

CASE REPORTS

HYPERTROPHIC SUBAORTIC STENOSIS WITH MYOCARDIAL FIBRE DEGENERATION

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During the past decade it has become evident that obstruction to left ventricular outflow may result from causes other than aortic valve disease and congenital subaortic stenosis associated with a demonstrable ridge or diaphragm below the aortic valve. Various types of obstruction have been demonstrated, sometimes associated with marked local hypertrophy of the myocardium, especially the interventricular septum, and sometimes with generalized hypertrophy of the left ventricle.

This obstructive syndrome has been described under a variety of names, functional obstruction of the left ventricle (Brock, 1957, 1959), pseudo aortic stenosis (Bercu *et al.*, 1958), asymmetrical hypertrophy of the heart (Teare, 1958), obstructive cardiomyopathy (Goodwin *et al.*, 1960), and hypertrophic subaortic stenosis (Brockenbrough, Braunwald, and Morrow, 1961). Under the title "Familial muscular subaortic stenosis" Brent *et al.* (1960) described a group of cases in which several members of two families were involved.

Necropsy studies have sometimes shown pronounced localized hypertrophy of the interventricular septum or generalized hypertrophy of the left ventricle. Histologically the only changes found have been hypertrophy of the muscle fibres, occasionally fine fibrosis and slight endocardial fibrosis over the area of obstruction.

The following is a report of a case which, in addition to hypertrophy, showed extensive myocardial fibre degeneration.

Case Report

The patient was first seen at the age of 35 in 1958. At this time she had noticed shortness of breath on exertion (e.g. climbing one flight of stairs) for about eight months. There had been no dyspnoea at night, no cough or sputum, and no swelling of legs. There was no family history of heart disease. She had not had rheumatic fever. On a medical examination before the removal of an ovarian cyst in 1953 she had been questioned on this point; possibly some cardiac abnormality had been noted at this time.

On examination the pulse was regular and of normal character. The blood pressure was 160/90 mm. Hg. There was no venous congestion or oedema. The apex beat was just beyond the mid-clavicular line and of a somewhat thrusting type. There was a loud mid-systolic murmur maximal in the left 4th interspace but conducted widely over the præcordium and into the neck. The phonocardiogram tracing had a shape typical of aortic stenosis. The chest radiograph showed some generalized enlargement of the heart. The lungs were normal. The electrocardiogram showed left ventricular preponderance and inverted T waves in I, VL, and the left side of the præcordium. The results of cardiac catheterization are given in Table I.

The cardiac index was 3.9 l./min./m.² The central aortic pressure tracing showed no evidence of aortic stenosis.

In September 1958 she began to develop severe pain in the front of the chest on exertion, occasionally passing through to the back. It was relieved after resting for ten minutes and, more quickly, by sublingual glyceryl trinitrate. During the next two years the pain gradually increased in severity and frequency and her breathlessness also became worse. At the beginning of 1961 she started to have attacks of breathlessness at night and found she needed to use four pillows.

TABLE I
RESULTS OF CARDIAC CATHETERIZATION

	Oxygen saturation	Pressure (mm. Hg)
Pulmonary artery	81	24/17 (19)
Right ventricular outflow	82	25/2
Right ventricular inflow	77	—
Right atrium	83	—
Superior vena cava	79	—
Aorta	97	142/82
Wedge	—	11

TABLE II
RESULTS OF CARDIAC CATHETERIZATION

	Pressure (mm. Hg)
Pulmonary artery	35/22
Wedge	20
Left ventricle	262/15
Brachial artery	170/105

She was admitted for further investigation at this time. The physical, radiological, and electrocardiographic findings were the same as before. A further cardiac catheterization was carried out together with left ventricular puncture (Table II).

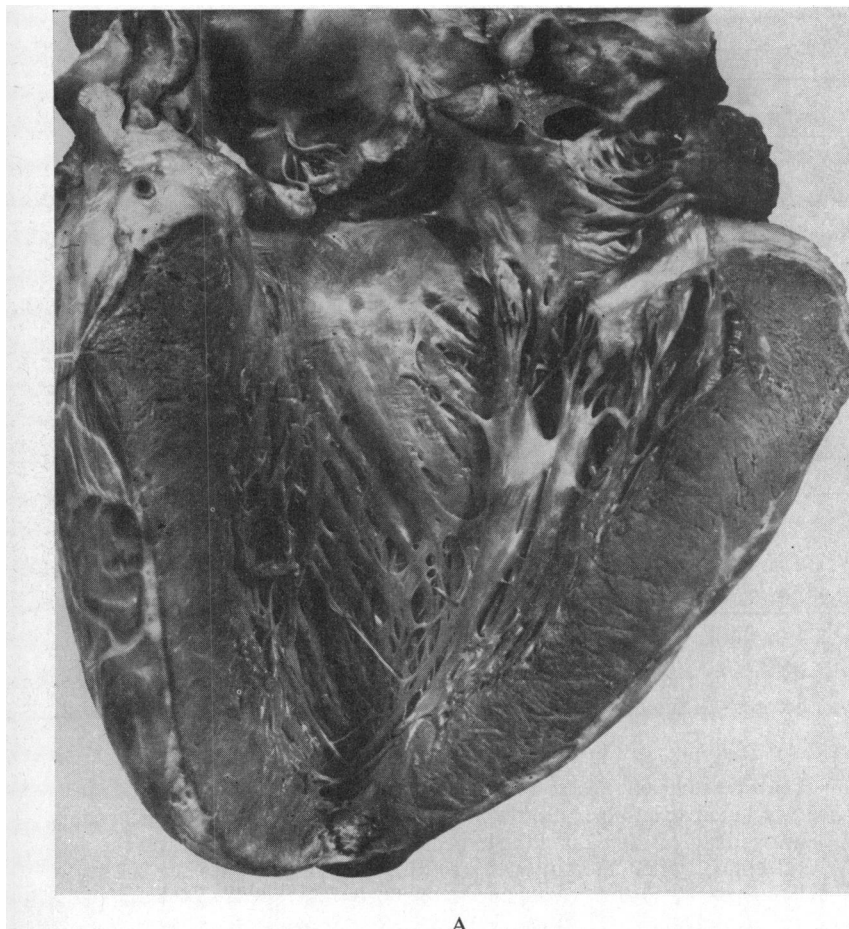
The cardiac index was 3.5 l./min./m.² The brachial arterial pressure tracing following a ventricular premature beat was suggestive of subaortic stenosis (Morrow and Braunwald, 1959).

