Torsade de pointes (TdP) is an uncommon and specific form of polymorphic ventricular tachycardia, associated with a prolonged QT interval. Prolongation of the QT interval is the most widely recognized electrophysiological abnormality in patients with liver cirrhosis. We observed a case of TdP leading to cardiopulmonary resuscitation after the induction of general anesthesia, in a patient with liver cirrhosis scheduled for emergency cadaveric donor liver transplantation. The patient had mild QT prolongation on preoperative electrocardiography with a corrected QT (QTc) interval of 455 ms. Drugs used in the preoperative period can elongate cardiac repolarization. Sevoflurane and 5-hydroxytryptamine type 3 receptor antagonists such as palonsetron, used during general anesthesia may have triggered further QT prolongation, producing a fatal condition such as TdP. More caution and consideration in selecting drugs for anesthetic management are necessary for liver cirrhosis patients, especially in patients with preoperative QT prolongation. (Korean J Anesthesiol 2014; 66: 80-84)

Key Words: Heart arrest, Liver transplantation, Long QT syndrome, Torsades de pointes.
Case Report

A 53-year-old male (height 173.6 cm, weight 75.6 kg) was scheduled for emergency cadaveric donor liver transplantation due to hepatitis B virus-related liver cirrhosis and hepatocellular carcinoma. Microvascular angina was diagnosed 2 years earlier with atypical chest pain. Coronary angiography at that time showed no significant stenotic findings. The patient was diagnosed with atrial fibrillation at the same time, and he was started on nicorandil, molsidomine, isosorbide dinitrate, digoxin, furosemide, and spironolactone. An anticoagulant was excluded due to bleeding tendencies. Furthermore, the patient had liver cirrhosis-related diabetes mellitus, portal hypertensive gastropathy, and esophageal varix.

ECG was performed just before surgery and showed atrial fibrillation with a normal heart rate (Fig. 1). The calculated QTc interval was 455 ms. The patient had mild mitral regurgitation and tricuspid regurgitation, but no regional wall motion abnormality was seen on preoperative echocardiography. The calculated left ventricular ejection fraction was 68%, and the mean pulmonary arterial pressure was 24 mmHg. The PT INR was 1.38, total bilirubin was 2.2 mg/dl, platelet count was 48,000 /μl, and albumin was 2.5 g/dl. Other blood test findings were within normal limits.

Without preoperative medication, the patient entered the operating room and his vital signs were measured immediately. His blood pressure (BP) was 117/73 mmHg, heart rate (HR) was 80 beats/min, and his pulse oximetry oxygen saturation (SpO₂) was 99%. After preoxygenation with a mask by applying 100% O₂ at 6 L/min for a few minutes, palonosetron 0.075 mg, lidocaine 40 mg, and propofol 120 mg were administered intravenously. After the patient lost consciousness, manual assisted ventilation was performed with 100% O₂ at 6 L/min and 5 vol% sevoflurane; in addition, rocuronium 50 mg was injected. With full relaxation, the patient’s trachea was intubated using a cuffed 7.5 mm endotracheal tube without difficulty. The radial and femoral arteries were cannulated, followed by continuous arterial blood pressure monitoring. A central venous catheter (AVA HF; Edwards Lifesciences, Irvine, CA, USA) was placed at the right internal jugular vein with no resistance or difficulty. A pulmonary artery catheter (Swan-Ganz CCOmbo; Edwards Lifesciences, Irvine, CA, USA) was inserted and pulmonary artery pressure monitoring was started. By ECG, no clinically significant change occurred during insertion of the pulmonary artery catheter. The catheter’s position was checked with a chest X-ray. Anesthesia was maintained with 0.7 L/min O₂, 1.3 L/min air, and 1.5–4.0 vol% sevoflurane. Initial arterial blood gas analysis (ABGA) revealed normal electrolyte levels and adequate oxygenation. ECG showed atrial fibrillation, but no clinically significant abnormal change was observed.

