CHLORPROMAZINE INDUCED T WAVE AND QT ALTERNANS — A CASE REPORT AND REVIEW

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SYNOPSIS

This paper describes a patient who after long-term high dose chlorpromazine developed an episode of diarrhoea followed by T wave alternans, QT alternans, prolonged QT interval and recurrent ventricular tachycardia of the "torsade de pointes" type. Electrical T wave alternans, a rare phenomenon in electrocardiography, has not been reported in association with chlorpromazine therapy. The electrical T wave alternans was due to changes in the repolarization phase from a combination of factors such as prolonged administration of chlorpromazine in high doses and possible intracellular potassium deficiency.

INTRODUCTION

Isolated T wave alternans without changes in the QRS complex is an intriguing and rare electrocardiographic phenomenon. It is characterised by changes in contour, amplitude or polarity of the T wave, occurring regularly in every other complex and without obvious changes in the P or QRS complexes. This phenomenon is often transitory.

This paper describes a patient who was treated for schizophrenia with long-term high dose of chlorpromazine (900 mgm daily) for 5 years. She presented with transitory isolated electrical T wave alternans, QT alternans, recurrent ventricular tachycardia of the "torsade de pointes" variety and prolonged QT interval after an episode of diarrhoea. As far as we are aware, chlorpromazine induced T wave and QT alternans has not been described previously in the literature.

CASE REPORT

A 55-year-old Chinese female was transferred from Woodbridge Hospital to Middleton Hospital with a diagnosis of infective enteritis. She had been treated in Woodbridge Hospital for schizophrenia since 1952, and had been on chlorpromazine since 1960. The dosage of chlorpromazine was gradually increased over the years because of frequent relapses. She had in addition received electroconvulsive therapy. She had been receiving 900 mgm chlorpromazine daily from October 1976 until the day of admission to Middleton Hospital on 2.11.80. On that day the patient momentarily lost consciousness after passing a large volume of loose stools. The medical officer, in Woodbridge Hospital, who examined the patient noted the pulse to be irregular at 80 per minute. On admission into Middleton Hospital, the patient was found to be "cyanosed with a temperature of 38°C and blood pressure of 90/60 mm Hg. The heart rate was 100 per minute and irregular. No cardiac murmurs were heard and the lungs were clinically clear. No abnormalities were detected on

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abdominal examination. The electrocardiogram revealed frequent ventricular premature contractions and runs of ventricular tachycardia. She was treated with an intravenous infusion of 500 mls of 5% dextrose saline containing 10 mls of 10% potassium chloride.

She was transferred into the Medical Intensive Care Unit at Tan Tock Seng Hospital for further management. The patient was conscious but dehydrated. There was a greyish blue pigmentation of the face, finger and toe nails from prolonged chlorpromazine therapy. Bilateral cataracts were also noted. The blood pressure was 130/60 mm Hg, and the heart rate was irregular at 100/minute. The electrocardiogram revealed sinus rhythm with frequent ventricular premature contractions and runs of ventricular tachycardia which showed features of "torsade de pointes" (Figure 1). The ventricular dysrhythmias were promptly suppressed with a bolus of 100 mgm lignocaine given intravenously. A subsequent monitoring strip showed electrical alternans of the T wave and QT interval without any obvious change in the morphology of the QRS complexes (Figure 2A). The T wave amplitude and contour was noted to vary with alternate beats. The QTC interval was increased and varied between 730 msec to 520 msec with alternate beats. A subsequent episode of "torsade de pointes" (Figure 2B) was again easily suppressed with an intravenous bolus dose of lignocaine after which the T wave alternans was noted to disappear. The QTC was however still prolonged to 620 msec. No recurrences of ventricular dysrhythmias were seen following continuous infusion of potassium chloride and lignocaine over the first 24 hours.

Investigations

The haemoglobin was 10.9 gm%, total white count 4,300/cc (neutrophils 86%, lymphocytes 12%, monocytes 2%, eosinophils 0%), serum urea 21 mgm/dl, serum potassium 4.5 mmol/L, serum sodium 135 mmol/L, serum chloride 103 mmol/L and the blood glucose 109 mgm/cc. The arterial pH was 7.403, $paCO_2$ 20.4 mm Hg, paO_2 86.4 mmHg, oxygen saturation 95.6% and the standard bicarbonate 16.2 mmol/L. The serum iron was 65 microgm/cc (normal 60-175 microgm/cc) and the total iron binding capacity 190 microgm/cc (normal 216-410 microgm/cc). The serum magnesium level was 2 mgm/dl, serum calcium 7.4 mgm/dl and the serum phosphate 2.3 mgm/dl. Methaemoglobin was not detected in the blood. The stool cultures were negative for Salmonella, Shigella and cholera micro-organisms.