Following this investigation she developed atrial fibrillation which later disappeared after administration of digitalis. One week later she developed a pleuritic pain in the left chest. A portable radiograph showed some shadowing at the left base and anticoagulant therapy was started. Four hours later she suddenly became unconscious and the blood pressure was too low to measure. Vasopressor drugs were given without effect and she died in a few hours.

Findings at Necropsy. Two small ovoid swellings 3 × 2 × 2 and 1 × 1.5 × 1 cm. were found in the left side of the neck: on histological examination these proved to be ganglioneuromata. The lungs were moderately oedematous and a recent infarct was present at the left base. The pleural cavities were dry and free from adhesions. The abdominal organs showed chronic venous congestion. The left ovary had been removed.

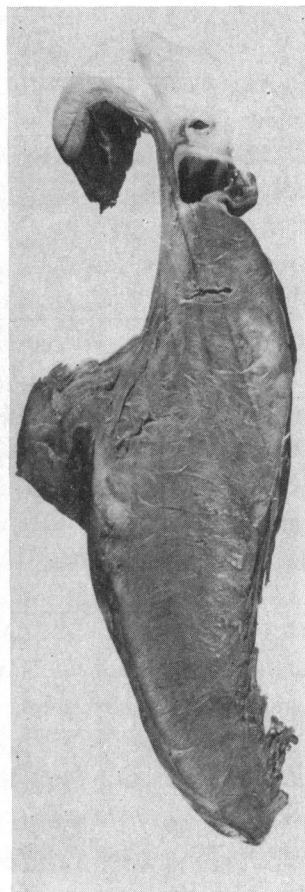
Heart. The pericardium contained 50 ml. of blood-stained fluid. The heart (580 g.) was enlarged and had an elongated shape. The right ventricle was slightly hypertrophied (7 mm.) and the left ventricle was hypertrophied (2.5 cm.). The aortic valve was not obstructed. The cusps showed fenestration but were not thickened. 2 cm. below the aortic valve a bulge could be felt on the interventricular septum. On opening the left ventricle an area of slightly opaque endocardium was noted at the site of the bulging part of the septum (Fig. 1A). The cavity of the left ventricle was not dilated. No abnormality was found in the other valves. The coronary arteries showed only slight fatty streaking and the lumina were patent. After fixation, section of the ventricular wall showed an irregular area of fibrosis extending into the muscle below the opaque endocardium (Fig. 1B). Similar smaller areas were also seen in other parts of the ventricle beneath the endocardium and the papillary muscles were extensively fibrosed.

Microscopy. In addition to hypertrophy of myocardial fibres extensive but focal degenerative changes were present. In the fibrotic areas there was destruction of muscle fibres with fibrous replacement and a mononuclear cell infiltrate was present at the periphery (Fig. 2A). The mononuclear cells had fairly large open nuclei and some of them were so-called Anitschow myocytes. There were a few lymphocytes also but plasma cells and polymorphonuclears were absent. These extensive changes were present in the interventricular septum and in the papillary muscles. Throughout the remainder of the left ventricle small focal areas of myocytolysis and areas of mononuclear cell infiltrate were present in which fibrosis was not yet evident.



A

FIG. 1A.—Hypertrophied left ventricle with whole area of endocardial fibrosis and bulging of the septum below the aortic valve. Note the fenestration of the aortic valve cusps. The endocardium over the papillary muscles is also white and opaque.



B

FIG. 1B.—Slightly oblique section through the interventricular septum. Note the bulging of the septum and the area of fibrosis.

