Sinuatrial disease in young people

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SUMMARY A survey at three cardiac centres disclosed nine patients under the age of 25 years with sinus node dysfunction in the absence of other forms of heart disease. All were male and seven were above the 90th centile for height. Ambulatory monitoring was performed on all the first-degree relatives of six of the patients and three families showed conducting system disturbances in the form of sinuatrial disorders or delayed atrioventricular conduction. A genetic factor may be involved in the aetiology of sinuatrial disease in young people.

The aetiology of sinus node dysfunction occurring without other forms of heart disease (sinuatrial disease) is often obscure.^{1,2} Sinuatrial disease is commoner in the elderly than in the young³ but little is known about the aetiology at any age. Older patients may have other diseases, such as coronary artery atheroma, which obscure the underlying cause of the sinuatrial disorder. Children and adolescents are unlikely to have additional diseases; so studies in this age group should be rewarding. But few accounts of sinuatrial disease in the young have been published as few patients of this age will be seen at any one cardiac centre.

Many of the young patients with sinus node dysfunction attending cardiac clinics were noticed by the author to be tall men or boys. In order to confirm this observation all the young patients with sinuatrial disease attending three cardiac centres were reviewed. An arbitrary upper age limit of 24 years was selected as it is similar to the age limit in other accounts of sinus node dysfunction in the young.⁴⁻⁶ Ambulatory monitoring was performed on the relatives of some of these young patients to document any familial incidence of conducting system disease and the results were compared with recordings from healthy young hospital staff.

Subjects and methods

All known patients, under the age of 25 years at the time of diagnosis, with *symptomatic* sinuatrial disease attending the cardiac departments at King's College Hospital, London, The Royal Sussex County Hospital, Brighton, and Papworth Hospital, Cambridge, were included in the study. Symptomatic sinuatrial disease was defined as syncope or dizziness suggestive of transient asystole together

with documented sinus node dysfunction on a resting electrocardiogram or during ambulatory monitoring. Sinus node dysfunction was defined as at least two of the following—sinus bradycardia less than 40 per minute during the day, atrial pauses greater than 2.25 seconds, or paroxysmal atrial tachycardias. Patients were excluded if they had any other form of heart disease except more distal conduction abnormalities. During an 18-month period the author was notified of any patients attending the cardiac departments who might fulfil these requirements. In addition, pace-maker records and departmental diagnostic indices were consulted for any suitable patient who might have been seen earlier. One patient and his family had been the subject of a case report in the past.⁷ All except two of the subjects identified had a bradycardia of less than 40 per minute during the day. The remaining two had unconsciousness produced by periods of asystole greater than eight seconds. The centiles for height were taken from the charts of The Hospital for Sick Children, Great Ormond Street, as compiled by Tanner and Whitehouse.

Twenty-one male medical students, doctors, and technicians were subjected to a 24 hour period of ambulatory monitoring. None had any heart disease and all showed a normal electrocardiogram. Twenty-nine potential subjects were approached individually and all except eight agreed to take part in the study. Medilog recorders (Oxford Instruments) and a Pathfinder analyser (Reynolds Medical) were used. A tape-check system was incorporated so that the cardiac rhythm was displayed only if the tape was running at the correct speed. The heart rates were measured from four consecutive RR intervals during sinus or junctional

rhythm. Pauses which might be secondary to premature beats were not included in the measurements of the maximum RR interval or the minimum heart rate. If a minimum of 18 hours analysable recording was not present the monitoring was repeated.

