Chest pain in an adolescent

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A 15-year-old boy presented to a private cardiology office for evaluation of a known congenital heart condition diagnosed shortly after birth. He had had episodes of mild dyspnea and chest discomfort associated with exertion which had

been worsening over the past 12 months. Diagnostic clues are shown below (Figures 1–4).

For diagnosis and discussion, see the following page.

Figure 1. Electrocardiogram taken when the patient was not experiencing symptoms.

Figure 2. Parasternal long axis shows massive septal hypertrophy (arrow). LV indicates left ventricle; LA, left atrium; PW, posterior wall.

Figure 3. M-mode through the mitral valve demonstrates the hyperthrophy of the septum and the systolic anterior motion of the mitral valve (arrows). S indicates septum; MV, mitral valve; PW, posterior wall; P, pericardium.

Figure 4. Chest x-ray shows severe cardiomegaly and the presence of an implantable cardioverter-defibrillator.

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DIAGNOSIS: Hypertrophic cardiomyopathy.

DISCUSSION

Hypertrophic cardiomyopathy (HC) is a genetic disorder that usually results in left ventricular hypertrophy. HC may or may not result in significant left ventricular (LV) outflow obstruction. Only 25% of patients have obstruction, and obstruction does not have to be present for diagnosis (1, 2). The HC terminology replaces prior descriptive names, such as idiopathic hypertrophic subaortic stenosis, that suggested obstruction was an integral part of the disorder.

HC occurs in 1 of 500 individuals and is the most common cause of sudden death in the first to second decades of life (1, 2). It has an autosomal-dominant pattern due to missense mutations in sarcomere genes. The most deleterious are associated with abnormalities of the β -myosin heavy chain and troponin-T that result in amino acid substitution, causing a change in the net charge of these proteins. Individuals with such mutations have a higher risk of sudden cardiac death, congestive heart failure, and atrial fibrillation. DNA evaluation provides a definitive diagnosis but is limited to research studies and evaluation of proband pedigrees.

HC is often discovered when patients are referred for evaluation of a heart murmur, an abnormal electrocardiogram, or symptoms such as chest pain or dyspnea or when another family member has the disorder. Two-dimensional echocardiography is the method of choice for diagnosis as it has a low cost and a high sensitivity. No electrocardiographic changes are unique to HC, although most patients have an abnormal tracing. The physical examination is also limited in its utility for diagnostic purposes except in the patient with LV outflow obstruction. In the patient with obstruction, there is typically a harsh, crescendo-decrescendo murmur best heard at the left sternal border. This murmur is very dependent on ventricular loading conditions. It increases during the Valsalva maneuver due to decreased venous return leading to underfilling of the left ventricle. Diagnosis of HC with an outflow tract obstruction requires demonstration of a resting gradient of ≥ 30 mm Hg or a provokable gradient of ≥ 50 mm Hg. Gradients may be provoked with maneuvers, which increase contractility and/or decrease preload (such as dobutamine, the Valsalva maneuver, or exercise).

Once the diagnosis of HC is made, there are several important considerations. The first pertains to an assessment of risk of sudden death and the amelioration and treatment of symptoms. Sudden death is the most devastating outcome related to HC, especially when it occurs in a young individual. Original estimates of mortality related to HC were 3% to 6% per year; however, these were derived from data of tertiary referral centers (1). Better estimates from community-based studies are lower (1% annually). The second consideration is the evaluation of first-degree relative, which is extremely important in families with adverse events related to HC. Evaluation must include a history and physical examination, electrocardiography, and 2-dimensional echocardiography.

The risk of sudden death is greatest when the patient has had a prior arrest or documented spontaneous ventricular tachycardia. Prevention of sudden death with an implantable cardioverter-defibrillator (ICD) is warranted in these patients. Prophylactic implantation of an ICD is considered for patients with one or more of the following risk factors: 1) family history of HC-related

sudden death in a first-degree relative, 2) syncope, 3) nonsustained ventricular tachycardia recorded by Holter electrocardiography, 4) abnormal blood pressure response to exercise (fall or failure to increase by 20 mm Hg), or 5) extreme LV hypertrophy (thickness of >30 mm Hg) (3). Studies of patients who have received an ICD have shown the presence of dangerous arrhythmias in 25% of the patients in a follow-up period of 3 years (1, 3). ICDs placed for primary prevention have a 5% annual rate of appropriate interventions, and those placed for secondary prevention have a rate of 11% (1, 3).

Additional treatment approaches for patients with HC are dependent on the presence of symptoms. Patients who are genotypically positive and phenotypically negative need longitudinal follow-up, as their phenotype may change over time. Patients with phenotypic findings but no symptoms require either no treatment or drug therapy with a negative inotropic agent (beta-blocker or verapamil). Symptoms are related to diastolic dysfunction (impaired relaxation), myocardial ischemia, atrial fibrillation, and outflow obstruction. Beta-blockers are the mainstay of therapy in symptomatic patients. Verapamil must be used more cautiously in patients with severe outflow obstruction and heart failure. Patients with end-stage disease may develop severe heart failure due to progressive systolic dysfunction and require diuretics, digitalis, and afterload reduction.

Patients with severe outflow obstruction refractory to medical therapy need more aggressive therapy. Studies have shown LV outflow tract obstruction to be an independent predictor of increased morbidity and mortality (1, 3). Ventricular septal myotomy-myectomy (surgical excision of a portion of the proximal septum) has been used successfully to remove the outflow obstruction and has an operative mortality of $<2\%$ (1). Dual-chamber pacing has had limited success and appears most useful in older patients and those with increased operative risk. The improvement in obstructive gradients observed during infarction or ischemia of the septum led to the development of alcohol septal ablation, a controlled induction of an infarction of the proximal septum. The most frequent procedural complication is infranodal conduction block. The short-term success of alcohol septal ablation approaches 90% (2), but long-term risks and follow-up data are not yet available. Cardiac transplantation is a limited option for medically refractory nonobstructive HC.

The patient was referred for evaluation for ICD for primary prevention of sudden death due to massive septal hypertrophy. Holter electrocardiography revealed nonsustained ventricular tachycardia, and his blood pressure failed to increase with exercise. An ICD has been placed, and 2 episodes of nonsustained ventricular tachycardia have been detected. Echocardiography revealed a resting gradient of 60 mm Hg and systolic anterior motion of the mitral valve septal leaflet. His dyspnea and exercise tolerance have worsened despite medical therapy and pacing. Alcohol septal ablation is being considered.

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