SYNCOPE, DEAFNESS, AND SUDDEN DEATH: REPORT OF A FAMILY FROM BAHRAIN AND LITERATURE REVIEW

KASIM OMAR ARDATI, MD, FAAP; A. NABI ABDULLA AL-SAIF, MD, MRCP(I), DCH

An extended Bahraini family with seven children having the cardio-auditory syndrome of Jervell and Lange-Nielsen is described. All of the children had deafness detected in infancy and sudden repeated episodes of syncope. Detailed clinical history of one of the affected children is presented. Six of the affected members died. The index case and his surviving cousin with this condition had prolonged QT interval. The electrocardiogram of the parents and siblings of the index case and the siblings of the surviving member are described; all had normal QT interval except the mother of the index case whose QT interval was borderline. The use of propranolol in the index case did not prevent the occurrence of syncope although it decreased the frequency of the attacks in the surviving member. Literature review of this condition is presented. Left cardiac sympathetic denervation has recently been reported to be of great value in the management of patients with prolonged QT interval. All children with unexplained syncope or with congenital deafness need a thorough medical evaluation that must include electrocardiography.

SUDDEN, RECURRENT EPISODES of syncope in children with congenital deafness was first described by Jervell and Lange-Nielsen in 1957.1 Since then, several reports2-10 describing this condition were published. Patients with Jervell and Lange-Nielsen syndrome (JLNS) have been reported to have deafness early in their infancy together with recurrent episodes of syncope and sudden death. This condition has an autosomal recessive inheritance. Prolongation of the QT interval has been noted in patients with this condition. A similar condition without congenital deafness and with autosomal dominant inheritance was described by Romano in 196311 and Ward in 1964.12 Adequate recognition of the condition is important because these patients often die suddenly with ventricular arrhythmias. We describe here an extended family from Bahrain where 7 members have this condition together with electrocardiographic findings of 12 individuals, including 2 members with prolonged QT interval. Review of the literature, emphasizing significant progress in the management of this condition, is also presented.

Case Report

The index patient was a 3 years- and 10-monthsold Bahraini boy who was referred to the pediatric clinic at Salmaniya Medical Centre for evaluation of repeated brief episodes of syncope. He was delivered by cesarean section 10 d prior to the expected date of birth; the cesarean operation was performed because of irregular fetal heart rate and suspicion of fetal distress. But his neonatal course was normal, and he was discharged home with his mother. At the age of 8 mo, his mother noted that he was not responsive to auditory stimuli; otherwise, his development was normal. At the age of 2 y, he was admitted to the hospital with Salmonella gastroenteritis. At that time, because of his deafness and speech impairment, he was referred to the ENT service where evaluation confirmed profound deafness. At the age of 3 years and 6 months, he was admitted to
the surgical service because of a brief episode of loss of consciousness that occurred when he fell while running. He was discharged after 2 d of observation. The mother reported that, since that time, he had several brief episodes of syncope that were not associated at any time with convulsions. The episodes would occur during times of emotional stress and anxiety, especially when he was separated from his mother.

On examination, his weight was 14.9 kg; height, 99.5 cm; blood pressure, 80/60 mm Hg; heart rate, 80 beats/min; and respiratory rate, 20/min. He was pleasant and cooperative but did not respond to auditory stimuli. His examination was normal except for a soft, grade I/VI systolic murmur and profound deafness. The electrocardiogram showed the corrected QT interval to be 0.57 s. He was started on propranolol.

At the age of 4 y the patient was admitted after he was found to be lying down, cyanosed, and unconscious. Resuscitation was initiated by the family with mouth-to-mouth breathing, and he was immediately brought to the hospital. Initial evaluation revealed that he was semiconscious and responsive only to painful stimuli. Soon after admission, he developed an episode of cardiorespiratory arrest. Despite resuscitative measures, he developed fixed dilated pupils. He died 12 d later without regaining consciousness.

**Family History**

The family pedigree is shown in Figure 1. The parents are first cousins. The index patient was the sixth of seven children. The first child died at the age of 11 mo following a brief febrile illness. The fifth sibling (a boy) died suddenly at the age of 5 y. He was also noted to be deaf since infancy and had recurrent episodes of syncope. One first cousin, a female aged 11 y, has deafness and recurrent episodes of syncope (the episodes are currently less frequent than in her early childhood). She is presently taking propranolol.

The corrected QT interval (QTc) was calculated according to the standard method. It was prolonged in the index case (0.57 s) and the surviving cousin (0.53 s). All other members of the family who had electrocardiographic recording had normal QTc except the mother of the index case whose QTc was 0.45 s.

**Discussion**

This report documents the occurrence of JLNS in a Bahraini family. Only one of the 7 patients reported is alive now. All of the children reported had deafness that was detected in early infancy and had repeated episodes of syncope. The index case and his surviving cousin had prolonged QTc.

The first report of JLNS was published in 1953 from Norway. Following that report, other cases were described in the United States, England, Ireland, Italy, Iran, and Pakistan. To our knowledge, this is the first description of JLNS in an Arab family.