The first-degree relatives of some of the young patients with sinuatrial disease were available for a 24 hour period of ambulatory monitoring. Recordings were made with Medilog or Avionics recorders and replayed on a Pathfinder analyser. The tapes of the relatives and the healthy volunteers were analysed in an identical fashion. No relative was taking any drugs likely to influence the cardiac rhythm. The rhythms discovered in one family during this study have been described in detail elsewhere.⁸

Results

Nine patients with sinuatrial disease under the age of 25 years were found. All nine were male. Their ages ranged from 15 to 24 years, with a mean of 19. Five had received permanent pacemakers to control their symptoms. Many of these young patients were tall (Table 1). Seven were above the 90th centile for their age. Four of the five with pacemakers had a height on or above the 97th centile. Two had been described as Marfanoid because of their body habitus. One (case 3) had a height of 187 cm with a metacarpal index of 9.4. The other (case 1) was 195 cm tall with a metacarpal index of 8.4. This index is above 8.3 in most cases of Marfan's syndrome.⁹

The results of the ambulatory monitoring of the young volunteers are shown in Table 2. The minimum heart rate was always during the night. Few arrhythmias were seen. Four subjects had more than five ventricular ectopic beats in the 24 hours

Table 2 Ambulatory monitoring in 21 healthy male volunteers

Case no.	Age (y)	Height (cm)	Max. RR (ms)	Min. heart rate (beats/min)	Arrhythmias
1	21	185	1340	45	None
2	21	185	1780	37	None
3	21	179	1440	43	None
4	21	165	1590	41	None
5	20	176	1780	38	Intermittent ectopic atrial or junctional rhythm
6	22	184	1740	39	Junctional escape beats
7	22	177	1690	41	None
8	21	179	1900	34	None
9	24	167	1580	44	None
10	23	180	1700	40	Single supraventricular ectopics
11	25	183	1880	37	Junctional escape beats
12	21	185	1450	49	Single ventricular ectopics
13	23	177	2040	33	None
14	33	188	2300	34	None
15	26	179	1730	38	None
16	28	184	1560	42	None
17	28	187	1440	46	Single ventricular ectopics
18	30	183	1560	44	Single ventricular ectopics
19	28	179	1700	44	Single ventricular and supraventricular ectopics
20	31	176	1790	36	None
21	25	171	1710	36	None

and two had more than five supraventricular ectopic beats in one hour. In two subjects the longer RR intervals were terminated by junctional beats. One volunteer had periods of a rhythm with an inverted P wave and a short PR interval suggesting an ectopic atrial or junctional rhythm.

The results in this group of volunteers were used to decide which arrhythmias should be sought in the tapes of the relatives. The following arrhythmias were looked for: sinus bradycardia less than 35 beats per minute; atrial pauses greater than 2 seconds; definite sinuatrial block (PP interval twice preceding interval); first, second, or third degree atrioventricular block; supraventricular tachycardias; and junctional rhythms.

Sinus bradycardias greater than 35 beats per minute, Wenckebach sinuatrial block, single junctional beats, and single supraventricular or ventricular premature beats were not recorded.

All the first-degree relatives of six of the nine patients were available for study. Some relatives of three patients showed uncommon rhythms indicating possible conducting system abnormalities (Table 3).

Such rhythm disturbances were discovered in the relatives of case 3. In an elder brother periods of asymptomatic supraventricular tachycardia were

Table 1 Heights of the young patients with sinuatrial disease

Case no.	Age (y)	Height (cm)	Height (in)	Centile for age
<i>With permanent pacemakers</i>				
1	19	195	77	99
2	18	193	76	99
3	17	187	73½	97
4	21	187	73½	97
5	24	171	67½	30
<i>Without permanent pacemakers</i>				
6	24	188	74	98
7	15	183	72	95
8	22	184	72½	92
9	15	171	67½	50

seen on the 24 hour electrocardiogram. A maternal uncle had received a pacemaker for the bradycardia/tachycardia syndrome two years previously. The mother had been invalided out of the fire service during the second world war after two unexpected episodes of syncope. At the time she also had palpitation and occasional dizziness. In recent years she had been asymptomatic and no arrhythmias were seen on ambulatory monitoring. In this family, blood was taken for ABO grouping and HLA typing from the patient, his brother with the

supraventricular tachycardia, the uncle with the bradycardia/tachycardia syndrome, and the common relative, the mother. The mother and the patient shared the HLA haplotype A2, B15, and the mother, uncle, and brother shared the haplotype A3, B7. As the same haplotype was not common to all the affected members, the HLA type was unlikely to be a marker of the conducting system abnormalities in this family and further relatives were not tested.

