Friedreich’s Ataxia Cardiomyopathy: Case Based Discussion and Management Issues

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Abstract
Cardiac involvement is common in Friedreich’s Ataxia and is a common cause of premature death. Evidence regarding treatment of congestive heart failure in patients with Friedreich’s Ataxia is lacking. The case of a 31-year-old male with advanced Friedreich’s Ataxia who presented with an acute diaphoretic illness and features of acute heart failure is discussed. We then review the reported cardiac manifestations of Friedreich’s Ataxia and discuss management options.

Introduction
Friedreich’s Ataxia is the most common inherited ataxia, with a prevalence of 1:29000 live births. Cardiac involvement is common and consists of a distinctive cardiomyopathy characterised by concentric left ventricular hypertrophy. This leads to congestive cardiac failure and is a common cause of premature death among these patients. Average life expectancy is reduced to between 40 and 50 years. There are few reports of optimal management of Friedreich Ataxia Cardiomyopathy.

Case Report
A 31-year-old male with a diagnosis of Friedreich’s Ataxia was brought to hospital complaining of feeling generally unwell with diaphoresis for one week, vomiting and feeling febrile. During this short history he developed a non-productive cough with shortness of breath. On examination he was hypotensive and had an irregular tachycardia. Cardiac, respiratory and abdominal exams were otherwise unremarkable. Neurological examination revealed sustained nystagmus on lateral gaze, absent reflexes and dysmetria. He was also diaphoretic. Investigations revealed leukocytosis (11.2) with neutrophilia, elevated inflammatory markers (CRP 3.62) and urea (7.3). ECG revealed atrial fibrillation with a ventricular response of 162/min. There were lateral repolarisation abnormalities. CXR revealed moderate cardiomegaly.

He was initially treated with metoprolol orally. bedside echocardiography demonstrated a dilated left ventricle with moderate to severe global hypokinesia. The impression was of a dilated cardiomyopathy with reduced ejection fraction. He was commenced on amiodarone, bisoprolol, lisinopril, diuretics and anticoagulation. The next day he demonstrated considerable haemodynamic improvement. Over the following days the patients doses of beta blocker and ACE inhibitor were uptitrated. On day 5 his heart rate had increased again to 140 and he received oral digoxin loading. This resulted in adequate rate control and digoxin was continued. Further investigations included thyroid function tests, which were normal. A departmental echocardiogram demonstrated an ejection fraction of 25 to 35%. (Figure 1). A diagnosis of Friedreich Ataxia cardiomyopathy was made, with intercurrent gastroenteritis and a tachycardia induced further impairment of left ventricular function. Discharge medications included a diuretic, high dose beta blocker and ACE inhibitor, and warfarin. Heart failure management also consisted of a low sodium diet, fluid restriction, and dietitian referral.

Discussion
Friedreich’s ataxia is an autosomal recessive neurodegenerative disorder caused by a GAA trinucleotide expansion on chromosome 9q13. The FRDA gene encodes a mitochondrial protein frataxin, whose function is uncertain. Mitochondrial dysfunction in frataxin deficient in frataxin show high concentrations of iron, with subsequent irreversible cell damage. The FRDA gene is preferentially expressed in heart and central nervous system tissue. The disease is manifested by a distinctive cardiomyopathy characterised by concentric left ventricular hypertrophy. This leads to congestive cardiac failure. The disease is manifest phenotypically by hypertrophy of the interventricular septum and increased left ventricular mass index. The cause of hypertrophy in patients with Friedreich’s Ataxia may be a consequence of myocardial energy deficiency.

The most common symptoms are shirghtness of breath at rest and palpitations. The most common findings are an ejection systolic murmur and a third or fourth heart sound. ECG abnormalities include repolarisation abnormalities, left axis deviation, widespread T wave inversion and ventricular hypertrophy. Echo abnormalities most commonly consist of concentric left ventricular hypertrophy. The majority of patients with Friedreich’s Ataxia have normal cardiac function and are not at high risk for heart transplantation. Treatment modalities are limited, particularly in the pre-transplant era. There is evidence that treatment with diabeneone, an antioxidant, prevents progression of the disease in animal models. Beta blockers and ACE inhibitors have been shown to improve myocardial energetics.

Treatment with these agents may attenuate the compensatory response of hypertrophy by improving myocardial energetics. We may hypothesize for this reason that these agents are particularly effective in Friedreich Ataxia Cardiomyopathy.

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References
1. Babcock M et al. Regulation of mitochondrial iron accumulation by Yfh1, a putative homolog of frataxin. Science 276 (1997), 1709–1712
4. Burns M et al. Cardiac energetics correlates to myocardial hypertrophy in Friedreich’s ataxia. Ann Neurol 52: 121-123
9. S1,2,3,4,5,6,7,8,9,10,11,12