

Familial Progressive Cardiac Conduction Disorder and Multiple Exostoses

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Introduction

Familial cardiac conduction disorder of a progressive nature has been reported in adult and paediatric patients¹⁻⁴. An underlying cardiomyopathy was found in most of these patients, either of hypertrophic^{1,2}, restrictive⁵ or dilated variety³. Systemic diseases like juvenile rheumatoid arthritis and other collagen disorders and familial dysautonomia infrequently have associated conduction abnormalities⁶⁻⁹. We present a family in which four of seven siblings had abnormalities of cardiac conduction and no concomitant cardiomyopathy or systemic disease. Additionally, there was an association of multiple bony exostoses in six siblings and deafness in two (Table I). The purpose of this presentation is to highlight the association of two familial abnormalities in one family.

Case Report

Case 1

SM, a thirteen year old boy, previously asymptomatic, presented with one 'day's history of syncope and tonic-clonic seizures occurring four hours prior to admission. Clinically, he was afebrile, had a heart rate of 30/min, a respiratory rate of 30/min and a blood pressure of 90/60 mm of Hg. He also had multiple exostoses around the wrists and elbow joints and had a severe bilateral conductive hearing loss of 90 decibels at a 2000 hertz frequency. The electrocardiogram showed complete heart block with atrial rate of 100 beats/min and ventricular rate of 25 beats/min with a QRS duration of 0.12 seconds (Table II).

Table II. Electrocardiographic findings in the siblings.

S.NO.	Atrial Rate/min	Ventricular Rate/min	PR Interval (sec)	QRS Duration (sec)	QTC Interval (sec)	QRS Axis	Complete Heart Block	Bundle Branch Block	Bi-Fascicular Block
1.	100	30	-	0.12	0.35	-24°	+	-	-
2.	100*	75*	0.28	0.12	0.35	-50°	-	+	+
3.	150	28	-	0.12	0.46	0°	+	-	-
4.	86	86	0.14	0.16	0.48	+120°	-	+	-
5.	100	100	0.12	0.08	0.37	+90°	-	-	-
6.	85	85	0.12	0.08	0.39	+90°	-	-	-
7.	125	125	0.10	0.08	0.36	+110°	-	-	-

* Averaged over six beats.

The echocardiography showed no structure and function abnormality in the heart, the left ventricular diastolic dimension being 37 mm, systolic dimension being 25 mm and the ejection fraction was 70% (normal 62-85%). The serum sodium was 134 meq/l, serum potassium was 4.2 meq/l, serum calcium was 9.4 mg/dl and serum cardiac enzymes were normal. Initially, he was managed with isoproterenol infusion at a dosage of 0.05 ug/kg/min and twenty-four hours later with a temporary pacemaker.

Unfortunately he succumbed to staphylococcus aureus septicaemia ten days later.

Case 2

U.M., a ten year old boy, presented to the emergency room with vomiting and abdominal pain. The heart rate was 25 beats/min, the respiratory rate was 40/min and the blood pressure was 50/30 mm of Hg. He had multiple bilateral exostoses around wrist, elbow, knee and ankle joints (Figure 1).



Figure 1. Bony exostoses (Case 2).

The hearing test was normal in this patient. The electrocardiogram showed a complete heart block (Table II) with atrial rate of 150 beats/min and the ventricular rate of 25 beat/min. The echocardiography showed a left ventricular diastolic dimension of 39 mm, systolic dimension of 25 mm and the ejection fraction of 73% (normal 62-85%). The serum sodium was 138 meq/L, serum potassium was 3.8 meq/L, serum calcium was 10.1 mg/dl. He had normal cardiac enzymes and the screening for collagen disorder was normal. The initial drug therapy included dopamine infusion in a dosage of 10 µg/kg/min and a temporary pacemaker which was later replaced by an epicardial VVI permanent pacemaker. The patient has remained well thereafter.

Case 3 and 4

JM and NM are eleven and nine year old boys respectively and are asymptomatic. They were screened for cardiac conduction defects and multiple exostoses. Both had exostoses of ends of long bones. Their electrocardiograms showed sinus rhythm and a heart rate of 70 beats/min and 80 beats/min respectively (Table II). There was a left bundle branch block in both and a left axis deviation in JM and right axis deviation in NM. After two years, the rhythm of JM deteriorated and he developed a first degree heart block, irregular heart rhythm with atrial extra systoles in addition to the left bundle branch block (bifascicular block). The echocardiography, serum electrolytes, serum calcium, cardiac enzymes and antinuclear antibodies were normal in both. Hearing tests revealed that JM had a conductive hearing loss of 60 decibels at 2000 hertz frequency, whereas NM had a normal hearing.

