CASE REPORT

Chest pain during exercise as first manifestation of Friedreich's ataxia

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Abstract

Cardiac function is affected in up to 90% of patients with Friedreich's ataxia, the most common spinocerebellar degenerative disease. Friedreich's ataxia typically causes motor abnormalities of the extremities, mainly impairing walking and the coordination of the legs and arms. The myocardium is affected at a later stage of the disease. The extent and timing of myocardial involvement determines the clinical course. Some patients have no cardiac symptoms and cardiac involvement can be established only by electrocardiographic or echocardiographic examination. In addition some pathological studies have found evidence of coronary abnormalities, mainly in the small vessels. There are no reports that such lesions cause angina.

In a 16 year old patient chest pain on exercise had been the presenting symptom of Friedreich's ataxia at the age of 9. Considerable alterations in ventricular repolarisation on the electrocardiogram suggested a congenital coronary abnormality or hypertrophic cardiomyopathy. The results of a Doppler echocardiography, Holter monitoring, and a haemodynamic study with coronary arteriography were all normal. An exercise test when the boy was 13 indicated significant changes in ventricular repolarisation. Myocardial scintigraphy ($^{99m}\text{Tc-MIBI}$) at that time, however, was normal. He improved slightly when he was treated with verapamil. When he was 15 neurological symptoms developed and Friedreich's ataxia was diagnosed. Typical angina during exercise seems to have been the first symptom of Friedreich's ataxia.

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Cardiac involvement in Friedreich's ataxia

Friedreich's ataxia is the most common degenerative spinocerebellar disease. It is caused by a recessive autosomal gene on chromosome 9.¹

Cardiac involvement is seen in 50-90% of cases.² Patients can remain symptom free for several years and the diagnosis is established by means of an electrocardiogram (ECG) or an echocardiogram or both. There are ECG alterations in 80-100% of patients¹⁻⁶ and echocardiographic abnormalities in 50-86%.^{1,3,6,7}

The most frequent cardiac pathology is hypertrophic cardiomyopathy,^{2,8} which is usually concentric, with preserved systolic function. Nevertheless, in some cases the septum is predominantly affected and there can be a subaortic gradient. A less common finding with a much poorer prognosis, is dilated cardiomyopathy with reduced systolic function. This is associated with tachyarrhythmias, development of congestive cardiac failure, and sudden death. It is not known whether these different forms are merely different stages of the disease or different effects.⁹

The pathogenesis of cardiac lesions still remains unknown. James *et al*¹⁰ in a post-mortem examination of three patients with Friedreich's ataxia who all died from congestive cardiac insufficiency (congestive heart failure) and atrial arrhythmias (one of these cases had already been reported¹¹) suggested the possibility of a multifactorial pathogenesis. Their mosaic concept of pathogenesis involved ischaemic factors affecting both small and large coronary arteries; neurological factors affecting nerves and lymph nodes (cardio-neuropathy); and myopathic factors with focal fibrosis and cellular lesions, especially at the level of the myocytes (cardiomyopathy).

Coronary involvement, especially of small vessels, has been described in several studies but in most its possible functional consequences were not evaluated.¹⁰⁻¹³ When Hewer reviewed necropsy specimens from 27 cases of Friedreich's ataxia, he found lesions in some small coronary arteries.¹³ However, he did not regard these lesions as important, because so often arteries (about 9%) were affected. He did not think that these lesions could be responsible for the extreme muscle fibrosis. Hewer thought that the arterial narrowing was secondary to degeneration of the cardiac muscle. We believe that the number of samples he studied represented only a very small part of the coronary arterial tree, too small a part to assess the overall involvement of the

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Figure 1 (Left) Repolarisation abnormalities in the electrocardiogram at rest with negative T waves in leads I, II, III and VF and all precordial leads. (Right) Significant ST segment elevation in leads V1-4 during an exercise test

coronary arterial tree, especially as any coronary abnormality is likely to have been focal. Nor is there any evidence that these lesions are secondary to the actual myocardial pathology. Russell¹⁴ found lesions causing stenosis of the large arteries in two of his four cases, and Boyer *et al*¹⁵ found atheromatous lesions in one (a 25 year old woman) of two necropsy cases. Such anatomical lesions may not be the sole cause of coronary ischaemia, however, both arterial tone and vasomotor reactivity are possible causes of ischaemic cardiomyopathy. Coronary spasm can affect both factors. Margalith *et al* described a case of Friedrich's ataxia in which coronary spasm was detected.¹⁶

Case report

We present the case of a 16 year old boy with an unremarkable personal and family history in whom angina during exercise developed when he was 9. A resting electrocardiogram subsequently showed abnormal ventricular repolarisation, with negative T waves in all leads (fig 1A). A standard echo-Doppler study was normal. Holter monitoring for 24 h showed no significant changes in ventricular repolarisation at the high cardiac rates at which the chest pain had occurred. While the patient was undergoing a standard Bruce protocol exercise testing he complained of precordial pain which made it necessary to stop the test. There were slight changes in the ST segment. Myocardial scintigraphy (thallium-201) showed signs of posterobasal and inferior hypoperfusion without redistribution. In view of this finding, a haemodynamic study with coronary arteriography was performed. This did not show any coronary lesions and confirmed that left ventricular systolic function was normal.

Given the absence of morphological abnormalities, the case was classified as "thoracic pain during physical exercise" with no clear evidence of myocardial ischaemia. The patient was instructed to have regular cardiological examinations. The symptoms continued but the patient learnt to stop exercising before becoming ill.

When he was 13 he was referred to our hospital. The clinical tests were repeated. The results were identical with those obtained earlier (fig 2), except for the exercise test, which showed that repolarisation had become more abnormal (fig 1B). Myocardial scintigraphy with ^{99m}Tc-labelled methoxyisobutyl isonitrile (MIBI), however, was normal. Treatment with nifedipine (30 mg/day) was started, without significant improvement. Verapamil was then tried (240 mg/day). This delayed the onset of thoracic pain on exercise, as confirmed in repeat standard Bruce protocol exercise testing.

During the physical examination kyphoscoliosis was found and he consulted an orthopaedic surgeon. At consultation, Friedrich's ataxia was suspected. Over the next year incoordination of the legs became progressively evident.

When he was 16 a new cardiac ultrasound study showed a slightly hypertrophied, non-dilated left ventricle (septum 12mm, posterior wall 11 mm) with normal systolic function (fig 3).

Comments

We believe that there are enough reported studies to confirm that coronary involvement is an integral part of the cardiomyopathy associated with Friedrich's ataxia. Our patient seems to be an example of such

Figure 2 Normal echocardiographic study when the patient was 13 years old

involvement. We cannot, however, rule out a vasospastic factor in our patient. No biopsy was carried out to assess whether there were lesions in the small coronary vessels, but in view of the published data and the clinical history of the patient, we think we have

sufficient evidence to regard coronary ischemia as the cause of thoracic pain in our patient. Angina is a rare symptom in children and adolescents and we have not been able to find any other cases that resemble our patient.

Figure 3 Echocardiogram showing slight hypertrophy of the left ventricle when the patient was 16 years old

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