At 50 minutes after the patient’s arrival, the surgeon started to prepare for surgery. At that time, sudden-onset large QRS tachycardia (Fig. 2B) appeared, and the femoral and radial arterial waves became flat. The end tidal CO₂ (ETCO₂) pressure dropped rapidly, from 35 to 13 mmHg. Epinephrine 100 μg and calcium chloride 300 mg were administered twice. One of the surgeons started cardiac compression immediately, and mechanical ventilation was continued with 100% O₂. Epinephrine 1 mg was injected intravenously. During CPR, defibrillation was performed four times using 150–200 J, and epinephrine 1 mg was administered intravenously every 3–5 minutes. Amiodarone 300 mg mixed with 100 ml of normal saline was administered. Additionally, magnesium sulfate 2 g and lidocaine 70 mg were injected intravenously. Calcium chloride, regular insulin, and sodium bicarbonate were also administered after checking ABGA (Table 1). During CPR, a bloody secretion started to come out of the endotracheal

![Fig. 1. Preoperative electrocardiography. The calculated corrected QT interval from lead II is 455 ms.](image-url)

![Fig. 2. Changes observed in lead II by electrocardiography (ECG) during anesthesia. (A) ECG after anesthetic induction (QTc = 492 ms) showed QTc interval prolongation. (B) At 50 min after the patient’s arrival, large QRS tachycardia appeared (QTc = 480–490 ms). (C) The R-on-T phenomenon and ventricular premature beats were observed during the occurrence of large QRS tachycardia. (D) During cardiac arrest, ECG demonstrated torsade de pointes. ECG: electrocardiography, QTc: corrected QT interval.](image-url)
Intraoperative torsade de pointes

After 30 minutes of CPR and the last defibrillation, large QRS tachycardia disappeared and ECG revealed a normal sinus rhythm. Simultaneously, the femoral and radial arterial waves recovered to normal wave forms. The patient’s systolic BP was 80–85 mmHg, his HR was 40–45 beats/min, and ETCO₂ was 17–19 mmHg. After the return of spontaneous circulation, we loaded 50 μg/kg milrinone intravenously and started continuous infusion of milrinone at 0.5 μg/kg/min and epinephrine at 0.1 μg/kg/min. Regular insulin, sodium bicarbonate, and vasoressin were also administered. The patient’s temperature was 34.7°C, and both pupils were dilated without a light reflex.

A few minutes later, the patient’s SpO₂ increased to 100%, and ECG showed atrial fibrillation with a HR of 80 beats/min. The patient’s pupil reflex returned to a normal response. Electrolytes and cardiac enzymes were evaluated. Neither hypokalemia nor hypocalcemia was detected, and all electrolyte values were within normal levels. The patient’s CK was 106 IU/L, CK-MB was 2.6 ng/ml, and Troponin I was slightly elevated to 0.10 ng/ml. Bedside echocardiography revealed no regional wall motion abnormality or evidence of myocardial ischemia.

On the second day of ICU admission, pulse-less large QRS tachycardia appeared twice. Both events were terminated after applying defibrillation using 150 J and cardiac compression for 2 minutes. Metabolic acidosis, intravascular volume loss, and pulmonary edema were aggravated and the patient’s BP and SpO₂ continued to decrease. On the fourth day in the ICU, the patient expired. ECG showed a marked prolonged QTc interval (Fig. 3). Nevertheless, cardiac echocardiography performed on the day of the patient’s expiry showed normal findings. No regional wall motion abnormality was observed, and the left ventricular wall thickness was normal with a calculated ejection fraction of 56%. The patient’s systolic pulmonary arterial pressure was 33 mmHg.

Discussion

Long QT syndrome is a congenital or acquired disorder of cardiac ion channels, characterized by heterogeneity in cellular repolarization and precipitation of tachyarrhythmias [2]. The character of this syndrome is a marked prolongation of ventricular repolarization, including QT interval prolongation and T wave abnormalities leading to ventricular tachycardia, such as TdP and ventricular fibrillation [3]. Although a normal value has not been established, QTc intervals longer than 440 ms are generally considered to indicate prolonged QT. As in the present case, a prolonged QTc interval is related to sudden death and poor survival in patients with various diseases [3,4].
Prolongation of the QT interval is the most widely recognized electrophysiological abnormality in liver cirrhosis and has been observed in about half of patients with liver cirrhosis [1,5,6]. Several investigations have reported that QT prolongation increases with the severity of liver disease, but it can also occur in patients with well-compensated cirrhosis [1,5,6]. Bal and Thuluvath [5] demonstrated an association between liver cirrhosis and QT prolongation, showing that a worsening of the Child-Pugh score was associated with further prolongation of the QT interval. Some investigators have demonstrated that the QT interval is an additional prognostic factor for life expectancy [7]. The present patient had Child-Pugh class C liver cirrhosis with numerous accompanying complications. The QTc calculated by preoperative ECG was 455 ms.

