active cellular reuptake of released noradrenaline, and this probably contributes to its antagonism of antihypertensive agents and to its hypertensive interaction with monoamine oxidase inhibitors. Although tricyclic antidepressants may theoretically potentiate the pressor effect of noradrenaline derived from levodopa, the combination of amitriptyline and levodopa is apparently safe, and there are no reports of hypertensive crises in patients on Sinemet and amitriptyline. Furthermore, hypertensive responses to other combinations of Sinemet, amitriptyline, and metoclopramide have not previously been described. These three agents are not uncommonly used together to treat patients with Parkinson's disease, and prescribers should be aware of the possibility of a potentially dangerous reaction to such treatment.

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1 Chase, T N, and Watanabe, A M, Neurology (Minneapolis), 1972, 22, 384.

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**Ventricular arrhythmias caused by prenylamine**

Prenylamine is a drug widely used to treat angina pectoris. We describe here two patients with prolongation of the Q-T interval complicated by serious ventricular arrhythmias and syncope due to prenylamine.

**Case 1**

A 78-year-old woman was admitted to hospital after collapsing at home. She had had palpitations and dizzy spells for a few weeks. An electrocardiogram taken during a visit to the casualty department the previous day after a faint had shown sinus rhythm at 52 beats/min and a Q-T interval of 0.62 s, but the significance of this was not recognised and the patient was sent home.

She had mild diabetes mellitus controlled by diet, and exertional angina pectoris, and she had had a left total hip replacement for osteoarthritis three years earlier. She was taking prenylamine 180 mg daily, as well as Feospan (dried ferrous sulphate), diazepam, allopurinol, and oxyphenbutazone.

During transfer to hospital in a coronary ambulance the monitoring oscilloscope showed only sinus rhythm with occasional ventricular extrasystoles. In hospital she had an episode of ventricular tachycardia, sinus rhythm being restored by DC countershock. The patient was then given intravenous lignocaine but then had 87 documented episodes of ventricular tachycardia over the next 90 minutes, many of them displaying the "torsade de pointes" phenomenon (fig 1). A full electrocardiogram showed sinus bradycardia, right bundle-branch block, giant bizarre T waves, prominent U waves, a much prolonged Q-T interval of at least 0.8 s, and coupled ventricular extrasystoles (fig 2).

As soon as the nature of the emergency was understood right atrial pacing was started at a rate of 120 beats/min, which immediately suppressed the arrhythmia. Pacing at fast rates was completely effective over 72 hours until spontaneous improvement occurred. Investigations showed: serum potassium 3.1 mmol (mEq)/l, normal serum calcium; and no enzyme evidence of myocardial infarction. After withdrawal of prenylamine serial electrocardiograms showed that the Q-T interval gradually returned to normal; four weeks after admission it was 0.40 s (fig 3).

**Case 2**

A 62-year-old woman presented with a history of four blackouts in the preceding four months. These blackouts lasted a few minutes and made her feel breathless for a short time afterwards but were not associated with palpitations. For the previous 20 months she had been taking Navidrex K (cyclophenthiazide 250 μg and potassium chloride 600 mg), propanolol, and prenylamine 180 mg daily to help control her angina and hypertension.

The pulse was regular at 48 beats/min and the blood pressure was 250/100 over the next 90 minutes, many of them displaying the "torsade de pointes" phenomenon (fig 1). A full electrocardiogram showed sinus bradycardia, right bundle-branch block, giant bizarre T waves, prominent U waves, a much prolonged Q-T interval of at least 0.8 s, and coupled ventricular extrasystoles (fig 2).

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**FIG 2—Case 1. ECG showing giant bizarre T-U segments and coupled ventricular extrasystoles.**

**FIG 3—Case 1. ECG showing improvement of Q-T prolongation over three weeks after withdrawal of prenylamine.**

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mm Hg. The electrocardiogram showed sinus rhythm at 48 beats/min with abnormal T waves, prominent U waves, and a prolonged Q-T interval of 0.64 s (fig 4). A 24-hour ambulatory monitoring tape showed several short runs of ventricular tachycardia with a maximum of six consecutive beats (fig 5). Prenylamine was withdrawn at the end of the monitoring period. After this the patient had no further blackouts. An electrocardiogram recorded four weeks after presentation showed a normal Q-T interval (fig 4).

Discussion

These cases emphasise the importance of the Q-T prolongation effect of prenylamine. There is little information about this subject in English reports though some reports have appeared in France1 and Italy.2 Q-T prolongation may be due to congenital abnormalities of repolarisation,1 myocardial ischaemia,3 hypokalaemia,4 hypocalcaemia,5 and hypomagnesaemia.6 Drugs which have been implicated include quinidine,7 procainamide,8 phenothiazines,9 10 and tricyclic compounds11 as well as prenylamine.

Several factors may coexist in prolonging the Q-T interval, and in particular hypokalaemia may be a contributory cause in combination with drug-induced or congenital Q-T prolongation.12 Our first patient was hypokalaemic on admission to hospital.

Q-T prolongation reflects a prolonged myocardial repolarisation time. This in turn is thought to favour a state of asynchronous depolarisation, which encourages re-entry processes and consequent arrhythmias. Ventricular arrhythmias caused in this way may show the torsade de pointes phenomenon, in which the QRS axis on the electrocardiogram changes direction radically during the space of several beats, as shown in case 1. Torsade de pointes may also arise during slow heart rhythms due both to sinus node disorders and atrioventricular block.13 14 Though the arrhythmia may resemble ventricular fibrillation electocardiographically, ventricular depolarisation occurs in an abnormal but still co-ordinated sequence. Loss of consciousness may occur due to inadequate diastolic filling at very high rates.

During treatment of ventricular arrhythmias associated with Q-T prolongation cardiac depressant drugs such as quinidine and procainamide should be used with caution as these may aggravate the arrhythmia.15 Lignocaine may also be contraindicated, for torsade de pointes has been observed after lignocaine overdosage.16 The repeated episodes of ventricular tachycardia which followed the use of lignocaine in case 1 were probably causally related. Parenteral potassium should be given, especially in the presence of even moderate hypokalaemia. Hypokalaemia and hypomagnesaemia should also be corrected if these metabolic abnormalities are suspected. Myocardial repolarisation time can be shortened by giving an isoprenaline infusion, though a very cautious trial will be needed to determine whether the rhythm disturbance is improved or worsened by this agent.

Cardiac pacing is effective, especially when the arrhythmia is bradycardia-dependent as in heart block.14 Ventricular pacing, however, carries the risk of inducing ventricular fibrillation,17 and atrial pacing is preferable if atrioventricular conduction pathways are intact. It was highly effective in the management of our first patient. The use of atrial pacing in the treatment of ventricular arrhythmias associated with Q-T prolongation is poorly documented, but it should be considered in cases similar to ours.

On the basis of our observation of these two cases and of other examples of Q-T prolongation resulting from treatment with prenylamine, we advise that patients on this drug should undergo regular electrocardiography, perhaps every three months. If the Q-T interval becomes greatly prolonged the drug should be stopped. If patients complain of syncope or dizziness the drug should be stopped immediately. Prenylamine is widely used and may be an important cause of tachyarrhythmias complicated by changes in consciousness.

10 Schoonmaker, F W, Ostren, R T, and Greenfield, J C, jun, Annuals of Internal Medicine, 1966, 65, 1076.

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