Cardiology in the Young (2015), **25**, 1418–1420
doi:10.1017/S1047951114002303

Brief Report

Treatment of depression in an adolescent with cardiomyopathy and arrhythmia

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Abstract Patients with cardiomyopathy have a higher incidence of mood and anxiety disorders, resulting in greater probability for hospitalisation and increased risk for arrhythmia and death. We report a case of a 16-year-old boy with Danon disease, Wolff–Parkinson–White syndrome, and hypertrophic cardiomyopathy, who later developed depression and significant weight loss. The patient was successfully treated for his anxiety and depression with mirtazapine without any adverse cardiac effects.

Keywords: Arrhythmia; Danon disease; depression; hypertrophic cardiomyopathy; mirtazapine

Received: 23 December 2013; Accepted: 15 October 2014; First published online: 17 November 2014

DEPRESSION AND ANXIETY ARE COMMON AMONG adolescents with heart disease, with an incidence of ~30–40% in young adults with complex CHD.[1–2] Depressed patients with heart failure have an overall poor quality of life with adverse outcome, while children with heart failure experience demonstrable neuronal loss in the areas of the brain responsible for mood regulation, autonomic function, and memory.[3]

Selective serotonin re-uptake inhibitors are generally recommended as first-line psychotropic agents for depressed patients with heart failure; however, if selective serotonin re-uptake inhibitor therapy is not well tolerated or if adjunctive therapy is required, bupropion, mirtazapine, venlafaxine, and duloxetine can be used as suitable alternatives.[4]

Case

A 16-year-old boy with confirmed Danon disease and associated cardiomyopathy was living with his father and stepmother. He had ceased school attendance because of his cardiac disease. His biological mother died due to a similar cardiac disease when he was 10 years old. He was referred to our clinic because of sustained supraventricular tachycardia that caused heart failure (Fig 1a). On physical examination, his height was 181 cm (85–95th percentile) and his weight was 42 kg (5–10th percentile). Genetic testing identified a pathogenic mutation in the lysosome-associated membrane protein 2. Echocardiographic examination demonstrated concentric left ventricular hypertrophy with interventricular septum and posterior wall measuring 18 mm each during diastole. The left ventricle was dilated and measured 50 mm at end systole and 60 mm during diastole. The left ventricular contractility was severely impaired with decreased ejection fraction of 28–32%. There was no evidence of either static or dynamic obstruction to the left ventricle outflow tract. A typical Wolff–Parkinson–White syndrome pattern was noted in his previously recorded electrocardiogram (Fig 1b). His tachycardia persisted despite anti-arrhythmic therapy – amiodarone infusion 10 mg/kg/day and propafenone 350 mg/m^2/day – for 5 days. In view of low ejection fraction (26%), catheter ablation of the accessory pathway was

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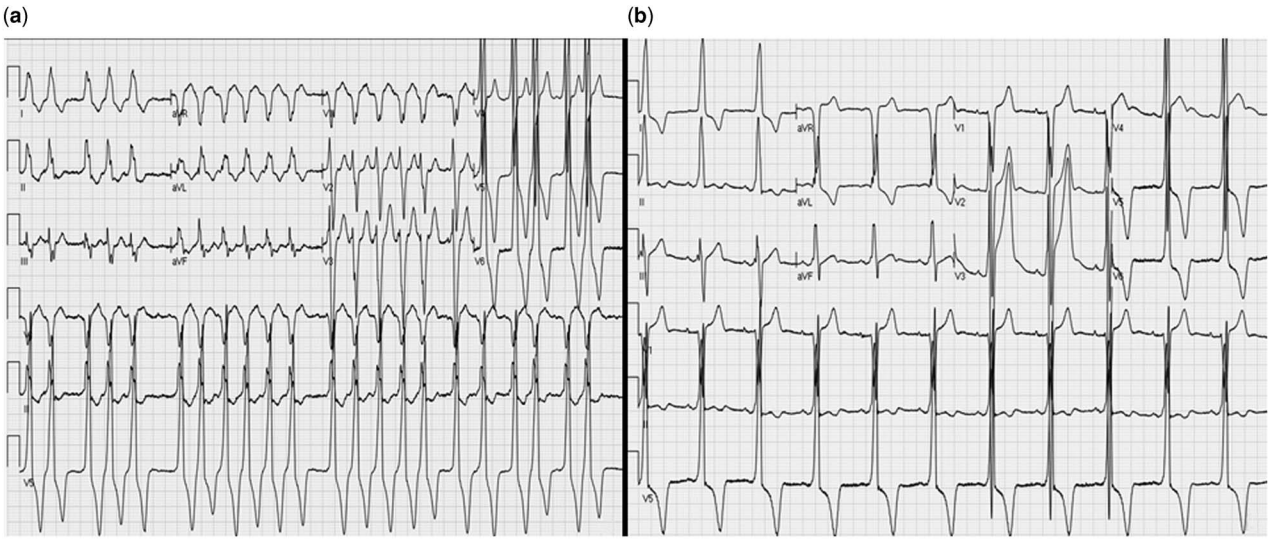

Figure 1.
*A twelve-lead electrocardiogram (**a**) during tachycardia and (**b**) after tachycardia.*

attempted. Attempts to cryoablate the parahissian accessory pathway were, however, unsuccessful. The tachycardia stopped on the 7th day while he was still on anti-arrhythmic therapy. A transvenous implantable cardioverter defibrillator was implanted and the patient was discharged on propafenone, amiodarone, enalapril, and warfarin.

