Usefulness of Valsalva manoeuvre and cold pressor test for evaluation of arrhythmias in long QT syndrome¹

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SUMMARY Ventricular arrhythmias were precipitated with reflex testing in a case of the long QT syndrome and were abolished after acute administration of propranolol.

Since the original description of a hereditary syndrome of prolongation of the electrocardiographic QT interval, syncope and sudden death, with congenital deafness (Jervell and Lange-Nielsen, 1957) or with normal hearing (Romano *et al.*, 1963; Ward, 1964), clinical evidence has accumulated to implicate the autonomic nervous system in the genesis of arrhythmia. The effects of catecholamine infusion (Garza *et al.*, 1970; Mathews *et al.*, 1972) and exercise (Roy *et al.*, 1976) have been reported to cause ventricular tachycardia and fibrillation in this syndrome. We tested the hypothesis that reflex manoeuvres would precipitate arrhythmias and found such testing useful for assessing the efficacy of antiarrhythmic therapy.

Case report

A 23-year-old white woman was referred to the University of California, San Francisco, for evaluation of recent postoperative arrhythmias. The patient was the product of a normal conception and delivery. During childhood she suffered 3 seizures and was treated with diphenylhydantoin until adolescence. She remained well until syncopal episodes occurred without warning during pregnancy: 1 episode during her first pregnancy and 2 during her second. For the past year she had been healthy, but was recently admitted to Alaska Hospital for minor pelvic surgery. Postoperatively she was noted to have frequent premature ventricular

contractions, a potassium of 2.8 mmol/l, and a magnesium of 1.6 mmol/l. Potassium correction was undertaken and the patient transferred to the coronary care unit for monitoring. After transfer, short runs of ventricular tachycardia were noted. Treatment with bolus and infusion of lignocaine and procainamide was begun, together with an oral dose of quinidine. Runs of ventricular tachycardia occurred, followed by ventricular fibrillation. Cardiopulmonary resuscitation and precordial electric shock restored normal rhythm. An electrocardiogram taken before cardiac arrest showed a QT interval of 0.46 second with a heart rate of 77. The calculated corrected QT (QTc) (Bazett, 1920) was prolonged to 0.52 second, with the upper limit of normal 0.425 second (Massie and Walsh, 1960). After treatment with bolus propranolol and supplemental potassium, the QT was 0.44 second at a heart rate of 71 (QTc = 0.48). There was an uneventful recovery. On the day of discharge, while on propranolol, 120 mg, and diphenylhydantoin, 300 mg, orally per day, she underwent progressive treadmill exercise with premature ventricular contractions at rest, which were abolished with exercise. Her dose of propranolol was subsequently increased to 160 mg per day. An audiogram was normal.

On admission she was a well-developed, well-nourished young woman in no acute distress. Vital signs, physical examination, and chest x-ray film were normal. Laboratory blood electrolyte values included a potassium of 4.0 mmol/l and a magnesium of 2.3 mmol/l. The electrocardiogram was normal, except for a QT of 0.48 second, with a heart rate of 55 (QTc = 0.46) at a time when the propranolol level was 200 ng/ml and the diphenyl-

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Fig. 1 Heart rate and QT during exercise. Heart rate (solid squares) increased during exercise and was associated with premature ventricular contractions (PVC). QT interval (open triangles) was prolonged at rest and at exercise, compared with the upper limit of normal for QT corrected for heart rate (open circles).

hydantoin level was 5 µg/ml. Her mother had been admitted to hospital for syncopal episodes with a reportedly normal QT interval; a brother had an electrocardiogram which showed right bundle-branch block; and a nephew had congenital unilateral deafness and motor difficulty.

HOSPITAL STUDIES

Exercise

All drugs, including antiarrhythmics, were stopped at least 24 hours before any studies. No arrhythmias

were observed with the patient at rest during continuous monitoring.

In the cardiac catheterisation laboratory the patient underwent progressive supine bicycle exercise. The QT interval, which was prolonged at rest, showed progressive shortening with exercise, but nevertheless remained prolonged above normal (Fig. 1). At 400 kiloponds/min ventricular ectopy was manifested with coupled beats. Cardiac metabolism at rest and with exercise was normal, as judged from positive lactate extraction between coronary sinus and arterial blood.

Reflexes

The cold pressor test was performed with the hand immersed in ice water at 1°C. After 1 minute of immersion, ventricular bigeminy developed (Fig. 2). During Valsalva manoeuvre blowing, heart rate increased. With release, ventricular bigeminy occurred (Fig. 3). These studies were repeated after a 6 mg intravenous dose of propranolol. Heart rate response was diminished and no arrhythmias were observed. Each reflex manoeuvre was performed twice, both before and after propranolol. The results were the same each time.

In the past 6 months of outpatient follow-up, the patient has remained symptom and arrhythmia free on propranolol, 160 mg/day in divided doses.

Discussion

This case represents a potpourri of clinical features previously reported separately in the long QT interval syndrome. The early childhood 'seizures' were provisionally treated with diphenylhydantoin, a drug said to shorten ventricular repolarisation (Bigger *et al.*, 1968). Further delay of syncopal episodes until young adult life is consistent with the previously reported onset of clinical manifestations

Fig. 2 Cold pressor test. After hand immersion in ice water, premature ventricular contractions and ventricular bigeminy were noted. With beta-blockade, the increment of increase in heart rate was similar, but no ectopy occurred.

Fig. 3 Valsalva manoeuvre. Heart rate rose during Valsalva manoeuvre and with release ventricular bigeminy occurred. After beta-blockade, repeat manoeuvre caused no ectopy.

with variable age (Garza *et al.*, 1970; Mathews *et al.*, 1972; Roy *et al.*, 1976). The occurrence of severe arrhythmic episodes while in hospital for surgery may, in part, be attributed to stress in the post-operative period, as well as metabolic derangement. A single dose of quinidine was also administered and may have contributed to ventricular vulnerability (DiPalma and Shults, 1950).

The clinical evidence for a role of the sympathetic nervous system in the long QT syndrome includes precipitation of arrhythmias with exercise, emotional excitement, and catecholamine infusion and abolition of arrhythmias with beta-blockade (Jervell and Sivertsen, 1967; Garza *et al.*, 1970; Schwartz *et al.*, 1975; Roy *et al.*, 1976). After stellate ganglion blockade or left sympathectomy, shortening of the QT interval has been invoked as evidence for a disparity between sides of the stellate ganglion in sympathetic nervous system outflow to the ventricle (Schwartz *et al.*, 1975). In our patient, precipitation of ventricular arrhythmia with the Valsalva manoeuvre and a cold pressor test, and abolition of arrhythmia with propranolol, also provide examples of the precipitation of arrhythmias in the long QT syndrome by an action on the sympathetic chain. Our observation that propranolol abolished the ventricular arrhythmias associated with reflex manoeuvres and exercise is in agreement with the beta-blocking effect of this drug and at variance with the suggested direct antiarrhythmic effect (Garza *et al.*, 1970).

Although a recent review of drug therapy suggests the superiority of propranolol (Schwartz *et al.*, 1975), we encourage an individual approach in this serious malady. Using electrocardiographic monitoring, simple exercise testing and reflex manoeuvres

may be useful to uncover ventricular ectopy and to assess drug therapy.

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