Familial Sinus Node Disease*

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A family with evidence of severe malfunction of the sinus node in two senior members and with electrocardiographic evidence of sinus node malfunction in four junior members and an additional adult is presented. Acquired heart disease has been clinically excluded in the patients described. None of the patients demonstrates QT interval prolongation, and there is no family history of congenital deafness. Family histories relative to syncopal episodes, serious cardiac arrhythmia, breath holding spells, or palpitations should be obtained from all patients presenting with serious malfunction of the sinus node regardless of age, and family members so affected should be carefully observed for the development of serious cardiac arrhythmias.

Malfunction of the sino-atrial node may be manifest as (1) persistent, severe, unexpected sinus bradycardia; (2) cessation of sinus rhythm for short periods with escape rhythms supervening; (3) long periods of sinus arrest without “rescue” rhythms; (4) absence of sinus rhythm after cardioversion; and (5) untreated atrial fibrillation with slow ventricular response.1 These findings are manifestations of the so-called “sick sinus syndrome.”1 Commonly described etiologies for this syndrome include major coronary artery disease,2,3 pericarditis,4 rheumatic, congenital, or acquired “primary” heart disease (cardiomyopathy),5 surgical injury to the nodal tissue,6 vagotonia and various drugs,7 and aging.8

Autopsy studies of children afflicted with the familial syndrome of hereditary QT interval prolongation, cardiac arrhythmias, syncope, and sud-

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Figure 1. Case 1. Forty-one year old woman. Twelve lead electrocardiogram demonstrating periods of sinus arrest with nodal and ventricular escape beats. Ventricular tachycardia is seen in lead V2.
FAMILIAL SINUS NODE DISEASE

den death occasionally associated with congenital deafness, have revealed obliterator changes of the intranodal portion of the artery to the SA node with degenerative changes in the node. Similar findings without electrocardiographic documentation in the hearts of two young athletes who died suddenly have been described. Extensive fibrosis with degenerative changes of the arterial blood supply to the entire conduction system in a young boy with QT interval prolongation who had a family history of sudden death has been reported.

This communication relates the findings in a family presenting with clinical evidence of SA node malfunction without QT interval prolongation or congenital deafness.

CASE REPORTS

CASE 1

A 41-year-old premenopausal woman was admitted to the hospital for elective hysterectomy. A history of a "slow heart rate" and palpitations for many years was obtained. No previous electrocardiograms had ever been taken. She was taking no medications. A routine electrocardiogram revealed periods of prolonged sinus arrest with AV nodal and ventricular escape beats and occasional short bursts of ventricular tachycardia. Procaine amide was administered and the patient discharged. She was readmitted to the hospital three days later with the interval history of three syncopal episodes and was seen in consultation on January 15, 1970.

There was no past history of syncope. A subtotal thyroidectomy had been performed 15 years earlier. Abnormal physical findings were limited to the cardiovascular system and were those consistent with her arrhythmia. An electrocardiogram revealed periods of prolonged sinus arrest with AV nodal escape beats and occasional short bursts of ventricular tachycardia. Procaine amide was administered and the patient discharged. She was readmitted to the hospital three days later with the interval history of three syncopal episodes and was seen in consultation on January 15, 1970.

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gram revealed periods of sinus arrest, nodal and ventricular escape beats, and runs of ventricular tachycardia (Fig 1). Right ventricular pacing was begun and procaine amide was discontinued. Laboratory data revealed normal serum enzymes, no evolution of an infarct pattern with her pacemaker turned off, normal thyroid parameters, negative "LE" preparations, normal electrolytes, sedimentation rate, and serum proteins.

Brief periods of sinus rhythm subsequently spontaneously recurred. Atropine and isoproterenol had no effect in maintaining sinus rhythm. Atrial pacing was attempted and resulted in the reappearance of an atrial vector with normal AV conduction and slight QT interval prolongation (Fig 2). Selective coronary angiography revealed no coronary artery disease with normal arteries to the SA and AV nodes. The left ventricular end diastolic pressure was normal.

The patient was discharged with a permanent pacemaker catheter in the right atrium and has continued to do well.

