Congenital Familial Cardiac Conduction Defects

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The familial occurrence of conduction system disturbances has been reported infrequently in medical literature. Morquio, in 1901, reported clinical signs of impaired atrioventricular conduction in five boys in a family of eight children. There was no evidence of consanguinity and the defect did not occur in immediate ancestors nor in collateral branches of the family. In 1903, Sir William Osler described a case of Adams-Stokes disease and mentioned that "many relatives of his family" had slow pulse rates.

Since then, the occurrence of different degrees of AV block has been reported in two or three siblings by Aylward, Canabal and Dighiero, and Wallgren and Agorio. A family study, involving more than 75 individuals and more than three generations, revealed no additional cases of conduction defects. Conduction defects have been reported in one parent of two or more children with congenital atrioventricular block. A more recent study revealed all four siblings of a family to have varying degrees of right bundle-branch block.

We have recently collected data on a family in which conduction disturbances were evident in three generations and the proband (III-7 in fig. 1), an intelligent white woman, said that two of her grandparents (I-1 and I-2) and an uncle (II-2) were also reported to have had "heart trouble" prior to their deaths.

The proband was initially seen by us having episodes of Adams-Stokes seizures with complete atrioventricular block. It was noted that, 2 years prior to being seen, she had a child (IV-7) who died shortly after birth, demonstrated by electrocardiogram to have advanced AV block with a 5:1 ratio. The history was obtained that her father (II-3) had experienced a slow heart rate as a young adult. Electrocardiogram subsequently obtained on him revealed 2:1 AV block with periods of complete dissociation. It cannot be proved definitely that this atrioventricular block was congenital, since no electrocardiogram was obtained in early life. He did say that his heart rate was unusually slow and there was no history of any other type of heart disease.

Electrocardiograms were then obtained on 35 members of the family, including all members of generations III and IV and most members of generation II. Five other cases with conduction defects were found. Three of these were in the proband's siblings, one in another of her six children, and one in the child of a sibling. This makes a total of 11 probable cases in four generations, eight of them documented by electrocardiograms and three reported by the proband. These three individuals were dead (I-1 and I-2, and II-2) and no electrocardiograms were available.

A summary of the clinical data concerning those members of the family with documented significant cardiac abnormalities follows.

II-3. A 67-year-old man was noted by electrocardiogram to have 2:1 AV block with periods of complete AV dissociation and with right bundle-branch block (QRS duration of 0.12 second). Even though no prior tracing was obtained, he was known to have a slow heart rate since childhood.

III-3. A 39-year-old man has had a slow heart rate since birth. He has been asymptomatic, and has no unusual physical findings except for a slow heart rate. Electrocardiogram showed a P-R interval of 0.16 second and QRS duration

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of 0.08 second, with a marked sinus bradycardia at 45 per minute.

III-5. A 34-year-old asymptomatic man was normal on physical examination. Electrocardiogram showed a regular sinus rhythm with a P-R interval of 0.16 second, a QRS duration of 0.16 second, and a rate of 60. Left axis deviation of -75 degrees was present. The terminal vector suggested right bundle-branch block except for aVL, in which there was no S wave even though the R wave was 14 mm. in height.

III-7. A 35-year-old woman was admitted to the hospital January 15, 1963, with Adams-Stokes seizures due to congenital atrioventricular heart block known to be present since age 2. At age 23 2:1 AV block was recorded. Electrocardiogram taken shortly after admission during an Adams-Stokes seizure revealed a run of ventricular tachycardia, ventricular flutter, and a short period of ventricular fibrillation. After therapy with isoproterenol and hydrochlorothiazide, the electrocardiogram revealed complete AV block. The Adams-Stokes seizures began after delivery of the sixth child.

III-11. A 26-year-old asymptomatic woman was normal on physical examination. Electrocardiogram revealed regular sinus rhythm with a P-R interval of 0.22 second and QRS prolonged to 0.10 second with right bundle-branch block.

IV-3. A 10-year-old asymptomatic girl was normal on physical examination. Electrocardiogram revealed regular sinus rhythm with a P-R interval of 0.14 second and QRS prolonged to 0.13 second with right bundle-branch block.

IV-7. A full-term newborn boy had been found to have a slow heart rate 2 months prior to birth by fetal electrocardiogram. At birth the heart rate was 36 per minute and electrocardiogram revealed advanced AV heart block with a 5:1 ratio and ventricular ectopic beats. The QRS complexes measured 0.08 second in duration. The patient died suddenly 3 days after birth. Autopsy revealed hypertrophy and dilatation of both ventricles. In the subendocardial area were cells thought to represent typical Purkinje fibers.

IV-10. An 11-year-old asymptomatic girl has been found to have a 2:1 AV block at birth. A subsequent tracing revealed 2:1 AV block with Wenckebach periods, nodal escape, and periods of complete AV dissociation. QRS duration consistently was 0.08 second.

Discussion

The scattered reports of familial cardiac conduction defects suggest a genetic basis for the disturbance. The occurrence of the defect in several siblings or in one parent and in some of the children provides little material for formulating a hypothesis as to the genetic mechanism involved.

We believe our study to be the most complete family history in the literature. The high incidence of congenital cardiac conduction defects in this family suggests a hereditary basis for the defects. The large number of affected individuals and the absence of consanguineous marriages provide evidence against the trait being transmitted by a re-
cessive gene. Sex-linked dominance can be ruled out, since an affected father transmitted the trait to sons. An autosomal dominant trait should appear equally in males and females and, in this family, the ratio of affected males to affected females is 4:4. Also, an autosomal dominant trait should be transmitted to 50 per cent of the offspring of an affected parent. Since III-9 produced a child with the trait, one must assume that she had the dominant gene but did not develop clinically detectable signs of the trait. With this assumption, the observed data (eight with the dominant gene) fit the expected number (nine) quite well. The data support the hypothesis that, in this family, congenital cardiac conduction defects are transmitted as an autosomal dominant trait with an incomplete but high degree of penetrance.

Summary

A family in which several members of three separate generations have evidence of congenital familial conduction disturbance has been described. The occurrence of Adams-Stokes seizures with congenital AV block was also noted. From the available information it is clear that the conduction disturbance was congenital in two generations, and the family history suggests that three or four generations were probably involved. The data suggest that in this family the congenital cardiac conduction defects were transmitted as an autosomal dominant trait with incomplete penetrance.

References


The Legacy of Greece

With the fall of the Roman Empire practically all of Greek science was lost to the West, although much of it survived in the Byzantine Empire. Recovery was slow: it came first from the Arab world by way of reconquered Spain, along with the significant contributions of Arab medicine. Arabic translations of Galen and Hippocrates and the Canon of Avicenna were translated in turn into Latin by Gerard of Cremona. Another source was the School of Salerno in southern Italy, a way station for the Crusaders, and the place where the Arab scholar Constantine of Africa established himself in the eleventh century. —André Cournand, M.D. Circulation of the Blood. Edited by Alfred P. Fishman, M.D., and Dickinson W. Richards, M.D. New York, Oxford University Press, 1964, p. 17.
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