Several drugs used in the perioperative period could induce the lengthening of cardiac repolarization [8,9]. In many ECG studies, sevoflurane has been shown to lengthen the QT interval during the induction of inhalational anesthesia [8,10]. 5-Hydroxytryptamine type 3 receptor antagonists commonly used to prevent or treat postoperative nausea and vomiting, have also been demonstrated to induce QT prolongation [11]. In our case, palonsetron was administered during the induction of anesthesia and sevoflurane was used to maintain anesthesia. Palonsetron is a 5-hydroxytryptamine type 3 receptor antagonist. Thus, palonsetron may have been an aggravating factor in QT prolongation, although its effect on the QT interval has not yet been specifically investigated. A few seconds before the occurrence of TdP, the QTc interval was prolonged to 492 ms (Fig. 2A). TdP only occurred before any surgical procedure, so the anesthetic agents used during induction are suspected to be the most probable cause. That no sympathetic hyperactivity was seen before the occurrence of TdP and ABGA performed just before the initiation of TdP was within normal limits support this. Although the patient had diagnosed microvascular angina, preoperative ECG showed only atrial fibrillation and no evidence of myocardial ischemia. Preoperative cardiac echocardiography and coronary angiography revealed normal findings. Furthermore, cardiac echocardiography and cardiac enzymes evaluated after CPR did not indicate any ischemic insult. Atrial fibrillation may have been a contributing factor in the occurrence of TdP; however it is hard to ascribe myocardial ischemia as a major cause of TdP.

We undertook a retrospective analysis of the ECG waveform during anesthesia and found that TdP was the initiating ECG form during the patient’s arrhythmia and arrest. Ventricular premature beats occurred, and the R-on-T phenomenon preceded TdP (Figs. 2C and 2D). Unfortunately, we did not know that TdP was the first ECG form at the time of arrest; thus, we managed the patient’s arrhythmia according to standard CPR guidelines. We administered amiodarone intravenously, which may have aggravated the QT prolongation. Amiodarone is known to prolong the QT interval, but with a low incidence of proarrhythmic events [12]. Nevertheless, QT prolongation with subsequent TdP after amiodarone therapy potentially resulting in ventricular fibrillation has been repeatedly reported [13]. Preoperative management of patients with long QT syndrome should be performed in a comfortable environment. Midazolam and fentanyl can be used to prevent anxiety without complications [14]. The use of drugs known to prolong the QT interval should be avoided as far as possible. Perioperative infusion of magnesium sulfate is recommended as prophylaxis against TdP [14]. A defibrillator and transvenous pacing wires and leads should be prepared for prompt use [2,15]. Hypothermia should be avoided since it may prolong the QT interval, possibly through the delayed recovery of inactivated sodium channels [2,14,15].

Magnesium sulfate is the treatment of choice for TdP [14]. Serum electrolyte levels should be checked and corrected within normal limits. Temporary transvenous pacing can be effective in some patients. Defibrillation and CPR may be necessary and lidocaine may be useful in terminating arrhythmia [14]. In conclusion, patients with liver cirrhosis may have preoperative QT prolongation, but insufficient awareness of this electrophysiological abnormality is common. Sevoflurane and 5-hydroxytryptamine type 3 receptor antagonists used during anesthesia can trigger further QT prolongation. This can lead to fatal conditions, including TdP, as in the present case. More caution and consideration when selecting drugs and inhalation agents during anesthetic management are necessary for patients with liver cirrhosis, especially patients with preoperative QT prolongation. In particular, 5-hydroxytryptamine type 3 receptor antagonists should be avoided and replaced with other antiemetic drugs, and sevoflurane should be used with caution. Vital signs and ECG should be carefully monitored, and the QTc should be evaluated continuously during anesthesia if possible. Furthermore, in vulnerable patients with preoperative QT prolongation, TdP should be considered as a possible cause when fatal arrhythmia occurs. Deterioration in a patient’s condition due to an inappropriate medication such as amiodarone can be prevented by scrupulous attention and an adequate diagnosis. Accurate and expeditious management is also required.
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