The relatives of case 6 also showed some rhythm disturbances. The father had a persistent first-degree atrioventricular block with a PR interval of 0.24 seconds. The younger brother had intermittent type I second-degree (Wenckebach) atrioventricular block and occasional appearance of an ectopic atrial focus.

The family of case 7 was unusual in that both the mother and father had some evidence of conducting system disturbances. The rhythms discovered in this family have been described in detail before.⁸ Briefly, the mother presented in 1964 with palpitation and dizziness. Electrocardiograms showed intermittent sinuatrial block and one paroxysm of a supraventricular tachycardia. As her symptoms failed to resolve with drug treatment a permanent pacemaker was offered two years later but declined. Ambulatory monitoring showed that she was now in permanent atrial flutter. The ventricular rate was satisfactory in the absence of any drug treatment. In 1970 the father had an unheralded episode of loss of consciousness. The electrocardiogram showed a PR interval of 0.24 second. His PR interval is now 0.22 second. The sister is asymptomatic; ambulatory monitoring showed periods of a regular rhythm with inverted P waves and a shorter PR interval.

Some members of the other three families had rhythm disturbances which are more difficult to assess (Table 3). The younger sister of case 1 had intermittent ectopic atrial rhythm. The father of case 2 and the sister of case 8 had episodes of sinuatrial block as shown by a PP interval equal to twice the preceding PP interval.

Discussion

All the nine patients with symptomatic sinuatrial disease were male. Early accounts of sinuatrial disease at all ages suggested that there was no sex bias or possibly an excess of women.^{10 11} But these reports were based on hospital cases which form a selected group. The comprehensive population survey of bradycardias in Devon³ is more likely to disclose the true picture and this shows that sinuatrial disorders are twice as common in men

Table 3 Relatives of six young patients with sinuatrial disease

	Age (y)	Height (cm)	Centile for age	24 hour tape	
Case 1					
Father	49	182	85	Normal	
Mother	45	174	97	Normal	
Brother	24	185	95	Normal	
Sister	16	170	90	Ectopic atrial rhythm	
Case 2					
Father	45	195	99	SA block	
Mother	47	175	98	Normal	
Sister 1	20	173	96	Normal	
Sister 2	16	168	80	Normal	
Sister 3	15	170	90	Normal	
Case 3					
Father	56	182	85	Normal	
Mother	57	173	95	Normal	Previous syncope and palpitation
Sister 1	32	158	25	Normal	Intermittent unsteadiness
Brother 1	29	190	98	SVT	
Brother 2	26	184	92	Normal	Nocturnal epilepsy
Sister 2	22	170	90	Normal	
Sister 3	17	180	99	Normal	
Maternal uncle	48	183	90	—	Twin sister of patient Pacemaker inserted for brady/tachy syndrome
Case 6					
Father	57	178	60	1° AV block throughout	
Mother	47	170	90	Normal	
Brother	21	193	99	1° and 2° AV block and ectopic atrial focus	
Case 7					
Father	41	187	97	1° AV block throughout	Unexplained syncope
Mother	42	165	70	Atrial flutter throughout	Brady/tachy syndrome, refused pacemaker
Sister	14	161	50	Junctional rhythms	
Case 8					
Father	65	190	98	Normal	
Mother	53	158	25	Normal	
Sister	30	170	90	SA block	

SA, sinuatrial; AV, atrioventricular; SVT, supraventricular tachycardia.

as in women. The proportion of men was even greater in the younger age groups.

