ABSTRACT

A case is reported of electrocardiographic QT prolongation that was presumably familial in origin. Torsades de points developed in association with the use of dothiepin, despite the prescription of a low dose of this drug.

Key words - Electrocardiogram, QT prolongation, torsades de points, dothiepin, adverse effects of dothiepin, antidepressant drug adverse effects.

Torsades de pointes (TDP) is a life-threatening ventricular arrhythmia which occurs rarely in patients receiving high doses of antipsychotic drugs, particularly by the parenteral route (Gelenberg, 1998). Recently, reports of TDP have appeared in association with conventional doses of oral antipsychotic agents (Jackson et al, 1997). TDP often occurs in a background of QT segment prolongation (Gelenberg, 1998). Tricyclic antidepressant (TCA) drugs slow cardiac conduction and may therefore, theoretically, increase the risk for TDP. In overdose, fluoxetine has also been reported to occasion QT prolongation and TDP (Graudins et al., 1997).

We present a case of QT prolongation of presumably familial origin; TDP developed in association with the use of low dose dothiepin, a drug which is commonly considered to be among the least cardiotoxic of the conventional TCA.

CASE REPORT

Ms S, a 21 year old unmarried female, presented to a general physician with a 2 hour onset of chest pain. A physical examination and electrocardiogram (ECG) were found to be within normal limits. The physician noted that she had been receiving dothiepin (25 mg at bed time) since two weeks for the management of anxiety associated with a psychosocial stressor, and therefore referred her for a psychiatric review.

At the hospital, she continued to complain of severe, non-radiating central chest pain associated with giddiness. There was no fear, restlessness, sweating, tremors, hyperreflexia or other characteristics of either panic anxiety or a cardiac event. Her behaviour appeared histrionic. Except for an irregular pulse, physical examination was entirely within normal limits. These observations appeared to confirm the referring physician's opinion.

The irregular pulse however prompted a second ECG, and clear abnormalities became evident; these included classical TDP, a prolonged QT interval, prominent U waves and complex premature ventricular contractions (PVCs). The patient was shifted to cardiological care, and she subsequently recovered with appropriate management of TDP complication of the prolonged QT syndrome. It was later discovered that the patient's sister had died suddenly and of unknown causes at age 20.

DISCUSSION

Several different genetic mechanisms
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have been identified in the familial transmission of the prolonged QT syndrome (Keating, 1996); therefore the diagnosis of a prolonged QT syndrome in this patient strongly suggests that the sudden, unexplained death of her sister was due to QT prolongation and complications thereof.

TDP often occurs in association with QT prolongation. Drugs which prolong the QT interval may thereby increase the risk for TDP; this may explain the rare occurrence of TDP in patients receiving psychotropic drugs, particularly when the drugs are administered intravenously or in high doses, or when the drugs are taken in overdose (Glenberg, 1998). Since TCA are known to slow cardiac conduction, dothiepin may have been the participating factor in the patient described in this report. To our knowledge, this is the first report of dothiepin associated with TDP; this report is further unusual because the dose of dothiepin used was low, and because dothiepin is conventionally considered to carry a low risk for cardiac adverse effects. The pre-existing familial vulnerability of this patient may explain why a conventionally safe drug precipitated a cardiac event.

It is likely that the known intermittence of the clinical syndrome was responsible for the normal findings at the time of the first physical examination and ECG. Therefore, this case also demonstrates that psychiatrists must guard against assuming a functional origin of syndromes even when the patient has received a clean chit from a physician.

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