Various stages of degeneration were noted in the myocardial fibres. Some of the muscle fibres around and within the lesions showed areas of vacuolation and extensive granular degeneration. At the periphery of the large lesions and in the smaller more recent lesions it was evident that the sarcoplasm was broken into irregular masses and the fibres were invaded by the mononuclear cells (Fig. 2B). The process appeared to be primarily degeneration of muscle fibres with a histiocytic response. Other myocardial fibres at the periphery of the lesions contained giant irregular nuclei. In the papillary muscles there was preservation of the reticulin pattern and mononuclear cells were arranged in rows between the reticulin fibres but in some of the large lesions in the septum the reticulin pattern was only partly preserved. The fibrosis as seen in the papillary muscles was only partly the result of collapse of the stroma as parallel reticulin fibres could be identified passing from the myocardium through the fibrotic areas with collagen fibre between.

The muscle of the right ventricle and the atria was not involved. No changes were noted in the vessels apart from fatty streaking in the main branches.

Discussion

The abnormalities in this case differ from those previously reported in that an active degenerative process is superimposed on the hypertrophied muscle fibres. It appears likely that hypertrophy

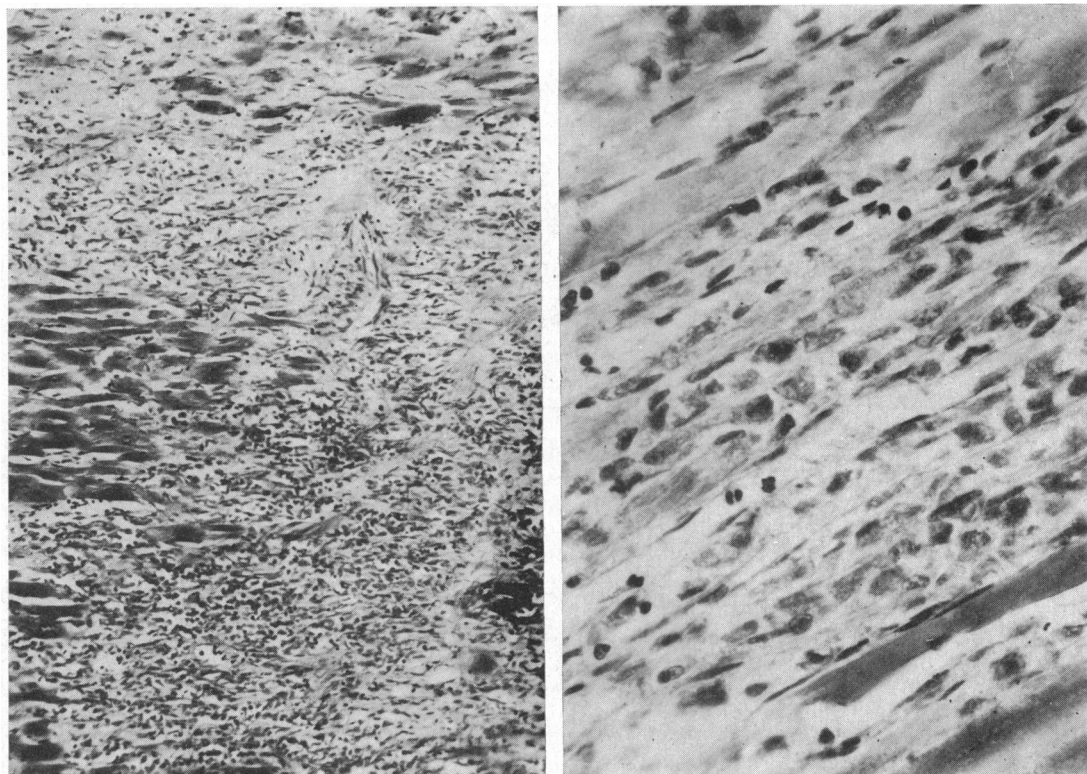


FIG. 2A.—Mononuclear cell infiltrate at the periphery of a fibrotic area. (van Gieson $\times 100$.)

FIG. 2B.—Broken-up myocardial fibres invaded by mononuclears. (H. and E. $\times 450$)

preceded the degenerative changes since many of the degenerated fibres were large. The history of angina, the distribution of the fibrous areas, and the presence of recent cytolysis suggest the possibility that ischæmia may be a factor, but if so the lesions are of a very unusual type. The absence of an interstitial inflammatory reaction makes a myocarditis unlikely.

The relationship of this type of case to other forms of cardiomyopathy is not clear. Some of the obstructive types are familial and other familial cardiomyopathies often associated with cardiac enlargement have been reported in several families (Evans, 1949; Battersby and Glenner, 1961; Whitfield, 1961; Bishop, Campbell, and Jones, 1962). The pathology of these cases usually shows hypertrophy with fine fibrosis but basophilic degeneration of myocardial fibres has also been reported (Battersby and Glenner, 1961; Bishop *et al.*, 1962).

The possibility that these conditions are primary metabolic disorders of cardiac muscle fibres must be considered and the findings in the present case favour the view that the abnormality lies in the myocardial fibres themselves.

Summary

A case of hypertrophic subaortic stenosis is described in which widespread myocardial fibre degeneration was present in the absence of coronary artery disease. The possibility of a primary abnormality of myocardial fibres is considered.

I wish to thank Dr. P. Harris for the clinical details of this case.

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