A case of prenylamine toxicity showing the torsade de pointes phenomenon in sinus rhythm?

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Summary

A case of torsade de pointes attributed to prenylamine is described. In addition, the authors show QRS axis variation of a similar nature in sinus rhythm. It is postulated that these changes of QRS axis direction, seen in ventricular tachycardia and sinus rhythm, are both manifestations of partial refractoriness, within the ventricle, producing gross changes in the mean QRS vector.

Introduction

The adverse effects of the anti-anginal drug prenylamine (Synadrin), involving the sequelae of Q-T prolongation, have been widely reported in Europe (Picard, Anzepy and Chauvin, 1971; Bens *et al.*, 1973; Jacovella and Vajola, 1976), but only occasionally in England (Puritz *et al.*, 1977). The mode of action of prenylamine is claimed to be reduced sympathetic stimulation by its effect on catecholamine uptake and release, in addition to a direct coronary dilating effect (Wade and Reynolds, 1977).

A case is now reported of repeated episodes of ventricular tachycardia attributed to prenylamine, and the arrhythmias produced are examined.

Case report

A 55-year-old woman, known to have had rheumatic fever at the age of 7 years and again at the age of 14 years, was treated with prenylamine following 2 episodes of 'wooziness' and sensations of heaviness down the left arm. She had been asymptomatic until this time, and her ECG was normal.

After starting treatment she experienced approximately monthly attacks of vertigo and rapid palpitation unassociated with any precipitant factors.

One month before admission the frequency of attacks increased and became associated with black-out and urinary incontinence. The day of admission the patient had experienced 5 such attacks at home.

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On arrival at hospital she was fully conscious, with no signs of general systemic illness. Pulse was irregular, rate 88/min, with a BP of 150/90 mmHg. There were signs of mixed mitral valve disease, with no evidence of heart failure. Serum potassium on admission 4.2 mmol/l. The patient admitted to taking prenylamine in therapeutic doses up to her admission.

Shortly after admission, whilst having an ECG, the patient became unconscious, with a weak and rapid pulse. The synchronous ECG recording leads 1, 2 and 3 (Fig. 1(a)) shows a ventricular tachycardia with the torsade de pointes (MacWilliam, 1923; Dessertenne, 1966) or twisting peak phenomenon displayed in lead 3. This episode reverted to sinus rhythm following a bolus of 100 mg of i.v. lignocaine. An electrocardiogram, taken between 2 such episodes, showed sinus rhythm with multifocal ventricular ectopics, grossly prolonged Q-T interval at 0.72 sec and wide irregular T waves.

Although this patient's situation was not initially attributed to prenylamine, the drug was withdrawn on admission.

Over the next 6 days, the phenomenon of rotating frontal plane axis in sinus rhythm was displayed (Figs 2, 3). Following this, the patient settled to a stable sinus rhythm with her Q-T interval returning to normal at 0.40 sec. There was no historical or enzymatic evidence of myocardial infarction, and she was discharged home feeling well on the 13th day.

Discussion

The torsade de pointes phenomenon is a distinct form of ventricular tachycardia characterized by QRS polarity oscillation over short runs of beats (Fig. 1(a)). It is typically found in ventricular tachycardia associated with Q-T prolongation, and has been clearly described before (Krikler and Curry, 1976). It is important to note that drugs such as lignocaine which act by increasing repolarization time, can themselves cause this arrhythmia, and

FIG. 1. (a) synchronously recorded ECG leads 1, 2 and 3 during ventricular tachycardia with torsade de pointes. (b) mean QRS vector plotted on Einthoven's triangle for beats A-E showing progressive counter-clockwise rotation.

therefore a drug such as isoprenaline which shortens repolarization time is the theoretical pharmacological treatment of choice (Krikler and Curry, 1976).

The authors show 2 further cardiographic abnormalities attributed to the use of this drug. Firstly, the way in which, even in sinus rhythm, the complexes became equiphase and then the QRS axis changed direction (Fig. 2). This was the dominant abnormality of days 2 and 3 of the patient's admission. Secondly, the continuing change of the frontal plane vector (Fig. 3) seen over the first week of admission. The appearances in Fig. 3 taken on their own are compatible with an alternating hemiblock. However, in conjunction with the progressive axis rotation implied by the monitor lead (Fig. 2), it is thought that the changes in Fig. 3 are more likely to be due to such axis rotation. It is unfortunate that full 12-lead ECGs could not be taken during the progressive changes recorded from the bedside monitor. Furthermore, no ECG changes such as those recorded in Fig. 3 were ever observed before or after the patient's illness, which resolved following withdrawal of prenylamine.

In an attempt to understand these changes, the synchronous recording of leads 1, 2 and 3 during the ventricular tachycardia displaying the torsade de

FIG. 2. Chest monitor lead 'I' showing rotation of frontal plane vector in sequential QRS complexes as in torsade de pointes.

pointes was used to plot the frontal plane vectors for successive beats. Although it is difficult to establish an isoelectric line with accuracy, the estimated vectors indicated an ordered anticlockwise rotation in the frontal plane (Fig. 1(b)).

FIG. 3. 12-lead cardiograms over the first week in hospital. Note grossly prolonged QT interval on day 2 and changing mean frontal plane vector.

The prolonged QT interval in sinus rhythm indicates delayed repolarization and increased refractory period. There is also greatly increased variance of repolarization time indicated by the wide irregular T waves. Partial refractoriness in certain areas of the ventricle is presumably sometimes still present after a normal R-R interval, producing a gross change in mean QRS vector between sinus beats (Fig. 2). This phenomenon is greatly exaggerated during tachycardia (torsade de pointes, Fig. 1). Here the spread of repolarization times produced a progressive anticlockwise rotation of the mean direction of electrical forces during sequential depolarization (Fig. 1(b)).

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