Case Report
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A Fatal Side Effect of Piperacillin/Tazobactam Use: A Case Report

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Abstract

Drug-induced QT prolongation with T wave inversion is a complex regulatory and clinical problem due to the rarity of this potentially fatal adverse incident. A 68-year-old female patient was receiving piperacillin/tazobactam therapy for a complicated urinary tract infection. She has had normal ECG findings before the antibacterial therapy. After the treatment, the patient worsens due to long QT which is predisposed to torsades de pointes. As a result of the researches, it was understood that the cause of long QT was piperacillin/tazobactam. We aimed to present a rare case in which we detected drug-induced QTc prolongation with piperacillin/tazobactam in clinical practice.

Key words: Torsades de Pointes, drug-induced long QT syndrome, piperacillin/tazobactam, T-wave inversion, urinary tract infection

Introduction

The QT interval seen on the electrocardiogram (ECG) reflects the electrical depolarization and repolarization of the ventricles. The normal range of the rate-corrected QT (QTc) intervals was determined as (<0.47s) and (<0.45s) in females and males, respectively[1]. The QT interval prolongation is a clinically and genetically heterogeneous syndrome characterized by syncope and sudden death due to a tendency to ventricular fibrillation, torsades de pointes and ventricular arrhythmia[2]. QT interval may be prolonged by hypokalemia, hypomagnesemia, hypocalcemia, myocardial ischemia, post-cardiac arrest, increased intracranial pressure, congenital long QT syndrome and drugs. It has been identified that many drugs such as antihistamines, antibiotics, antidepressants and prokinetics may cause drug-induced prolonged QT syndrome (diLQTS)[3]. The mechanism for the drug that prolongs the QT time is due to the inhibition of the one encoded by KCNH2. HERG (the human Ether-à-go-go-Related Gene) prolongs QT interval by inhibiting the potassium channel, causing delayed action potential[4]. We present a rare case report by using piperacillin-tazobactam-induced long QT syndrome.

Case Report

A 68-year-old female patient with a history of hypertension was admitted to the emergency department with the complaint of fainting and feeling like her heart would stop.

ECG was notable for QT prolongations in multiple leads and deep symmetrical T wave inversion(Figure1) (QTc, Bazett correction = 542 ms). Patient was admitted to the critical care area of the emergency department clinic with the pre-diagnosis of the acute coronary syndrome and cerebrovascular event by emergency medicine specialists.

On arrival, the patient's vital signs were: blood pressure of 110/ 70 mmHg, heart rate of 65 beats per minute, respiratory rate of 18 breaths per minute, temperature of 36,5 degrees Celsius, and an oxygen saturation of 96% on room air. Blood glucose measurement from the fingertip is 100 mg/dl. No intracranial pathology was detected in cranial CT and MRI. Laboratory findings were WBC 11.9 103 / mm3 (4 - 10.5), NEU 8.7 103 / mm3 (1.82 - 7.42), LYM 2.8 103 / mm3 (0.85-3), Blood Urea Nitrogen 25 mg / dL (8 - 20), Creatinine 0.96 mg / dL (0.81 - 1.44), Alanine aminotransferase (ALT) 40 U / L, Aspartate transaminase AST- (SGOT) 52 U / L, CRP 20.8 mg / L (0 - 5), potassium (K): 3.6 mmol / L (3.5-5.0), sodium (Na): 136 mmol / L (138 - 145), Troponin T: 22 ng \ L (0-14) calcium: 8.6 mg / dL (8.5-10.5), magnesium 1.91 mmol / L (1.8-2.6).Transthoracic echocardiography performed in the emergency department revealed degenerative mitral and aortic valves and mild left ventricular hypertrophy (Figure 2). She was hospitalized to the coronary intensive care unit because at her ECG, a prolonged QT was also detected. She was under home treatment with valsartan/hydrochlorothiazide and acetylsalicylic acid. One hour after hospitalization in the coronary intensive care unit, CPR was initiated and defibrillation was performed rapidly

