ANGINA PECTORIS AND NORMAL CORONARY ANGIOGRAPHY*

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SUMMARY

Thirteen cases of angina pectoris with normal coronary arteriograms are described, 9 of which occurred in females. A 14th patient, a woman aged 28, had angina pectoris with an abnormal cardiogram and a positive after-effort test. Postmortem examination showed completely normal coronary arteries, and there was no cardiac muscle or valve pathology. The pathophysiological basis for the angina pectoris in these cases must, we consider, still be regarded as obscure.

In most patients with symptomatic or electrocardiographic evidence of ischaemic heart disease, coronary artery obstruction or narrowing provides a pathophysiological basis for the myocardial hypoxia. The pioneering and development of selective cine-coronary angiography by Sones and colleagues[1-3] has made possible the correlation of clinical syndromes of arterial obstruction during life.

Several angiographic studies have demonstrated that obstruction can be shown in at least 1 major coronary artery in most patients with angina pectoris, and often disease of two or three vessels has been demonstrated.[4-9] The electrocardiogram in most patients is abnormal at rest or on effort.

The demonstration of the wide distribution of coronary artery disease in these patients is in keeping with earlier reports on comparison between clinical and postmortem studies in coronary artery disease. These correlations do not necessarily apply in the presence of valvular or other forms of organic heart disease.[10] The problem of myocardial infarction with normal coronary arteriograms has been well discussed by Campeau.[11]

In the large series of patients with coronary heart disease reported by Proudfit *et al.*,[12] 2 - 5% had normal coronary arteriograms, and in the series of Kemp *et al.*[13] 8% had normal coronary arteriograms. In the latter series 62% were females. Angina with normal coronary arteries has also been reported by other workers.[14-17] Whiting *et al.*[18] report a case of variant angina pectoris with normal coronary arteriograms. We are reporting a significant group of patients with angina pectoris without demonstrable heart disease, who do not show abnormalities of the coronary arteries on the angiocardiogram.

MATERIAL

For the past 8 years we have performed selective coronary angiography in patients for the elucidation of chest pain and in the investigation of heart disease of uncertain aetiology. Among these cases there have been 13 patients with a history which we accepted as angina pectoris. Some had superadded symptoms of anxiety and hyperventilation. These 13 comprised 6 White females, 3 White males, 3 Coloured females and 1 Coloured male. Their ages ranged from 26 to 53 years. None of the patients had diabetes or hypertension. The Wassermann reaction when done was negative. The blood cholesterol, when done, was within the normal range. No patient had valve disease or cardiomegaly The duration of the chest pain varied from 2 months to 11 years in the patients when first seen in the Cardiac Clinic.

A fourteenth case, a 28-year-old White female, is included in this report. This patient had typical angina pectoris. She had a story of 6 months' substernal chest pain, burning in character across the chest, through to the back, down the left arm, occurring on effort or after emotion. There was a marked anxiety factor in her make-up. She did not have selective coronary arteriography, but the coronary arteries were studied at postmortem examination. Thus, of our total series, 70% were females.

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METHODS

A careful routine history was taken from all the patients. The diagnosis of angina was made on the history by at least two of us. The effort electrocardiogram was obtained by exercising on the Master 2 step until the patient complained of pain or was too tired to do more trips. Tracings were then recorded immediately and continuously thereafter for variable periods up to 10 minutes.

We have used strict criteria for positive after-effort tests. A depression of 1 mm of the S-T segment, with or without inversion of the T wave, was considered a positive response.[19,20] Depression of lesser degree, and S-T segment depression of abnormal shape, were described as probably positive. Selective arteriography was performed by the Sones technique through the brachial artery with injections of 6 - 8 ml of radio-opaque dye, directly into the coronary arteries. The injections into both vessels were filmed in left anterior and right anterior oblique positions on 35-mm film at 40, and more recently, 60 frames per second.

The resting electrocardiogram was normal in 9 cases and abnormal in 4 cases. After exercise, the electrocardiogram was positive in 4 and probably positive in 2 cases. One case had postextrasystolic T-wave inversion after effort. Six had normal after-effort tracings.

Our fourteenth patient, who had typical angina pectoris with abnormal resting and after-effort electrocardiograms, committed suicide by falling from a 6th floor window. As stated, she did not undergo coronary angiography, but a

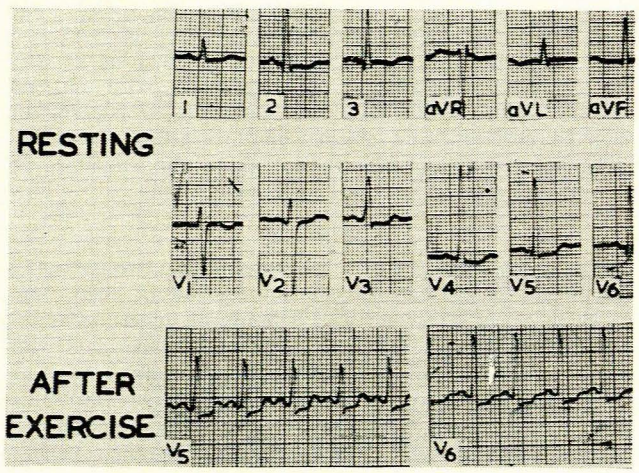

Fig. 1. Resting and after-exercise electrocardiogram of case 14.

detailed postmortem examination of the heart failed to reveal any pathology in the coronary vessels or the myocardium. This case is our only postmortem study and is thus of special significance (Fig. 1).

DISCUSSION

The demonstration of normal patency of the large coronary arteries by selective cine-arteriograms imposes an obligation to consider other aetiological factors—either anatomical or functional for the anginal pains. It has been claimed that cine-arteriograms may underestimate the severity of the atheroma, or that the arteriograms are incorrectly interpreted.[21] It may be that some peripheral coronary branches were not visualized in the angiogram, but obstructive disease of the peripheral vessels is exceptional, unless the major arteries are similarly involved.[16] The microcirculation is not visualized in arteriography and its involvement could not be appraised, but pathological involvement of these intramuscular vessels is not, at present, considered to be a factor in ischaemic heart disease, and is at most, an unproved postulate.[22-25] Eliot and Mizukani[26] and Eliot and Bratt[27] described 15 premenopausal women under 40 years of age, with myocardial ischaemia and normal selective coronary arteriograms. Three women died later with single or multiple subendocardial infarcts. These 3, at postmortem examination, had no disease of the large or small coronary arteries. Abnormal haemoglobin-oxygen dissociation was found in 14 of the 15 cases. Neil *et al.*[28] and Gorlin[29] in their cases with normal coronary arteries, found an increase in the coronary venous blood-lactate - pyruvate ratio. The blood showed normal oxygen affinity and thus they did *not* find abnormal oxygen dissociation as a cause of the hypoxia in *their* cases. *Finally,* a most difficult question arises. Were our cases examples of anxiety and hyperventilation precipitating angina pectoris? S-T and T changes have been described in hyperventilation.[30,31] Many of our patients were anxious and did hyperventilate. The abnormalities of myocardial lactate metabolism in the patients reported by Neil *et al.*[28] and Gorlin[29] with angina and normal coronary arteriograms, argue strongly against psychoneurosis *alone,* being a sole cause in their patients.

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