Diuretic-induced hypokalaemia inducing torsades de pointes

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Torsades de pointes (TP), an unique polymorphous type of ventricular tachycardia, is associated with either an acquired or congenitally prolonged QT interval. Several reports have demonstrated TP to follow an acquired prolonged QT interval secondary to chronic hypocalcaemia, hypomagnesaemia, or hypokalaemia. We report a rapid onset, acute extracellular hypokalaemia not associated with other electrolyte disturbances inducing a prolonged QT interval followed by TP. This is the first case report of a rapid onset isolated acute extracellular hypokalaemia inducing TP. Since anaesthetists are involved in therapies that will rapidly reduce extracellular potassium (diuretic, catecholamine, and/or insulin administration, hyperventilation), this case report serves as a warning that such therapy may have the risk of arrhythmia induction.

Les torsades de pointes (TP) sont un type particulier de tachycardie ventriculaire. Elles sont associées à l'allongement acquis ou congénital de l'intervalle QT. Plusieurs observations ont décrit des TP après l'allongement du QT consécutif à une hypocalcémie, une hypomagnésémie ou une hypokaliémie. Les auteurs rapportent une hypokaliémie extravasculaire d'installation rapide sans association à d'autres dérangements électrolytiques capables d'allonger le QT et qui a été suivie de TP. C'est là la première description de TP causées par une hypokaliémie extravasculaire aiguë. Comme les interventions anesthésiques provoquent souvent des baisses rapides du potassium extracellulaire (l'administration de diurétiques, de catécholamines, d'insuline, l'hyperventilation), cette observation signale le risque de ces manœuvres relativement à la genèse des arythmies.

Key words

COMPLICATIONS: arrhythmia, hypokalaemia;
HEART: arrhythmia, torsades de pointes;
IONS: potassium.

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Torsades de Pointes (TP) is an unique type of ventricular tachycardia, characterized by QRS complexes of changing amplitude preceded by a prolonged (>500 msec) QT interval, most frequently observed with anti-arrhythmic drug therapy and electrolyte disturbances.¹ While hypokalaemia has been commonly associated with TP,² it is usually chronic hypokalaemia with concomitant anti-arrhythmic drug administration and/or hypomagnesaemia.³ While many episodes of TP terminate spontaneously, some degenerate to a more typical ventricular fibrillation resulting in death.⁴ We report a case of TP occurring during orthotopic liver transplantation in a child caused by an acute extracellular hypokalaemia with normal serum magnesium concentration and no previous anti-arrhythmic drug exposure.

Case report

A four-yr-old 18 kg caucasian boy was scheduled for orthotopic liver and small bowel transplantation because of cirrhosis secondary to short bowel syndrome. No symptoms of central nervous system dysfunction were observed. Preoperative laboratory values included a serum potassium of $3.9 \text{ mEq} \cdot \text{L}^{-1}$ (3.5–4.7 normal) and magnesium of $2.3 \text{ mg} \cdot \text{dl}^{-1}$ (1.7–3.0 normal). There was no history of arrhythmia or prolonged QT interval, or family history of sudden death. A corrected QT interval (QTc) of 370 msec was measured preoperatively (Figure A). After uneventful induction and maintenance of anaesthesia with isoflurane and muscle relaxation with pancuronium, the native liver was excised and the donor liver placed. During the anhepatic phase, the urine output was noted to be minimal, so furosemide, 15 mg *iv*, was given. During donor graft placement, the aorta was cross-clamped above the renal arteries for a total of 40 min. Following unclamping, anuria was noted. Furosemide, 180 mg, *iv* in divided doses was given over three hours with no effect. At that point, the Foley catheter was found to be occluded. Upon recatheterization, 2.7 l urine were measured over the ensuing 2½ hr. Over the same time, serum potassium concentration decreased from 3.9 to 2.9 $\text{mEq} \cdot \text{L}^{-1}$, while serum magnesium concentration remained unchanged at $2.3 \text{ mg} \cdot \text{dl}^{-1}$. Serum ionized calcium concentrations during this time were 1.17 to 1.18 $\text{mmol} \cdot \text{L}^{-1}$ (1.18 to 1.30, normal), and arterial blood pH

FIGURE Electrocardiogram obtained before surgery demonstrating sinus beats with a corrected QT interval (QTc) of 370 msec (Figure A). Intraoperative electrocardiogram obtained demonstrating sinus beats with prolonged corrected QT interval (QTc) (l) progressing to torsades de pointes (TP) ventricular tachycardia (Figure B). Electrocardiogram obtained after termination of TP showing a normal QTc (Figure C).

was consistently between 7.38 to 7.45. The heart rate was never observed to be <100 bpm. In spite of potassium replacement (40 mEq over five hours), $5\frac{1}{2}$ hr after revascularization of the liver and small bowel and during biliary reanastomosis, a prolonged corrected QT interval (QTc) of 600 msec was noted, followed rapidly by TP of 5.6 sec duration resulting in severe systemic hypotension (Figure B). Treatment with lidocaine 40 mg *iv*, magnesium 400 mg *iv* and KCl (10 mEq *iv* over 20 min) restored sinus rhythm with a QTc of 380 msec (Figure C).