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following the transition of the patient into an unconscious state and development of torsades de pointes, known as a fatal dysrhythmia, seen in the monitor. 2 gr Magnesium IV was administered. Coronary angiography was performed after rhythm recovery. Coronary angiography revealed uncritical plaques in the left anterior descending coronary artery (LAD) and right coronary artery (RCA). There was no detected abnormality in the laboratory results. There were no substantial reasons explaining prolonged QT. When the hospital registry system was checked, it was seen that the patient was discharged from our hospital about 15 hours ago. When the summary of discharge from the hospital was reviewed, it turned out that she was treated with piperacillin/tazobactam due to a complicated urinary tract infection due to E Coli producing ESBL in urine culture. Previous ECG taken before piperacillin/tazobactam treatment, shows no QT prolongation and T wave inversion(figure 3). It was found that the prolonged QT finding and deep T wave inversion of the patient, who was followed up in the coronary intensive care unit, resolved spontaneously. After ruling out other causes that could cause prolonged QT, it was thought that the cause of prolonged QT was likely to have resulted from piperacillin/tazobactam administration.

Discussion

Long QT syndrome (LQTS) is associated with fatal arrhythmias such as torsades de pointes and ventricular fibrillation[2]. As a matter of fact, torsades de pointes, which is a fatal rhythm, developed in our patient. The rhythm improved with fast and effective intervention in coronary intensive care. Electrolyte disorders such as hypokalemia, hypomagnesemia, and hypocalcemia that could cause long QT in our patient were ruled out with normal laboratory values. Intracranial pathologies were ruled out with cranial imaging. Since noncritical plaques and strictures were detected in coronary angiography, acute coronary syndrome that could cause long QT was also ruled out. Abnormal QT/QTc prolongation can be categorized into two groups as the congenital and the acquired variant the latter of which can generally be related with a certain group of drugs prolonging the QT/QTc interval. Arizona Center for Education and Research on Therapeutics (CERT) have issued a specific list of drugs with suspected TdP liability. Analyzing data from the United States Food and Drug Administration (USFDA) Adverse Event Reporting System, Poluzzi et al. reported additional drugs that can cause QT prolongation and TdP, which includes piperacillin/tazobactam and metronidazole[5]. In a study, using data between 2004 and 2008, conducted by the US Food and Drug Administration (FDA) Adverse Event Reporting System, it was found that overall 374 reports of diLQTS/TdP had been associated with antimicrobial drugs, more than half of which (62%) were detected to have links to antibacterial agents mostly to macrolides and fluoroquinolones[6]. 3.581 people who had adverse effects when taking piperacillin/tazobactam were reported between 1997 and 2018 from FDA reports on Feb, 25, 2018. Among them, total of four people, two in 2011, one in 2012, and one in 2014 (0.11%) had long QT syndrome. Our patient who developed long qt due to piperacillin/tazobactam intake is the fifth case report in the literature in this sense. Accumulating publications mostly in the form of case reports and case series pertaining to affected patients indicate that diLQTS/TdP with T wave inversion constitutes a problem cannot be unnoticed. Since it can lead to long QT and cause torsades de pointes, a fatal rhythm, piperacillin/tazobactam used in the treatment of patients with severe lower respiratory tract infections involving hospital-acquired pneumonia and ventilator-associated pneumonia, complicated urinary tract infections (including pyelonephritis), complicated intraabdominal infections, neutropenic fever, high-risk cancer patients, the ones with bacteremia associated, or likely to be associated with various infections as complicated skin and deep tissue infections (mainly in the form of diabetic foot infections)[7], are recommended to be administered with cardiac monitoring.

Conclusion

The real number of cases pertaining to drug-induced prolonged QTc with piperacillin/tazobactam in clinical practice is not exactly known. The present case clearly emphasizes the significance of reconsidering and even avoiding the administration of QT-prolonging drugs in hospitalized patients, due to the fact that hospitalized patients often have the potential to exhibit a proarrhythmic response resulting from various risk factors. Early recognition and appropriate management may lead to normalization of the ECG changes and prevent hemodynamic deterioration or death as in our case.

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