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Familial Discrete Subaortic Stenosis

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Summary: Discrete subaortic stenosis (DSS) accounts for 8 to 20% of all cases of congenital left ventricular outflow tract obstruction. There have been few scattered reports of left ventricular obstructive lesions occurring in immediate family members of patients with DSS. This is a report of four cases of DSS in one family: one brother with a fibrous ring, and two sisters and the son of one of the sisters with a fibrous membrane. The occurrence of multiple cases of DSS in this family suggests an autosomal dominant mode of inheritance.

Key words: discrete subaortic stenosis, subaortic membrane, familial, autosomal dominant

Introduction

Discrete subaortic stenosis (DSS) accounts for 8 to 20% of all cases of congenital left ventricular outflow tract obstruction.[1–4] The lesion usually consists of a thin crescent-shaped fibrous membrane immediately below the aortic valve or, less commonly, a thicker fibromuscular ring in the left ventricular outflow tract. The aortic leaflets are frequently malformed and thickened on their ventricular surfaces, resulting in aortic regurgitation.[4]

There have been few scattered reports of left ventricular obstructive lesions occurring in immediate family members of patients with DSS.[5–9] In this report we present a cluster of four cases of DSS in one family.

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Case Reports

Patient No. 1

A 38-year-old man had first been told of having a cardiac murmur at the age of 8 years. At the age of 18 years, he was first seen at our Center in 1977 with a history of pressure-like chest discomfort on mild effort, and dyspnea, dizziness, and blurring of the vision on moderate exertion over the preceding 6 or 7 years. He had also reported a fainting episode after severe exertion. On physical examination there was left ventricular (LV) hypertrophy with a strong, sustained precordial impulse. A grade 4/6 harsh ejection systolic murmur in the aortic area and a grade 2/6 early diastolic murmur at the left sternal border were noted. The electrocardiogram (ECG) showed LV hypertrophy with strain pattern. Cardiac catheterization demonstrated severe subaortic stenosis with an outflow tract gradient of 170 mmHg and mild aortic valvular regurgitation. Inspection of the aortic valve and the LV outflow tract during surgery revealed a tricuspid aortic valve with mild thickening of the cusps, but no stenosis or calcification. There was, however, very severe subaortic stenosis in the form of a fibrous ring extending anteriorly and posteriorly around to the mitral valve leaflet. A wedge incision below the right coronary cusp, removing a 2–3 mm thick ring of fibrous tissue, was carried out. The patient's postoperative course was very satisfactory. He has remained asymptomatic ever since, with no residual obstruction in the LV outflow tract, and no LV hypertrophy. Left ventricular function, as assessed by Doppler echocardiography, is normal. Mild aortic valve regurgitation persists.

Patient No. 2

A 50-year-old woman, sister of Patient No. 1, was evaluated for easy fatiguability 19 years after the evaluation of Patient No. 1. She reported a history of a cardiac murmur discovered 20 years earlier. A grade 3/6 harsh midsystolic ejection murmur was heard in the second and third intercostal spaces radiating to the neck and the left sternal border. The LV impulse and all peripheral pulses were normal. Chest radiogram was unremarkable and ECG was within normal limits. Echocardiography showed normal cardiac chambers, normal ventricular wall motion, and no ventricular hypertrophy. A linear echo in the LV outflow tract extending from the anterior septum to the anterior mitral leaflet indicated the presence of a fibrous membrane. Interrogation of the LV outflow tract

using pulsed-wave Doppler echocardiography, with the sample volume placed below the fibrous membrane, revealed a maximal systolic flow velocity of 0.80 m/s. By placing the sample volume between the membrane and the aortic valve, the maximal systolic flow velocity increased to 1.60 m/s, indicating discrete subvalvular aortic stenosis of mild degree. In our echocardiography laboratory, the normal range for resting maximal systolic flow velocity in the LV outflow tract is 0.70 to 0.95 m/s. By continuous-wave Doppler echocardiography, the maximal systolic flow velocity across the LV outflow tract and the aortic valve was 2.00 m/s. The aortic valve was tricuspid. Minimal aortic valvular regurgitation was detected by continuous-wave and color-flow Doppler echocardiography.