Progress

The patient improved in the ward and no further episodes of ventricular dysrhythmias were seen after the first day. Oral diphenylhydantoin 100 mgm t.d.s.

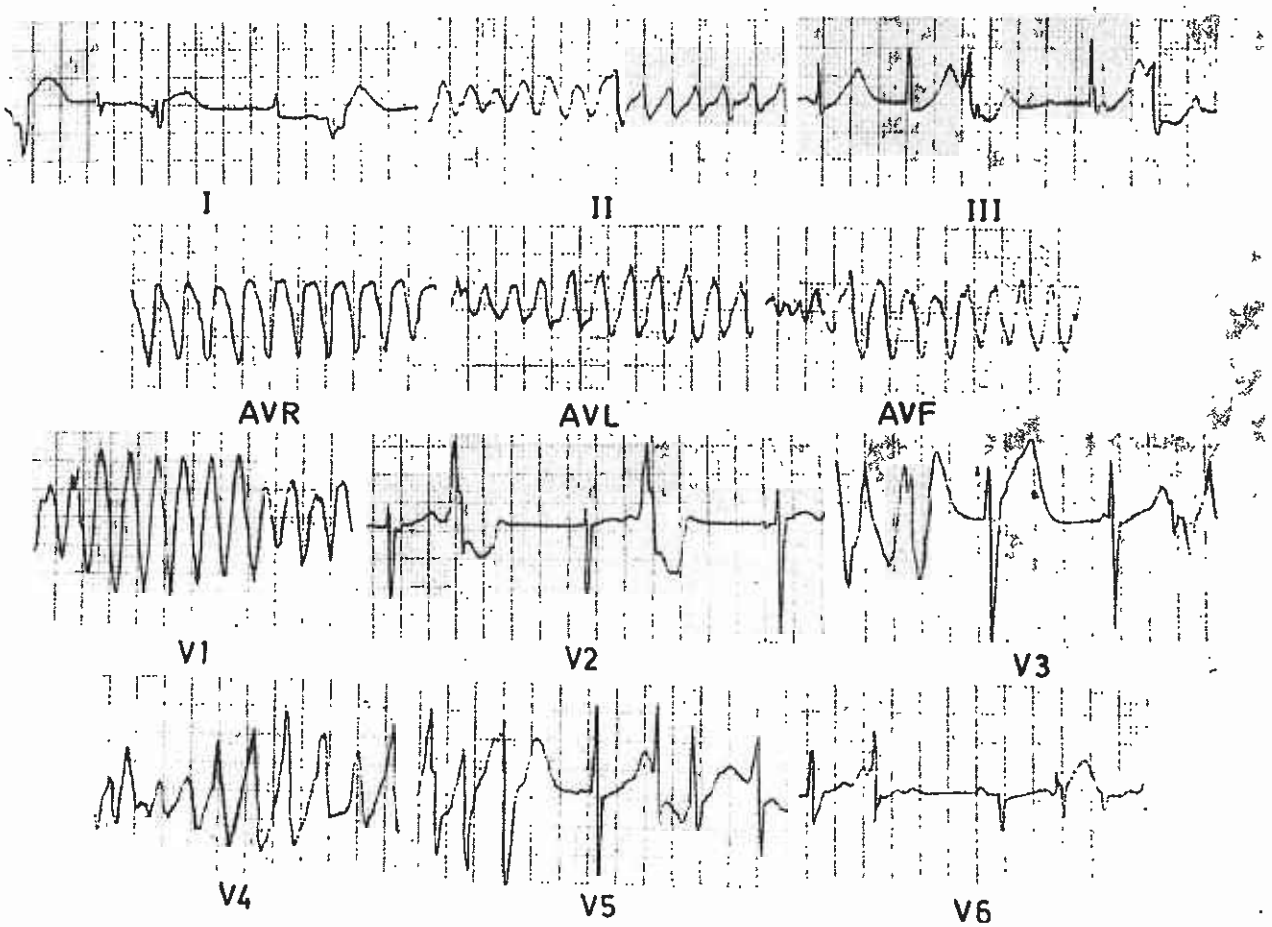

Figure 1
2.11.80. 12 Lead electrocardiogram showing frequent premature ventricular contractions with R on T phemomenon and tachycardia of "torsade de pointes" type.

