Case Report

A case of Ventricular Tachycardia and Cardiac Arrest Associated with Sertraline and Mirtazapine Combination

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A 67-year-old male suffering from depressive symptomatology was admitted to the inpatient clinic at Firat University School of Medicine; and his psychiatric evaluation revealed major depressive episode according to DSM-IV. He developed chest discomfort, chest pain and shortness of breath of acute onset accompanying pulseless ventricular tachycardia (VT) leading to cardiac arrest following sertraline and mirtazapine combination treatment. He died after two days in the Intensive Care Unit. The present case suggests that psychiatrists should be aware of unexpected cardiac events, especially when they use combination treatments.

Keywords: *Sertraline, Mirtazapine, Cardiac arrest*

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The cardiotoxic properties of some antipsychotic drugs (thioridazine, ziprasidon, etc.) and antidepressants, especially tricyclic antidepressants are well established. These properties seem to link their interactions with ion channels. However, despite their relatively and safety profile, the newer antidepressants also interact with voltage-dependent ion channels and lengthen the phases of both depolarization and repolarization, prolong the QT interval and affect the cardiac action potential. Thus, they do not have absolute sterility. On the other hand, psychiatric patients have been identified as a population at risk for cardiovascular problems (1, 2). It has been demonstrated that mortality rates are higher in psychiatric patients than in the general population (3) and that the pharmacological treatment itself might produce side effects that affect mortality from causes other than suicide (4). In the present paper, we report a case without any cardiac problems who developed ventricular tachycardia and cardiac arrest after being treated by the combination of sertraline and mirtazapine.

Case Presentation

The case was a 67-year-old married male. He was admitted to the inpatient clinic at Firat University School of Medicine nine months ago due to a major depressive episode according to DSM-IV. The Structured Clinical Interview for DSM-IV–Patient Version (SCID-I) was used to assess Axis I psychiatric comorbidity, and it revealed no comorbid diagnosis. He had no history of cardiac disease, other medical conditions, alcohol use or smoking. In addition, no personal history of fainting, a familial history of prolonged QTc syndrome or unexpected deaths were detected.

After asking him and his wife about the history of depressive symptoms, we found that his depressive complaints had started a year ago. He had been admitted to a local mental hospital for three months because of obvious weight loss and thoughts of suicide. His admission had continued for two weeks, and afterwards he had been discharged with the treatment of venlafaxine and alprazolam. However, he had not used the treatment regularly. Then, having depressive symptoms, he referred to our out-patient clinic and was admitted to the in-patient clinic. The follwing tests were carried out for a routine medical evaluation: blood sample for biochemical tests, posterior-anterior lung radiography and electrocardiography (ECG). All the routine results were evaluated as normal. Clinical Global Impressions Severity Scale (CGI-S) (5) was scored as 6 (severely ill) at baseline. Hamilton Depression Rating Scale (HDRS) (6) score was determined as 23 at baseline. QTc value at baseline ECG was 420 msn. Sertraline was started with the dose of 50 mg per day, and it was increased to 100 mg per day within three days. At the seventh day of the admission, 15 mg of mirtazapine was added to the ongoing treatment at bed time, especially for loss of motivation and concentration difficulties which are associated with the neurotransmitter, norepinephrine. His sleeplessness was improved after mirtazapine addition. On the other hand, it was observed that his depressive complaints significantly improved at day 12 and his HDRS score was 17 at that time. His relatives also said he looked well. On the same day, after dinner,

he began to complain about chest discomfort, chest pain and shortness of breath of acute onset, so ECG was performed. QTc in ECG was measured as 520 msn. Pulseless VT (ventricular tachycardia) occurred at the 9th minute. Sinus rhythm was recovered at the 9th minute with a pericardial thump. At the 16th minute, a further pulseless VT occurred and led to cardiac arrest. He was administered cardiac massage, and an immediate defibrillation of 200 J was performed. In the meanwhile, respiratory arrest developped. Bag valve mask ventilation was begun, but was complicated by increasing abdominal distention and oral secretions. He was endotracheal intubated and had several peripheral i.v. lines started. A foley catheter was placed and laboratory and arterial blood gas draws were obtained. He was transferred to the Intensive Care Unit of the same hospital, but he died in the Intensive Care Unit after two days.

Discussion

The combination treatment may have induced ventricular tachycardia and cardiac arrest in this patient because of the following reasons: (a) the patient had no history of cardiac illness, as mentioned by him and his first degree relatives; (b) his routine ECG examination was absolutely normal; (c) while the baseline QTc was 420 msn, it was 520 msn at the day he complained about chest discomfort, chest pain and shortness of breath of acute onset; (d) his ventricular tachycardia and cardiac arrest developed after sertraline and mirtazapine combination, he was not taking any agent which may have led to cardiotoxicity. In different combinations of psychoactive drugs, two main mechanisms seem to play a role in occurring the prolongation of QTc interval. The first may be the synergic blockade of the human ether-a-go-go-related gene (HERG) potassium channels, and the second may be the increase in the drug levels due to metabolic interactions between the drugs that share the same metabolic pathway whose mechanism seems to be associated with genetic-determined impairment of CYP2D6 and CYP3A4 drug-metabolizing enzymes (7). Clinical studies (8-10) did not reveal any QT prolongation with sertraline in the therapeutic dose interval. In a case report, Boer et al. (2005) reported that sertraline might cause QT interval prolongation up to 520 ms in an overdose. On the contrary, only in a case report, Amin et al. (11) described a clinically significant increase in QT interval after starting treatment with 200 mg of sertraline. Mirtazapine has two enantiomer: S+ and R-. S+ enantiomer is responsible for cardiac effects. On the other hand, kinetics of R- mirtazapine was found to be only marginally dependent on CYP2D6 genotype, but total clearance of the S+ enantiomer was determined as 1.3, 2.3, and 3.4 L min-1 in poor, extensive, and ultrarapid metabolizers of CYP2D6 substrates with apparent substantial first-pass metabolism in rapid and ultrarapid metabolizers. Consequently, the interaction via CYP2D6 seems to be individual-specific. Thus, detecting ventricular tachycardia and cardiac arrest in our case led us to consider the personalized psychotropic drug interactions. Furthermore, it can be speculated that genetic polymorphisms of potassium-channel-encoding genes may have a role in the individual risk of cardiac arrhythmias and the limits of QTc.

In conclusion, the present case leads us to conclude that it may be beneficial to take into consideration possible unexpected cardiac events of certain combination treatments like mirtazapine plus other antidepressants.

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