

## SHORT REPORT

## Friedreich's ataxia presenting after cardiac transplantation

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### Abstract

**A 4 year old boy underwent cardiac transplantation because of cardiomyopathy with ischaemia. Following transplantation he developed neurological signs of Friedreich's ataxia and the diagnosis was confirmed with genetic testing. Cardiomyopathy is a rare presentation of Friedreich's ataxia and to our knowledge this is the first reported transplant operation for the cardiomyopathy associated with this condition.**

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Keywords: cardiac transplantation; Friedreich's ataxia; cardiomyopathy

Cardiomyopathy is the indication for transplantation in at least half of the recipients in most paediatric series.<sup>1,2</sup> Most of these are idiopathic dilated cardiomyopathies or acute myocarditis but occasionally there are other unusual causes.

### Case report

A 2 year 9 month old boy presented with a two month history of cough and increasing shortness of breath. Clinical examination revealed signs of cardiac failure with tachypnoea, tachycardia, displaced apex beat, gallop rhythm, and hepatomegaly. Chest x ray showed cardiomegaly and a small left basal effusion. Electrocardiography showed some depolarisation changes in the lateral leads. Echocardiography showed a dilated heart with very poor function but which was structurally normal with normal coronary arteries. This was confirmed at cardiac catheterisation. Investigations for viral and metabolic causes of cardiomyopathy were uninformative.

There was a good response to frusemide, captopril, and digoxin and, as ventricular function improved, symmetric hypertrophy of the left ventricle became more apparent. Four months later he started to complain of chest pain on exertion. An exercise test showed evidence of ischaemia and a radionuclide uptake scan (technetium-99 sestamibi SPECT) showed perfusion defects, particularly apically and anteriorly. He was referred and accepted for cardiac transplantation. While on the waiting list, in the months leading up to his fourth birthday, he developed intermittent

symptoms of leg weakness, difficulty in getting up from sitting, and had occasional falls. There was mild proximal leg weakness, tendon reflexes were present, and otherwise neurological examination was normal. Investigations performed at the local centre, including creatine kinase, lactate, and muscle biopsy including histochemical stains for mitochondrial enzymes (NADH-TR, cytochrome oxidase, phosphorylase, phosphofructokinase, succinate dehydrogenase, and adenylate deaminase) were non-contributory. It was felt that his symptoms were caused by his general debilitation and poor cardiac function.

He underwent cardiac transplantation at age 4 years 4 months. He had an uneventful post-transplantation recovery and no problems with rejection. By six weeks post-transplantation he had excellent cardiac function but continued to struggle when walking distances, climbing stairs, or standing up. Repeat muscle biopsy performed at the transplantation centre (including enzymatic assays of mitochondrial respiratory chain function) was normal apart from an increased proportion of type "2C" (intermediate) fibres, probably caused by restricted physical activity. By three months post-transplantation he was also developing a mild scoliosis and pes cavus. A neurologist at the transplantation centre diagnosed limb and truncal cerebellar signs, diminished tendon reflexes in the upper limbs, absent reflexes in the lower limbs, and bilateral upgoing plantars. He did not have Gower's sign, dysarthria, or any hearing or visual defects. Genetic testing confirmed the clinical diagnosis of Friedreich's ataxia.

By six months post-transplantation his neurological symptoms had not progressed further. He maintained normal blood glucose (both Friedreich's ataxia and the immunosuppressive drug tacrolimus predispose to glucose intolerance). His transplanted heart function remained excellent.

### Discussion

Friedreich's ataxia is an autosomal recessively inherited spinocerebellar degenerative disease, associated with a triplet GAA repeat expansion in the first intron of the frataxin gene on chromosome 9.<sup>3</sup> Frataxin is a protein involved in regulation of mitochondrial iron content.<sup>4</sup> Incidence is 1 in 50 000<sup>5</sup> and typical presenta-

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tion is before 25, with gait or stance ataxia and dysarthria, lower limb areflexia, and an extensor plantar response. Reduced vibration sense, pes cavus, and scoliosis are often present.<sup>5,6</sup> Cardiomyopathy is frequent later in the course of the disease.<sup>7</sup> Triplet repeat lengths range from 7 to 29 in normal people and 66 to 1360 in Friedreich's ataxia patients.<sup>8</sup>

Since the location of the frataxin gene in 1988<sup>3</sup> and availability of genetic testing for Friedreich's ataxia, a broader clinical spectrum in terms of age and presenting features is now recognised.<sup>8,9</sup> Early onset and rate of progression are predicted by large expansions.<sup>5</sup> However, it is very unusual for cardiomyopathy to be the presenting feature and we can identify only five cases described in the literature where this has occurred.<sup>10-12</sup> None were as young as our patient, in keeping with the large repeat length in this child.

To our knowledge this is the first case published of a patient with Friedreich's ataxia undergoing cardiac transplantation. This is probably because cardiomyopathy usually occurs after neurological disease is well established and the poor prognosis precludes transplantation. Our patient is unusual in that he had early life threatening cardiomyopathy but mild neurological disease. If we had recognised the genetic abnormality before transplantation, the prognosis of neurological disease and survival after cardiac transplantation (50-60% at 10 years)<sup>13</sup> would have been discussed with his parents before making a decision with

them. The cardiac transplantation has almost certainly improved his life expectancy.

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