CASE REPORT

Familial Himalayan P Wave and Left Ventricular Hypertrabeculation/Noncompaction

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Background: "Himalayan P waves," are reported in congenital heart disease and cardiomyopathies.

Methods: We report a family with hypertrophic cardiomyopathy, Himalayan P waves, extensive focal right atrial wall thickening and left ventricular hypertrabeculation/noncompaction (LVHT).

Results: The father received a pacemaker and underwent heart transplantation because of hypertrophic cardiomyopathy. His daughters showed Himalayan P waves and right atrial wall thickening. LVHT was diagnosed in sister A at age 23 years and developed in sister B between 42 and 46 years. In sister A the heart rate continuously declined. She refused implantation of a pacemaker and died with 49 years. Sister B, suffers from bradycardia.

Conclusions: Himalayan P waves are due to focal right atrial wall thickening, may be familiarly and associated with LVHT.

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giant P wave; cardiomyopathy; hypertrophic cardiomyopathy; left ventricular noncompaction

Giant P waves in the ECG are also termed "Himalayan P waves." They are reported in congenital heart disease, various cardiomyopathies including left ventricular hypertrabeculation/noncompaction (LVHT), and in the setting of severe hypoxemia (Table 1).^{1–8} Familial Himalayan P waves have not been described. We report a family, in whom the father underwent heart transplantation because of hypertrophic cardiomyopathy and his two daughters showed extensive focal right atrial wall thickening associated with LVHT.^{9,10}

DESCRIPTION OF THE FAMILY

The father of the two had received a pacemaker in 1963 at age 33 years because of Adams-Stokes attacks. At age 58 years, polycythemia vera and polyglobulia (erythrocytes 7.000.000/ μ L) were

diagnosed and treated by phlebotomies. At that time a dilated left ventricle with decreased systolic function was diagnosed, and he underwent heart transplantation at age 60 years. The explanted heart showed right ventricular lipomatosis and disarray of the hypertrophic cardiomyocytes with bizarre hyperchromatic nuclei, perinuclear vacuoles, degenerated myofibrils and interstitial fibrosis, and the pathologic diagnosis of hypertrophic cardiomyopathy was established. The patient died due to lymphoma at age 62 years.

Sister A was born in 1962 as the first child to nonconsanguineous parents. Since the age of 18 months a systolic heart murmur and pathological P waves were mentioned. During her first pregnancy at age 23 years she developed shortness of breath and cyanosis during exercise. The ECG showed sinus rhythm with giant sharp P waves, higher than the R waves, in leads II, III, aVF,

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Table 1. Cases with “Himalayan” P Waves, Reported in the Literature

Ref.	Age/sex	Cardiac findings	Therapy, outcome
1	8 years/f	Tricuspid valve stenosis and regurgitation, pulmonary valve stenosis, enlarged right atrium	Cardiac surgery
2	55 years/f	Respiratory insufficiency, emphysema, hypoxemia	Intubation, ventilatory support
3	8 months/f	Tricuspid atresia	Bialock–Taussig shunt, single ventricle palliation planned
4	28 years/m	Right ventricular cardiomyopathy, tricuspid regurgitation, heart failure, ventricular tachycardia, atrial flutter	Beta-blocker, amiodarone
5	15 years/f	Hypertrophic cardiomyopathy, concentric hypertrophy of both ventricles, reduced systolic function, right atrial hypertrophy and dilatation	Heart transplantation
6	36 years/m	Heart failure, supraventricular tachycardia, enlarged atria and ventricles, left ventricular noncompaction	Pharmacotherapy, sudden cardiac death
7	22 years/f	Sudden cardiac death of the brother, heart failure, systolic dysfunction, increased septal thickness, biatrial dilatation, restrictive cardiomyopathy	Pharmacotherapy, implantable cardioverter defibrillator, listed for heart transplantation
8	14 years/f	Heart failure, dilated right atrium, restrictive cardiomyopathy	Pharmacotherapy

Figure 1. Electrocardiogram of sister A taken in 1986 at age 24 years. Standard, Goldberger, Wilson, and Nehb leads (25 mm/s).

and V₁–V₂ (Fig. 1). Right atrial wall thickening and LVHT were visualized by echocardiography and cardiac magnetic resonance imaging. She refused endomyocardial biopsy. She delivered a healthy child by caesarean section. A continuous decline of the heart rate was observed over time (Fig. 2). Right atrial wall thickening as well as LVHT remained unchanged (Fig. 3). She refused implantation of a pacemaker, and died suddenly at age 49 years. No autopsy was carried out.