The index case was delivered by cesarean section which was performed because of suspicion of fetal distress; this probably was related to arrhythmia occurring in utero. A previous study also described a patient with JLNS who was delivered by cesarean section because of fetal bradycardia, possibly a consequence of QTc prolongation. Our index case was initially referred to the pediatric clinic because of suspicion of seizure disorder. Seizure, as a

![Pedigree](image)

**Figure 1.** The pedigree of the extended family is shown. Affected numbers are indicated by the black circles (females) or squares (males), and the index patient is identified by the arrow. The corrected QT interval in seconds is shown under the symbols of each individual.
manifestation of this syndrome, was misdiagnosed as primary seizure in 3 patients who later were confirmed to have JLNS. In another study, a mother and three of her children presented with syncopal attacks precipitated by exercise or emotional stress; these syncopal attacks were initially misdiagnosed as epilepsy. Ventricular and supraventricular arrhythmias were documented in all the affected family members. The mother had decreased frequency of episodes after a pacemaker was inserted. However, she died after an episode of loss of consciousness, even though the pacemaker was functioning normally. Her three affected children improved upon treatment with propranolol, suggesting a disorder of the sympathetic innervation of the heart with a normal QT interval. These observations, together with the description of our index case, suggest that patients presenting with atonic seizures and unexplained syncope must have a complete evaluation, including electrocardiographic examination to rule out a cardiac cause of syncope. Such evaluation is essential because syncope on exertion or during emotional stress, even when associated with convulsions, is rarely due to a primary epileptic disorder.

Prolongation of the corrected QT interval has been described in patients with JLNS and with the Romano-Ward syndrome. Some patients with manifestations of syncope and unexplained syncpe must have a complete evaluation, including electrocardiographic examination to rule out a cardiac cause of syncope. Such evaluation is essential because syncope on exertion or during emotional stress, even when associated with convulsions, is rarely due to a primary epileptic disorder.

The inheritance of JLNS is autosomal recessive in nature, whereas it is thought to be autosomal dominant in the Romano-Ward syndrome. In a family with JLNS where consanguineous marriage is common, such as the family described here, it is very important to identify markers of the disease. Such identification is necessary in order to provide adequate genetic counseling. The search for disease markers in the parents of the affected individuals would be very helpful because these parents are obligate heterozygotes for the condition if the inheritance is autosomal recessive in nature. A report on an extended family with long-QT syndrome found strong correlation between inheritance of this condition and the Harvey ras-1 gene located on the short arm of chromosome 11. This finding, however, was not confirmed in a recently published study of another family with the same syndrome.

Thus, it appears that there is evidence of genetic heterogeneity in the long-QT syndrome. An evaluation of the family described would help in the understanding of the effect of certain genetic markers on the electrical activity of the heart and would help in providing adequate genetic counseling.

An important issue in the management of children with life-threatening dysrhythmias is whether parents of such children should be taught cardiopulmonary resuscitation. A report on this issue clearly showed the advantage of parent-initiated cardiopulmonary resuscitation. Of the 28 children who had cardiac arrest and whose resuscitation was initiated by the parents, 13 survived (46%); 17 of these children had primary electrocardiographic recordings. The siblings of these two family members and the father of the index case have normal QTc (Figure 1). The mother of the index case is asymptomatic and her QTc is 0.45 s. Although previous reports have mentioned the upper limit of normal QTc to be 0.44 s, a recent report defines long QTc to be 0.45 s or greater in individuals with symptoms or 0.47 s or greater in the absence of symptoms. Another report of an extended family with long-QT syndrome defines the limit of normal QTc in children, adult males, and adult females. According to the above definition, the 0.45 s QTc of the mother of the index patient is not considered prolonged but is considered equivocal according to a more recent publication.

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cardiac dysrhythmias and 7 of them survived (41%). None of the children whose parents were not instructed on cardiopulmonary resuscitation survived. A great effort should be made to properly instruct family members of children with congenital heart disease or with life-threatening cardiac dysrhythmias in cardiopulmonary resuscitation.

Another important issue in the management of these patients is proper understanding and reassurance to these patients during periods of stress. A patient with JLNS has been reported to have a good outcome following two cesarean sections. This patient was accompanied by a relative during the induction of anesthesia; the relative acted as an interpreter and also reassured the patient during the stressful period of anesthesia induction. Our index patient had repeated episodes of syncope during periods of emotional stress when he was separated from his mother. Adequate support to patients during emotional stress should be provided and strenuous exercise should be avoided or kept to a minimum.

The deafness that is detected in early infancy in patients with long-QT syndrome differentiates between JLNS and the Romano-Ward syndrome. The cause of deafness in JLNS was studied in a report describing autopsy findings of the ears of two siblings. Widespread degeneration of the sensory end organs of the cochlea and the vestibular apparatus, together with atrophied nerve fibers were noted. Periodic acid Schiff-positive hyaline nodules were also noted throughout both cochlea and vestibular portions of the membranous labyrinth. The implications of these findings are not clear, and it is also not clear whether any of these findings may relate to the cardiac abnormality that these patients have. It is important, however, to emphasize that patients with JNLS have normal intelligence and when their auditory handicap is managed properly by speech therapy that includes sign language instruction, they are expected to have adequate scholastic achievements.

The modalities of treatment of long-QT syndrome include the use of beta-adrenergic blocking drugs, insertion of pacemakers, implantation of cardioverter-defibrillators, and various surgical procedures that aim at decreasing or abating the cardiac sympathetic tone. A recently published worldwide study demonstrated the benefit of left cardiac sympathetic denervation in patients with congenital long-QT syndrome who remained symptomatic despite the use of beta-adrenergic blocking drugs. The use of propranolol in one of the patients described in this series was successful in decreasing the frequency of syncopal episodes. It appears that left cardiac sympathetic denervation should be the therapeutic modality of choice in patients with congenital long-QT syndrome who do not respond to the use of betaadrenergic blocking drugs.

References