Case 2

The 65-year-old maternal aunt of patient 1 was investigated in 1965 because of a four-year history of palpitation, dizziness, and syncopal episodes. Her exercise tolerance remained normal and no history of chest pain was obtained. A resting electrocardiogram revealed sinus rhythm with minor ST segment changes (Fig 3). She was exercised to a maximum heart rate of 120 (70 percent of predicted normal), without ischemic ST segment changes. A monitored electrocardiogram (Fig 4) revealed episodes of sinus arrest, nodal escapes, and runs of supraventricular tachycardia with aberrant conduction. She experienced syncopal episodes simultaneous with these periods of documented arrhythmia. Treatment with oral ephedrine was begun in 1965 and syncopal episodes have not recurred.

Case 3

This 68-year-old woman is the mother of patient 1 and sister of patient 2. She relates a history of dizziness, palpitations, and syncopal episodes all of her life, frequently precipitated by emotion and increasing in frequency over recent years. She has not experienced chest pain and has not been taking medications. Physical examination was unremarkable except for moderate hypertension (180/90) and an aortic
flow murmur (normal aortic closure sound, no third heart sound, and no early systolic click). Her resting electrocardiogram revealed ST segment changes in the lateral leads, slight sinus arrhythmia and prolongation of AV conduction (Fig 5).

The patient was monitored electrocardiographically for ten hours daily for seven days. No symptoms were noted during

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**Figure 5.** Case 3. The 68-year-old mother of patient 1 and sister of patient 2. Note the ST segment changes, and absence of QT prolongation. First degree AV block is present.

**Figure 6.** Case 3. Representative sections of a continuously monitored precordial ECG lead demonstrating the appearance of premature ventricular contraction during periods of sinus slowing.
this entire period of time. Premature ventricular contractions were recorded when the basic sinus rate slowed to below 60 per minute (Fig 6). She has declined further investigation or treatment.

Six children of patient 1 were investigated. Four children, ages 13 to 20, have mild sinus bradycardia, wandering pacemaker or evidence of ectopic pacemaker activity or abnormal ST segment changes. One boy has prolonged AV conduction. A representative ECG of an 18-year-old daughter is presented (Fig 7).

**DISCUSSION**

Cardiac arrhythmias occurring in the hereditable QT prolongation syndrome result primarily from premature contractions occurring during an enhanced vulnerable period.\(^{16-17}\) SA node disease, QT prolongation, and occasionally congenital deafness, are independently genetically determined\(^{16-17}\) but their coincident occurrence results in serious clinical manifestations. The SA node disease is the source of the extrasystoles which result in cardiac arrhythmias during periods when the QT interval is prolonged.\(^{16-17}\)

Further evidence for genetically determined SA node, AV node, and conduction system degeneration has been described by James and associates in other hereditable or possibly hereditable clinical conditions, associated clinically with syncope, atrial arrhythmias, and sudden death. These include primary pulmonary hypertension,\(^{18}\) Friedreich's ataxia,\(^{19}\) Marfan's syndrome,\(^{20}\) cardiomyopathy,\(^{20}\) and progressive muscular dystrophy.\(^{21}\)

In light of this knowledge, we postulate that the members of the family described in the current report have hereditable disease of the SA node without concurrent genetically determined QT interval prolongation or congenital deafness. In the absence of autopsy material we cannot document this conclusion, but the following points should be considered: (1) patient 1 has no angiographically demonstrable coronary disease and no clinical explanation for her severe SA node malfunction; (2) patient 2 with documented sinus node arrest and serious atrial arrhythmia has no history to suggest ischemic heart disease, a negative treadmill test, and has been completely asymptomatic for five years on oral ephedrine alone; (3) patient 3 demonstrates sinus slowing associated with ventricular ectopic beats during a period of time in which she experienced no symptoms. It is possible that her symptoms are related to more serious escape rhythms which we are unable to document; (4) four children in this family demonstrate moderate sinus bradycardia, and/or pacemaker wandering, and unusual ST segment changes. Exercise in two
young boys produces submaximal increase in their heart rates with further wandering of the pacemaker and no evidence of QT interval prolongation.

We therefore suggest that the members of this family have hereditary disease of the SA node, that the disease tends to be progressive with age, that the most severely affected members do not demonstrate QT interval prolongation, and that symptoms result from sinus slowing or arrest rather than subsequent to ectopic beats occurring during an enhanced vulnerable period. This conclusion suggests that a family history be obtained from all patients presenting with evidence of sinus node arrest, even in the absence of QT interval prolongation, and that symptoms associated with electrocardiographic abnormalities, fainting attacks and sudden death. A recessive syndrome. Quart J Med 33:361, 1964

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REFERENCES


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