Case 5, 6 and 7

RF, a seven year old girl; AM and MM, three and five year old boys were also screened. RF and MM had multiple exostoses (Figure 2),

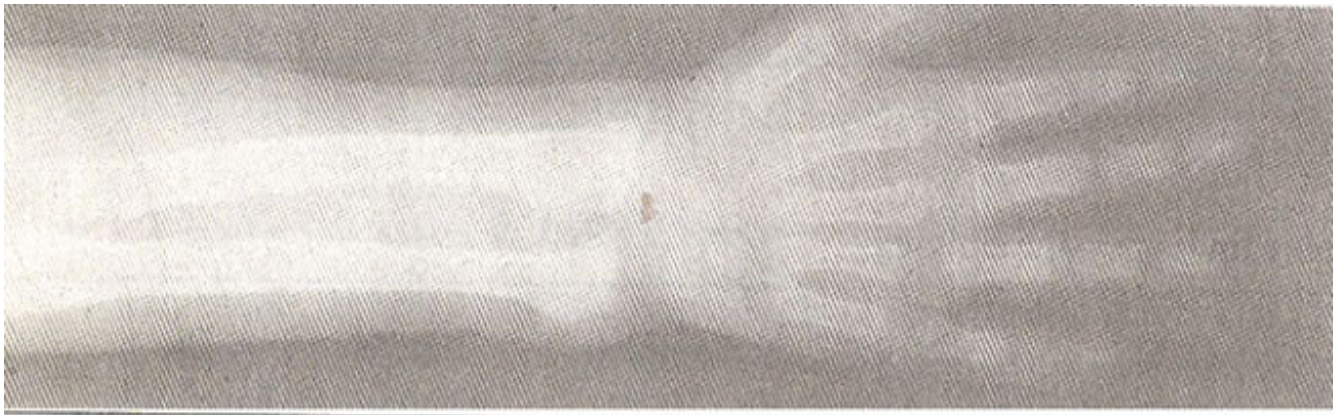


Figure 2. Bony exostoses (Case 5).

whereas, AM did not. All the three had nonnal electrocardiograms, a normal cardiac function on echocardiography and normal serum electrolytes, calcium and cardiac enzymes. Antinuclear antibodies and hearing tests were not performed..

Other family members

Mother, father and maternal grandmother did not have any abnormality on electrocardiogram or echocardiography. The mother's screening for autoimmune disease was normal. Four maternal uncles had unexplained deaths at the ages of four, nine, thirty and forty years. The other uncles and aunts could not be screened (Figure 3).