The patient seemed withdrawn, ate very little, and talked rarely with the nursing staff. He appeared to be very depressed and demonstrated significant weight loss during his stay in the paediatric cardiac ICU, and therefore he was referred to the child and adolescent psychiatric clinic at a mental health hospital, which was located at a distance. During his psychiatric examination, the patient exhibited a depressed mood and anhedonia. He had loss of appetite and sleep disturbances, and his intelligence quotient was in the borderline range. He displayed anxiety about the medical procedures and fear of eating solid food, losing 6 kgs in 1 month.

As the patient had limited intelligence and poor verbalisation skills, and as the psychiatric clinic was at another hospital requiring ambulance transportation, pharmacotherapy was preferred over psychotherapy. Mirtazapine was chosen for his depression and anxiety because of its antidepressant and anxiolytic actions, its positive effect on weight gain, and its availability in liquid form. A few weeks after starting 15 mg/day mirtazapine, his mood improved, anxiety decreased, and he gained weight. After 4 months, he was admitted to the cardiology clinic for 8 days because of heart failure and was treated with intravenous inotropic agents. At that point, he weighed 46 kg and showed a better mood. He was re-admitted to the clinic for 10 days after 6 months, again because of heart failure, at which point he weighed 52 kg and his mood was euthymic.

During the follow-up period of 10 months, mirtazapine was continued at the same dose (15 mg/kg/day). None of his serial electrocardiograms or 24 hour Holter monitor recordings showed tachyarrhythmia. Unfortunately, this patient died after 15 months of his initial diagnosis because of his hypertrophic cardiomyopathy complicated by life-threatening arrhythmias and heart failure, which are natural consequences of Danon disease.

Discussion

Danon disease is a rare X-linked multi-system disorder that has been more commonly described in boys. The disease is characterised by hypertrophic cardiomyopathy, skeletal myopathy, and mental retardation in young men, and is caused by a deficiency of the lysosome-associated membrane protein 2. The electrocardiogram usually reveals Wolff–Parkinson–White syndrome characterised by a pre-excitation pattern, as was seen in our patient, and therefore these patients are at a risk for life-threatening arrhythmias.[5] This is a serious health problem for the affected men, where survival beyond 25 years without a cardiac transplant is unlikely.[6]

In our patient, the heart failure developed due to long-standing tachycardia, and medical treatment with anti-arrhythmic drugs failed to control this arrhythmia. Ablation was attempted, but it failed because of the precarious location of the accessory pathway in close proximity to the His bundle. Atrioventricular node ablation with the implantation of a pacemaker was also one of the options, but it was not considered because long-term pacing can potentially worsen the left ventricular function.

https://doi.org/10.1017/S1047951114002303 Published online by Cambridge University Press

Before discharge from the hospital, the options of defibrillator implantation and heart transplantation were discussed, and an implantable cardioverter defibrillator was implanted for short-term benefit.

Living with the risk of a life-threatening disorder having an uncertain course is known to cause anxiety.[2] In addition to his medical conditions, he had additional risk factors such as loss of his biological mother because of a similar cardiac disorder, which may have been a constant stress factor for him. Multiple unsuccessful attempts at the treatment of his arrhythmic episodes were also responsible for an increase in his anxiety level. The factors that led to depression included the early death of his mother, multiple hospital admissions, inability to enrol in an educational programme, not having a job, limited social support, and the numerous medications with their potential side effects.

Mirtazapine belongs to a new class of drugs referred to as noradrenergic and specific serotonergic antidepressants. It enhances both central noradrenergic and serotonergic neurotransmission by directly inhibiting noradrenergic α2-autoreceptors and α2-heteroreceptors. Preliminary clinical data suggest that it is safe and well tolerated.[7] Weight gain, as seen in our patient, is a frequent and most commonly reported side effect of mirtazapine therapy. Being a moderate peripheral α1 adrenergic antagonist, mirtazapine occasionally causes orthostatic hypotension; however, clinical experience in patients with concomitant systemic illness is limited. In a particular study involving a retrospective analysis of electrocardiographic data collected from patients admitted to the emergency department due to citalopram, mirtazapine, and venlafaxine overdose, citalopram was found to be associated with prolonged QT and torsades de pointes, whereas this arrhythmia was not reported after mirtazapine or venlafaxine overdose.[8] In another study that compared the cardiac safety of antidepressants, mirtazapine was found to be associated with a marginally higher arrhythmogenic risk, but it was concluded that there were no large differences in arrhythmogenic risk among the antidepressants.[9] Our patient, fortunately, did not develop any arrhythmias on mirtazapine despite having cardiomyopathy and Wolff–Parkinson–White syndrome.

Although selective serotonin re-uptake inhibitors are first-line psychotropic agents in the treatment of depression in individuals with heart failure, we decided to use mirtazapine because of its availability in liquid form, its effects on weight gain, and because of the presence of sleep disturbances in our patient. Our past experience with mirtazapine, in children with choking phobia who were afraid of eating solid food, showed that it rapidly improved symptoms of anxiety associated with choking phobia. Our patient also had a fear of eating solid food, besides depression, and thus we decided to use mirtazapine instead of a selective serotonin re-uptake inhibitor. Knowing that he would be under the supervision of cardiologists, the concern over cardiac side effects was much less. Although our patient had significant cardiac risk factors, mirtazapine did not worsen his cardiac status, but it improved his depressed mood and increased his appetite.

Conclusions

Depression and anxiety are common and often affect the quality of life in patients with significant heart disease. Such patients must therefore be referred to a child and adolescent psychiatrist for the management of their mood disorder. Mirtazapine, as seen in our patient, appears to be a safe option for the treatment of depression in patients with cardiac problems; however, further prospective studies in a larger number of patients with a longer follow-up period are necessary to examine the effects of mirtazapine on the cardiovascular system.

Acknowledgement

None.

Financial Support

This research received no specific grant from any funding agency, commercial or not-for-profit sectors.

Conflicts of Interest

None.

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