Oesophageal temperature measurement remained $>35^{\circ}\text{C}$ throughout the TP and the entire surgical procedure. The remainder of the case was uneventful.

Discussion

Hypokalaemia predisposes to ventricular arrhythmias following myocardial infarction⁵ and during epinephrine infusion in dogs.⁶ Electrophysiological studies characteristically demonstrate a depolarization hump during phase 3 repolarization (early after depolarization, or EAD), as being the underlying electrical event responsible for TP.² Phase 3 repolarization corresponds to the T wave of the surface ECG; therefore, an EAD would correspond to the "R on T" phenomenon.^{2,7} Since major surgical stress is known to be associated with elevated plasma epinephrine concentrations,⁸ the pro-arrhythmic effects of diuretic-induced hypokalaemia was possibly potentiated by an epinephrine-induced hypokalaemia.^{5,6} Kwon *et al.*⁹ reported that an acutely hypokalaemic (induced by hyperventilation) rat model was surprisingly more resistant to the arrhythmogenic effect of an epinephrine infusion than was a normokalaemic control group.

Magnesium replacement acts by shortening the QT in-

terval,¹⁰ and suppressing EAD's.¹¹ In chronic hypokalaemia a 42% incidence of hypomagnesaemia has been reported.¹² Ventricular arrhythmias are commonly associated with combined hypokalaemia and magnesaemia.¹³ Under these conditions, magnesium and potassium replacement are required for ventricular arrhythmia control.¹¹ While TP has been commonly reported with normal serum magnesium concentrations,¹⁰ exogenous magnesium administration has been shown to be effective in terminating TP despite normal serum levels.¹⁴ Fiacadori *et al.* found no correlation between muscle and serum magnesium concentrations in chronically ill patients,¹⁵ thus a normal serum magnesium concentration may be found with total body hypomagnesaemia.

The extracellular potassium concentration is the primary determinant of resting membrane potential in human cardiac muscle; decreased extracellular potassium will prolong action potential duration; i.e., prolonged QT interval, as well as increase the rate of spontaneous phase 4 depolarization (increase automaticity), and hyperpolarize the resting membrane potential.^{16,17} In the potassium deficient state, extracellular potassium decreases more than intracellular⁷ and, as described by the Nernst equation,¹⁸ results in membrane hyper-polarization. Isolated chronic hypokalaemia is known to induce TP,^{2,18} but this is the first report demonstrating that a rapid onset extracellular hypokalaemia may also induce TP. Curry *et al.*¹⁹ reported two cases of TP associated with isolated chronic hypokalaemia, one secondary to hyperaldosteronism, the other due to familial periodic paralysis. Tamura *et al.*²⁰ reported a single case of TP with isolated hypokalaemia. Soroker *et al.*²¹ reported two cases of intraoperative TP associated with combined chronic hypocalcaemia and rapid onset hypokalaemia. The first two^{19,20} of these case reports fail to report serum magnesium concentrations, while one²⁰ report was complicated by simultaneous digitalization.

Complications described with furosemide have been generally related to its primary effect of sodium, potassium, magnesium, and water loss secondary to inhibition of active chloride transport in the loop of Henle.²² Large dose ($7\text{ mg} \cdot \text{kg}^{-1}$) furosemide administration has little direct cardiovascular effect,²³ while $1.5\text{ mg} \cdot \text{kg}^{-1}$ has been demonstrated to be without cardiovascular effects while causing a rapid (15 min) reduction of plasma potassium concentration.²³ While supraventricular tachycardia due to furosemide treatment per se (without secondary electrolyte alteration)²⁴ has been observed, no report has demonstrated that ventricular arrhythmias have been induced by furosemide.

In summary, this is the first description of a rapid onset, isolated, extracellular hypokalaemia resulting in an acquired prolonged QTc followed rapidly by TP. Even-

with a normal serum magnesium concentration, exogenous magnesium helped restore a normal QTc and terminate TP. This report serves as a warning that a rapid decrease in extracellular potassium concentration with no other risk factors may precipitate TP.

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