Published accounts of sinuatrial disorders in children show a male preponderance, though the number of cases is inevitably small. Yabek and Jarmakani⁴ described 30 patients under the age of 26 years with sinus node dysfunction; most also had congenital cardiac defects. Nineteen were male (male/female ratio 1.7:1). In a similar group of 20 patients under the age of 19 years, Radford and Izukawa⁵ found 13 boys (male/female ratio 1.9:1). Two groups of young patients with symptomatic sinus node dysfunction in the absence of other forms of heart disease also showed a male bias. In one account eight out of nine patients under the age of 25 were male.⁶ In the other report all six patients, whose ages ranged from 10 to 15 years, were boys.¹² None of these studies is large enough to provide conclusive evidence, but taken together with the present series they confirm an apparent male predominance among young people with sinuatrial disease. Some other cardiac arrhythmias also seem to be commoner in boys than girls. Examples include atrial fibrillation,¹³ atrial flutter in infancy,¹⁴ and Wenckebach atrioventricular block.¹⁵

Seven of the nine patients in this survey had a height above the 90th centile for their age. The significance of this finding is difficult to assess. Children with sinus node dysfunction in the absence of other forms of heart disease are often athletic^{12 16} but little attention has been paid to their heights in most reports. An occasional young patient has been noted to be particularly small in stature.¹² Conducting system disorders have been described in young patients with Marfan's syndrome but the disturbance is usually in the atrioventricular node or bundle-branches.⁹ Atrial flutter in infancy seems to be commoner in large babies.¹⁴ But the excess of tall subjects found in this survey of sinuatrial disease does not seem to have been noticed before.

If tallness is indeed related to symptomatic sinuatrial disease in the young, two explanations can be put forward. The first is that the height and the sinuatrial disease have a similar, probably genetic, origin. In the group of volunteers described here no correlation could be found between height and maximum RR interval or minimum heart rate. But this does not exclude a linkage between height and disordered node function in a few subjects. The other explanation is that both tall and short people can have the electrocardiographic abnormalities, but the tall subjects are more likely to develop symptoms. The tallness results in the patient being aware of the abnormal bradycardias and tachycardias. At present no further information

is available to help decide between these two explanations.

A fundamental problem with the ambulatory monitoring of the relatives was the lack of a clear division between normal and abnormal rhythms. Almost any rhythm can occur in a young asymptomatic subject with no previous evidence of heart disease.¹⁷ A division into common and uncommon rhythms is probably better than a division into normal and abnormal rhythms. So hospital staff were monitored to assess which rhythms would probably be detected in normal people by the recording and analysis system used in this study. A high incidence of sinus bradycardia, particularly during the night, was found; but no examples of atrioventricular block or abnormal tachycardias were seen. Published accounts of ambulatory monitoring in healthy volunteers have produced similar findings in the young.¹⁸⁻²⁰

Different results were obtained from the relatives. The monitoring showed atrial tachycardias or atrioventricular block in 20 per cent of these first-degree relatives. In addition, an uncle required a pacemaker to control his bradycardia/tachycardia syndrome. The number of affected relatives is small and it would be a mistake to draw a definite conclusion. It is possible, however, that a genetic factor may encourage the appearance of either sinus node dysfunction or more distal conduction abnormalities in members of the same family.

Familial sinuatrial disease is a rare, but well-recognised, entity which can take several forms. In some families the sinus node dysfunction occurs in the absence of other conducting system abnormalities.²¹⁻²⁴ But the commoner pattern seems to be for some members to have more distal conduction disturbances, in particular first-degree atrioventricular block.²⁵⁻³¹ Gambetta *et al.*²⁸ described a family with one member having pronounced sinus node dysfunction and seven other relatives showing a prolonged PR interval. Sarachek and Leonard²⁶ described a large family with 15 members affected by different combinations of sinus bradycardia and some degree of atrioventricular block. Thus, a familial factor can produce either sinus node dysfunction or atrioventricular conduction disturbances in close relatives. Such a factor could be present in some of the families of the young patients described here.

Sinuatrial disease is a rare condition in young people and the number of patients available for this study was small. Any conclusions must be tentative as it is possible that the subjects studied are not truly representative. Sinuatrial disease, however, does seem to be commoner in young men than in young women. Many of the sufferers are tall and

there is a suggestion of a familial factor in the aetiology. The demonstration of an inherited factor in the young might affect our understanding of the disease in all age groups. The identification of subjects at risk at any age would enable the diagnosis to be made earlier and would reduce unnecessary suffering.

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