Patient No. 3

A 47-year-old woman, sister of Patients Nos. 1 and 2, was examined for atypical chest pains during the same week of evaluation of Patient No. 2. She reported a history of a cardiac murmur discovered several years earlier. A grade 2/6 harsh midsystolic ejection murmur was heard in the second and third intercostal spaces. The LV impulse and all peripheral pulses were normal. The ECG was within normal limits. Echocardiography showed normal cardiac chambers without ventricular hypertrophy. A linear echo in the LV outflow tract suggested the presence of a fibrous membrane. Doppler interrogation of the LV outflow tract using pulsed wave, with the sample volume placed below the linear echo, revealed a maximal systolic flow velocity of 0.75 m/s. By placing the sample volume between the membrane and the aortic valve, maximal systolic flow velocity increased to 1.80 m/s, indicating subvalvular stenosis of mild degree. In our echocardiography laboratory, the normal range for resting maximal systolic flow velocity in the LV outflow tract is 0.70 to 0.95 m/s. The maximal systolic flow velocity by continuous-wave Doppler echocardiography was 2.00 m/s. Following exercise while lying on the examining bed (leg elevations), the patient's maximal systolic flow velocity increased to 2.40 m/s. The aortic valve was tricuspid. No aortic valvular regurgitation was detected by continuous-wave or color-flow Doppler echocardiography.

Patient No. 4

A 16-year-old male student, the son of Patient No. 3 and nephew of Patients Nos. 1 and 2, was found to have a cardiac murmur at the age of 3 years. At that time, evaluation with chest radiogram, ECG, and two-dimensional echocardiogram was inconclusive. The patient remained entirely asymptomatic and had normal growth and development. When seen recently at our Center he had a grade 3/6 harsh midsystolic ejection murmur maximal in the second right intercostal space, with radiation to the neck and along the left sternal border. The LV impulse and all peripheral pulses were normal. Chest radiogram and the ECG were within normal limits. Echocardiography revealed normal dimensions of the cardiac chambers, normal contractility of the ventricles, and normal wall thickness. A linear echo (Fig. 1) in the LV outflow tract extending from the anterior septum to the anterior mitral leaflet indicated the presence of a fibrous membrane. M-mode echocardiogram showed early systolic closure of the aortic valve and systolic aortic valve fluttering. Doppler interrogation of the LV outflow tract using pulsed wave, with the sample volume placed below the fibrous membrane (Fig. 2), revealed a maximal systolic flow velocity of 0.75 m/s. By placing the sample volume between the membrane and the aortic valve (Fig. 3), the maximal systolic flow velocity increased to 2.0 m/s, indicating discrete subvalvular aortic stenosis of mild degree. The flow appeared to be laminar with pulsed-wave Doppler interrogation in the apical 5-chamber view (Fig. 3), but it was turbulent when interrogated in the parasternal long-

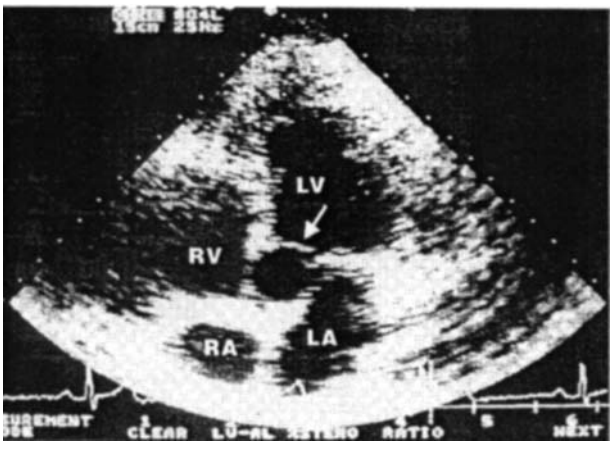

FIG. 1 Apical five-chamber echocardiographic view of Patient No. 4. A linear echo (arrow) in the left ventricular outflow tract extending from the anterior septum to the anterior mitral leaflet indicates the presence of a fibrous membrane. LA = left atrium, LV = left ventricle, RA = right atrium, RV = right ventricle.

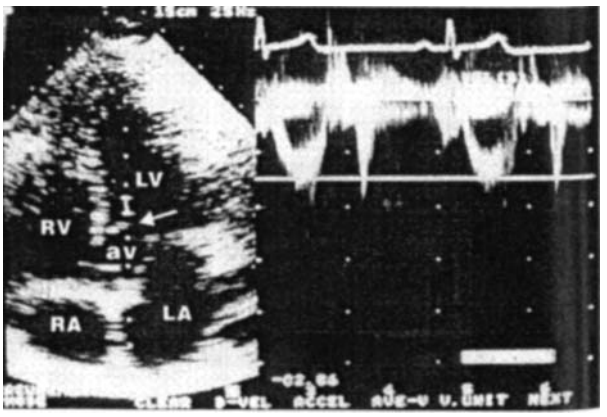

FIG. 2 Apical five-chamber echocardiographic view of Patient No. 4. Interrogation of the left ventricular outflow tract, using pulsed-wave Doppler echocardiography with the sample volume placed below the fibrous membrane. Arrow indicates the fibrous membrane. av = aortic valve, LA = left atrium, LV = left ventricle, RA = right atrium, RV = right ventricle.