and oral Bactrim 2 b.d. were prescribed. The dosage of oral chlorpromazine was reduced to 200 mgm t.d.s. The electrocardiogram recorded on 6.11.80 revealed sinus rhythm with QTC interval of 540 msec. The patient was discharged well on 14.11.80

DISCUSSION

Isolated T wave alternans without any change in QRS complex was first described by Mines in 1913 (1). Littman provided an example in 1933 (2) and in 1963, Kimura et al (3) provided a complete 12 lead electrocardiogram illustrating T wave alternans. Navarro-Lopez et al (4) in 1978 reviewed the literature on T wave alternans and was able to find 11 published cases (3, 9-14) from 1931 to 1975, and added two more cases of their own. Schwartz et al recognised 13 examples of T wave alternans after re-examining 28 cases of Romano-Ward Syndrome with prolonged QT interval which had previously been reported (5). Puletti et al reported in 1980, alternans of the ST segment and T wave in a patient with acute myocardial infarction (6).

The electrocardiographic features of the T wave and QT alternans in our patient consisted of changes in T wave amplitude and QT interval occurring with every alternate beat without any visible change in the QRS complex (Figure 2A). The QTC intervals alternated between 730 msec and 520 msec, and the Twave amplitude alternated between 5 mV and 1 mV. There was no change in the T wave polarity in contrast to some of the previously reported cases (8-11). The T wave and QTC alternans in our patient were recorded between episodes of ventricular tachycardia, which was of the "torsade de pointes" variety (Figure 2B). This dysrhythmia was promptly suppressed with a bolus dose of intravenous lignocaine following which T wave and QT alternans were observed to disappear. The QTC interval however, remained prolonged at 620 millisecs (Figure 2C).

The mechanism underlying electrical alternans remains unknown. Electrical alternans of components of the action potential has been studied experimentally at the level of the single cell (16-17). Experimentally, electrical alternans has been produced in both contractile and conductive tissue in a number of species of animals. The phenomenon was often transitory, was unrelated to heart rate, and was usually not associated with decreased cardiac contractility. Alternation of four types have been described:-

1) Rate of depolarization resulting in QRS alternans;
2) Rate of repolarization resulting in T wave alternans;
3) Magnitude of action potential; and
4) Magnitude of hyperpolarization.

The action potential of single cell could be separated into a spike (fast) component and plateau (slow) component. Electrical alternans of both com-

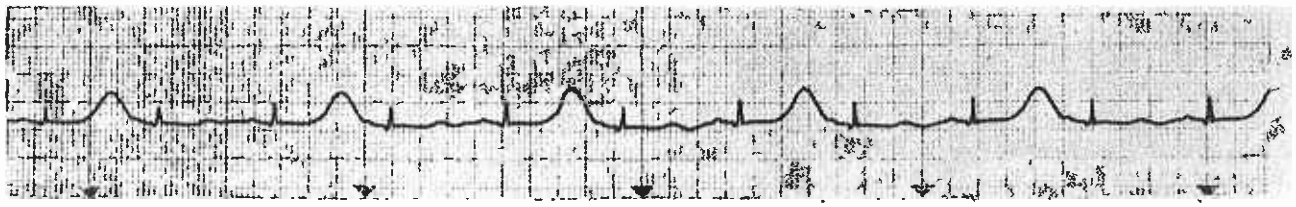

Figure 2A: Electrocardiogram showing T wave and QT alternans without changes in QRS complex.