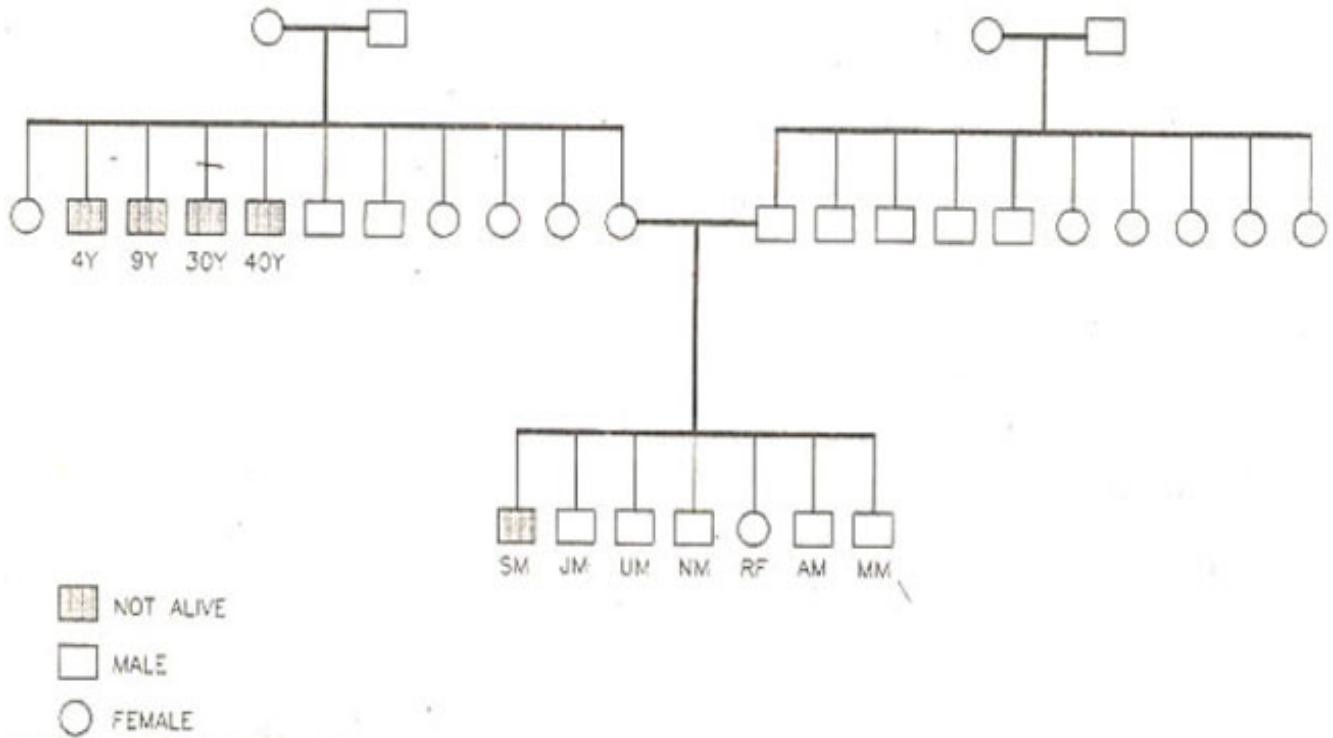


Figure 3. Family pedigree.

To summarize, out of seven siblings, four had cardiac conduction defects with multiple bony exostoses and two of them also had conductive deafness. Two of the remaining three siblings had only multiple bony exostoses.

Discussion

Heart block, which is discovered in early childhood, in the absence of any known cause, is usually regarded as congenital. Morquio in 1901, had described a family in which several siblings had bradycardia, syncope and died in childhood and proposed that complete heart block could be congenital and familial⁹. Congenital complete heart block may not present itself until the child is a few years old. The mean age of patients with complete heart block at presentation to The Hospital for Sick Children, Toronto, was 4.9 years⁹. The mean age at presentation in this family was 11.5 years. Four of seven (57%) had conduction defects with normal cardiac structure and function and six (85%) had multiple bony exostoses. Complete heart block in childhood is either congenital or acquired. Congenital complete heart block not associated with a structural heart disease may be familial in association with cardiomyopathy or systemic lupus erythematosus^{1,2,5,10}. Familial heart block of a progressive nature is an autosomal dominant disorder presenting at variable ages¹¹. The presence of a left anterior hemiblock associated with a right bundle branch block and a prolonged P-R interval (trifascicular block) on the electrocardiogram may provide a clue to patients at risk of progressing to a complete heart block¹². The progressive nature of the cardiac conduction disorder was seen in case number 3 in our series in whom the cardiac rhythm deteriorated and he developed, in addition to his previous dysrhythmia, a prolonged P-R interval and atrial extra systoles.

The exact pathogenesis of progressive conduction defect is not known. Cardiac conduction tissue develops in response to a genetic control different from that forming the rest of the heart. Anderson et al have hypothesized that a primary malformation of the conduction tissue, whereby after its formation it becomes interrupted by fibrosis, is responsible for the heart block¹³. Lev and his colleagues, in their extensive work, have sub-divided complete heart block in "normal" hearts into cases with discontinuity between atria and the node and those with discontinuity between the node and the ventricular conducting tissue. They proposed that the disrupted conducting tissue becomes replaced by spaces containing strands of collagenous and elastic tissue thereby producing a progressive conduction block^{14,15}. There have been no reports on any bone abnormalities occurring in association with cardiac conduction defects. Multiple exostoses are benign bone tumors, inherited as an autosomal dominant trait. They are rarely detectable even radiologically before three years of age¹⁶. Symptoms develop when the exostoses are large enough to compress neurovascular bundles or obstruct the external auditory meatus causing conductive hearing loss. This was the cause of conductive deafness in two siblings in our series (Table I).

Table I. General characteristics of the siblings.

S. NO.	Name	Age (years)	Sex	Conduction defect	Multiple exostoses	Deafness	Ejection Fraction (%)
1.	SM	13	M	+	+	+	70
2.	JM	11	M	+	+	+	88
3.	UM	10	M	+	+	-	73
4.	NM	9	M	+	+	-	67
5.	RF	7	F	-	+	-	72
6.	AM	5	M	-	-	-	74
7.	MM	3	M	-	+	-	75

Since cardiac conduction defects were present in four siblings and multiple exostoses in six, it seems

likely that cardiac conduction abnormality is genetically transmitted and the gene responsible is probably in close proximity to the one causing multiple exostoses or this may be an association by chance. Apart from the possibility of genetic transmission, congenital cardiac conduction defects could represent a developmental error encountered in the early embryological period¹³, the progressive nature manifesting in childhood. Follow-up of the two children who have multiple exostoses but no dysrhythmia would throw more light on the issue. In conclusion, serious conduction defects are present in a significant number of siblings of this family with structurally nonnal hearts. The association of exostoses raises interesting possibilities of gene location and transmission.

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