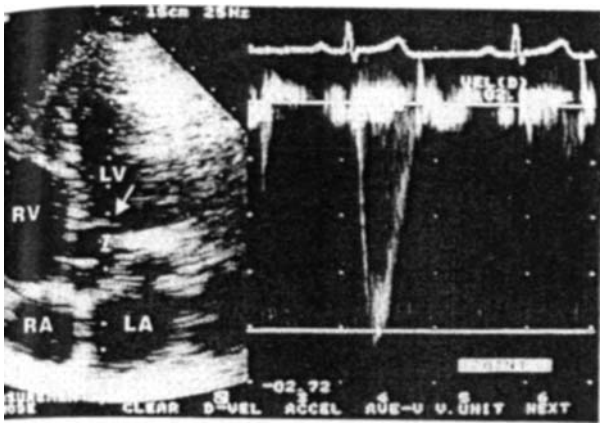

FIG. 3 Apical five-chamber echocardiographic view of Patient No. 4. Interrogation of the left ventricular outflow tract using pulsed wave Doppler echocardiography with the sample volume placed between the fibrous membrane and the aortic valve. Arrow indicates the fibrous membrane. LA = left atrium, LV = left ventricle, RA = right atrium, RV = right ventricle.

axis view. The maximal systolic flow velocity by continuous-wave Doppler echocardiography was 2.40 m/s. Following exercise, the maximal systolic flow velocity increased to 2.70 m/s. The aortic valve was tricuspid. No aortic valvular regurgitation was detected by conventional or color-flow Doppler.

Discussion

The occurrence of LV obstructive lesions in immediate family members of patients with DSS has been noted.[5–9] Levin *et al.* reported on monozygotic twins with the same complex of defects, consisting of subaortic stenosis, severe aortic coarctation, and large ventricular septal defect.[5] Coarctation of the aorta, valvular aortic stenosis, and DSS were found in immediate family members of patients with DSS in the series reported by Katz *et al.*[6] In 1974, Gale *et al.*[7] used the term "familial subaortic membranous stenosis" for the first time in their report of two siblings with discrete subaortic membranous stenosis, one of whom was mildly mentally retarded with unusual facies. The authors of the report pointed out that the presence of DSS in one member of a family should suggest its occurrence in other members with similar clinical signs. In 1985, Urbach *et al.*[8] reported on seven patients with DSS in three families, and proposed that first-degree relatives of patients with DSS should be evaluated for the presence of this anomaly. Recently, Abdallah *et al.*[9] reported on one family member of a patient with DSS presenting with findings suggesting a forme fruste of this disease and no other congenital defects. They, too, recommended increased surveillance of family members of individuals with DSS, as the clinical findings of mild subaortic obstruction may be indistinguishable from those of an innocent flow murmur.

In this report we present a cluster of four cases of DSS in a family: one brother with a fibrous ring causing severe subaortic stenosis, and his two sisters and the son of one of the sisters with a fibrous membrane producing mild subaortic obstruction. The familial occurrence was suspected when Patient No. 4 was evaluated for a cardiac murmur 19 years after his uncle's surgery and was found to have a subaortic membrane. His mother (Patient No. 3), who brought him for cardiac evaluation, was studied next with similar findings. Patient No. 2 was then studied and was found to have a subaortic membrane with mild subaortic obstruction and mild aortic valvular regurgitation. Patients Nos. 1, 2, and 3 belong to a family of 10 (6 brothers and 4 sisters). Two other brothers underwent cardiac evaluation, but no evidence of DSS was found. Several members of this family are not Cyprus residents.

Although Patient No. 1 had severe symptomatic DSS at a young age, his relatives (Patients Nos. 2, 3, and 4), even his middle-aged sisters, demonstrated only a mild form of this disease. Discrete subaortic stenosis tends to be a progressive abnormality, yet cases of patients surviving into the sixth decade have been reported.[10]

It is interesting that the flow in the LV outflow tract appeared to be laminar with pulsed-wave Doppler interrogation in the apical five-chamber view (Fig. 3); however, it was turbulent when interrogated in the parasternal long-axis view. A probable explanation is that the ultrasonic beam, being parallel to the flow in the apical five-chamber view, selectively registers the maximal flow velocities in the center of the jet. Another factor could be the mildness of the stenosis caused by the subaortic membrane, producing limited disturbance of flow.

Conclusion

The occurrence of multiple cases of DSS in this family suggests an autosomal dominant mode of inheritance.

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