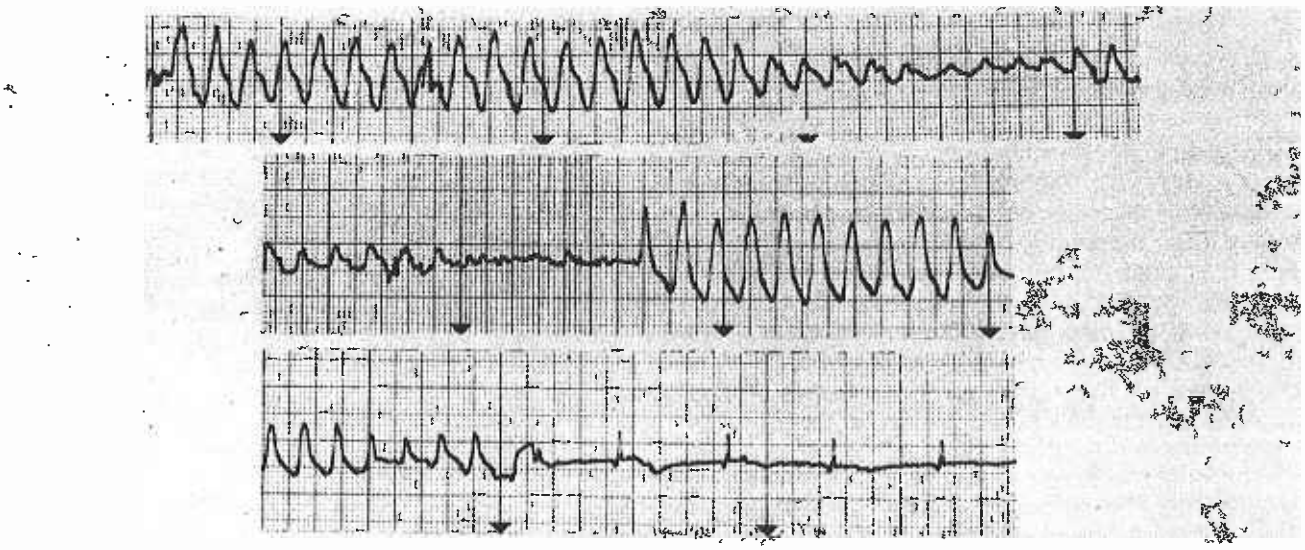

Figure 2B: Continuous electrocardiographic strip showing "torsade de pointes"

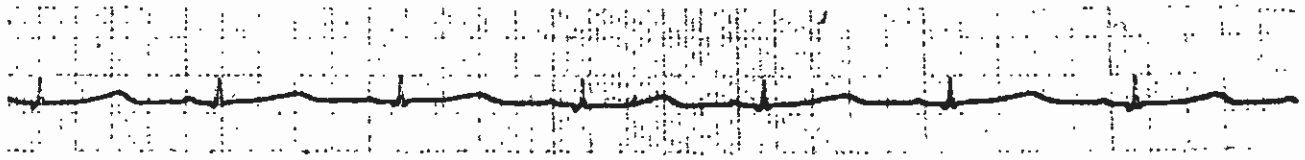

Figure 2C: Electrocardiographic strip showing sinus rhythm with prolonged QT interval after suppression of "torsade de pointes"

ponents could be produced experimentally (16, 17). It was postulated by Kleinfeld et al (16, 17) that alternation of the rate and extent of transport of ions across the myocardial membrane was involved. As the plateau (slow component) was dependent on calcium ion transport, reduction in serum calcium has been postulated to be one possible cause of isolated T wave alternans (18). Hypocalcaemia has indeed been found in some of the reported cases where serum calcium levels were available (3, 4, 13, 14) as in this patient. This, however, does not explain the mechanism in cases where serum calcium levels were reported to be normal (10, 12). Hypokalaemia and hypomagnesaemia have also been implicated in the production of electrical T wave alternans in a patient with alcoholic cardiomyopathy (9). It is possible that these ionic changes may affect the repolarization phase, contributing eventually to electrical T wave alternans. Isolated T wave alternans could be produced in experimental coronary artery occlusion (19). Puletti et al (6) described a patient with isolated T wave alternans of the ST segment and T wave in a 71-year-old man with acute myocardial infarction. It was postulated that delayed electrical activity of the ischaemic tissue may be the cause of the ST-T wave alternans. Schwartz et al (5) reviewed the reported cases of long QT Syndrome of the Romano-Ward type and found to their pleasant surprise, 13 instances of T wave alternans out of the 28 published cases. Prolonged QTC intervals and T wave alternans usually occurred during stress, suggesting that alternation of the T wave was related in some way to sympathetic nervous system. In one recent report (21) the workers were able to produce ventricular tachycardia and T wave alternans after Valsalva manoeuvre in some patients with prolonged QT Syndrome.

T wave alternans has also been reported after episodes of supraventricular and ventricular tachydysrhythmias (11, 12, 15). The actual mechanism in these situations is not known, but it has been suggested that the post-tachycardic state and myocardial disease could be contributory factors (12).

It has been well established that phenothiazines can produce electrocardiographic abnormalities and dysrhythmias (20). The changes include prolongation of QT interval, prominent U waves, supraventricular tachycardia and ventricular tachycardia, particularly of the "torsade de pointes" type as in our patient. Although electrical alternans was mentioned in one report (20), no electrocardiogram was available for inspection. T wave and QT alternans due to chlorpromazine has not been previously described to the best of our knowledge.

The T wave alternans in this patient could be due to a combination of factors affecting mainly the repolarization phase of the action potential. Although the serum potassium was normal, intracellular deficiency in potassium could not be excluded. Recently Kitazawa et al (22) have suggested that the dysrhythmogenic effect of chlorpromazine is due to decreased mitochondrial Ca+ + binding activity.

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