Sister B was born in 1966. At age 39 years, she presented with exertional dyspnea and

Figure 2. Electrocardiogram of sister A taken in 2000 at age 38 years (25 mm/s). The morphology of the P waves has changed. New repolarization abnormalities and one supraventricular ectopic beat are visible.

Figure 3. Cardiac magnetic resonance imaging of sister A at age 38 years showing right atrial wall thickening (asteriks) and left ventricular hypertrabeculation/noncompaction (arrow).

Figure 4. Electrocardiograms of sister B taken in 2006 at age 39 years (A) and in 2012, at age 45 years (B and C) (25 mm/s). Two different P-morphologies with different heart rates are visible in Panel B and C (arrows).

generalized fatigue with a history of palpitations, recurrent syncope with cloni, migraine, double vision, exercise-induced muscle aching, recent history of nausea, vomiting, diarrhea, renal insufficiency, hypothyroidism, and depression. ECG showed sinus rhythm with giant sharp P waves, higher than the R waves, in leads II, III, aVF, V₁-V₂ (Fig. 4). Twenty-four-hour Holter monitoring showed sinus rhythm with episodes of ectopic atrial bradycardia. Echocardiography and cardiac magnetic resonance imaging showed marked thickening of the right atrial wall and normal left-sided cavities (Fig. 5).⁹ Right atrial myocardial biopsy disclosed diminished myofibrils, perinuclear and intracytoplasmic vacuoles, but no fibrosis. Electron microscopy showed a diffuse increase of the number of mitochondria but no abnormalities. DNA-investigations for Fabry's disease showed two heterozygous polymorphisms for *GLA* 5'UTR, -10C/T in exon 1 and *GLA* 10115A >

G in intron 4. At age 45 years LVHT of the left ventricular apex was diagnosed.¹⁰ The morphology of the P waves changed and she suffered from bradycardia with a minimal heart rate of 28/min (Fig. 4). She refuses implantation of a pacemaker and genetic testing for sarcomere mutations, so far.

DISCUSSION

Most probably, the father and his two daughters suffered from the same cardiomyopathy associated with bradyarrhythmia. Since no ECG of the father is available it remains uncertain if he showed also Himalayan P waves. The substrate for Himalayan P waves was right atrial thickening which did not increase over time, whereas the decline in heart rate, changes in the morphology of the giant P waves, and development of LVHT may indicate progression of the cardiomyopathy.

Figure 5. Cardiac magnetic resonance imaging of sister B at age 45 years showing right atrial wall thickening.

As shown on Table 1, more females than males are reported with Himalayan P waves.^{1–8} It is unknown if this is just coincidence or if females are more prone than males to develop Himalayan P waves. Himalayan P waves are attributed to right atrial dilatation due to volume or pressure overload in cardiac or pulmonary diseases. Right atrial wall thickening associated with Himalayan P waves, like in our patients, is only rarely reported in the literature.^{4,5} Himalayan P waves associated with atrial tachycardia have been already reported in a 36-year-old man with LVHT who died suddenly, however it is not mentioned if the atrial walls were thickened or not.⁶ Bradyarrhythmias in LVHT have been already described, however not associated with Himalayan P waves.¹¹

Thickened atrial walls might also be due to right atrial hamartoma. However, Himalayan P waves have not been described in patients with hamartoma.¹² Hamartoma is rather unlikely in our patients since the findings at biopsy were not suggestive of a hamartoma, and the family history favors the diagnosis of a cardiomyopathy.

LVHT is a cardiac disorder of unknown etiology which might be congenital or acquired.¹³ LVHT has been reported as an isolated cardiac abnormality as well as associated with various cardiac and extracardiac abnormalities, including neuromuscular disorders. Familial occurrence of LVHT is frequent with autosomal dominant and X-linked transmissions. Different mutations in sarcomere protein genes were identified and there seems to be a shared molecular aetiology of different cardiomyopathic phenotypes, including LVHT, hypertrophic, and dilated cardiomyopathies.^{14,15} Unfortunately, no genetic studies of the presented patients are available so we cannot assess if the father's hypertrophic cardiomyopathy and the sisters atrial wall thickening and LVHT were due to the same mutation. Furthermore, it is uncertain if LVHT in the sisters is congenital or acquired. Review of previous recordings disclosed that LVHT was documented in sister A starting from the first investigation in 1986, thus LVHT was either congenital or acquired during adolescence. Since the follow-up period of sister B is only 6 years, it is uncertain whether LVHT is acquired or of "undulating" type, as described in children.¹⁶

This family shows that Himalayan P waves may be familial, that they are due to focal right atrial wall thickening, that LVHT may be associated with Himalayan P waves, and that focal right atrial thickening may be associated with bradyarrhythmia and sudden death.

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