete blood count, urinalysis, chemistry profile including liver enzymes, and electrocardiogram were normal. The chest roentgenogram revealed extensive bronchiectasis with scarring and retraction (Fig. 1). Sputum culture grew mucoid Pseudomonas aeruginosa. Her FEV1 was 0.7 liter and FVC was 1.3 liters. Arterial blood gas levels while breathing room air were PaO2 42 and pH 7.44. Positive sweat chlorides were confirmed at a cystic fibrosis center (Dr. W. J. Warwick, University of Minnesota). Four sweat tests were done with pilocarpine iontophoresis (Gibson-Cooke technique) and were positive: 96, 101, 101 and 102 millimoles of chloride per liter of sweat with adequate quantities of sweat on all four tests. Fecal fat analysis after a minimum intake of 100 gm of fat per day averaged 120 gm/24 hours and serum carotenes were undetectable. After treatment with parenteral antibiotics, vigorous pulmonary toilet and pancreatic enzyme supplementation, she was symptomatically improved.

DISCUSSION

The diagnosis of cystic fibrosis is firmly established in our patient. She fulfills the diagnostic criteria with elevated sweat chlorides, chronic pulmonary disease and clinical exocrine pancreatic insufficiency.5 Pansinusitis and the presence of the mucoid variant of Pseudomonas

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Figure 1. Chest roentgenogram demonstrates scarring and retraction with bulla formation predominantly in the upper lung fields.