Case Report
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Quetiapine Induced Myocarditis

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Abstract

This article reports myocarditis related to overdose of quetiapine. An 18-year-old female patient who used 25 mg of quetiapine for anxiety disorder attempted suicide with twenty quetiapine pills. The patient developed palpitations, shortness of breath, pleuritic chest pain, and confusion in the emergency room. ST-elevation and right bundle branch block were detected on D1-aVL lead in the patient's ECG. The cardiac markers were significantly elevated. The patient was hospitalized and treated in the internal medicine intensive care unit. Drug-induced myocarditis was resolved by two weeks of treatment. This case report presents a case of myocarditis induced by quetiapine overdose.

Keywords: Quetiapine, myocarditis, drug-induced myocarditis

Özet

Bu makale, ketiapin doz aşımına bağlı miyokarditi bildirmektedir. Anksiyete bozukluğu nedeniyle 25 mg ketiapin kullanan 18 yaşında kadın hasta, 20 adet ketiapin hapı ile intihar girişiminde bulundu. Acil serviste hastada çarpıntı, nefes darlığı, plöretik göğüs ağrısı ve konfüzyon gelişti. Hastanın EKG'sinde D1-aVL derivasyonlarında ST elevasyonu ve sağ dal bloğu saptandı. Kardiyak belirteçler önemli ölçüde yükseldi. Hasta dahiliye yoğun bakım ünitesinde tedavi altına alındı. İlaca bağlı miyokardit, iki haftalık tedaviyle düzeldi. Bu vaka raporu, ketiapin doz aşımının neden olduğu bir miyokardit vakasını sunmaktadır.

Anahtar Kelimeler: Ketiapin, myokardit, ilaca bağlı myokardit

Introduction

Drug-induced cardiotoxicity is one of the most severe adverse reactions associated with the use of antidepressants and antipsychotic drugs[1]. Although rare, several drugs can cause potentially fatal side effects in psychiatry clinics, including myocarditis. Myocarditis is an inflammatory disease of the myocardium [2,3].

Although the most common cause is viral infections, seldomly drugs can cause myocarditis. Myocarditis due to quetiapine, an atypical antipsychotic drug used in the treatment of schizophrenia, bipolar disorder, and major depressive disorder, is extremely rare [4,5].

Case report:

An 18-year-old female patient who took 25 mg of quetiapine a day because of her anxiety disorder was brought to the emergency room after using 20 quetiapine tablets for suicide. In her anamnesis, it was learned that she had taken the tablets one hour before she was brought to the hospital. She was admitted to the internal medicine intensive care unit after developing palpitations (evaluated as sinus tachycardia) while observing the emergency room.

ST-elevation and right bundle branch block were detected in the DI-aVL leads in the patient's first ECG. The patient's initial troponin value was below 0.01 pg/ml (reference value: 0-60 pg/ml), and CK-MB was 3,62 ng/ml (reference value: 0-5 ng/ml) in the emergency room. When the measurement was repeated 3 hours later, troponin was measured as 7168 pg/ml and CK-MB was measured as 32,47 ng/ml. The patient, who was being treated in the intensive care unit, had dyspnea, pleuritic chest pain, and confusion in the 6th-hour examination. Acute myocardial infarction, aortic aneurysm, coronary spasm, cardiomyopathy, pulmonary embolism and myocarditis were considered as the differential diagnosis of the patient. It was seen the level of cardiac markers was elevated in the blood samples collected from the patient in the intensive care unit. Results of the blood sample tests were measured as Troponin I: 10416 pg/ml, CK-MB: 19.5 ng/ml. WBC count was 7880 µl (reference value: 4500-11000/µl).

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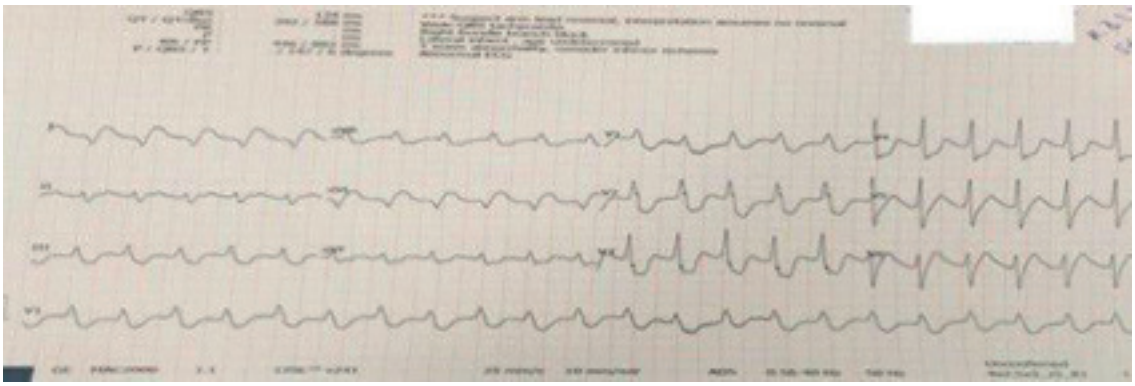

Figure 1: Electrocardiogram showing ST elevation in DI - aVL leads.

There were no signs of eosinophilia in the blood count of the patient (eosinophil count was 100/µl; reference value:0-700/µl). The eosinophil count was normal in the blood counts performed daily during hospitalization. In addition, CRP levels were within the normal range. Pulmonary embolism diagnosis was ruled out because of the D-dimer value was normal (0,22 mg/L; reference value:<0,55 mg/L).

Invasive coronary angiography was performed because the cardiac markers of the patient were rose, S-T segment elevation in D1-AVL leads and right bundle branch block were also found to be high in the first ECG (Figure 1).

There was a deterioration in left ventricular function on her echocardiography (ECHO). Left ventricular ejection fraction (LVEF) was found to be reduced by 40% (typically 50-70 percent). Apart from this, no finding suggesting myocardial infarction, such as reduced wall motion, was found on ECHO. Coronary arteries were normal in coronary angiography.

In addition, Psychiatric consultation was requested for the patient. Quetiapine was discontinued after the psychiatric evaluation. The patient was given ramipril 2,5 mg, fraxiparine 5700 IU/0,6 ml once a day, and ibuprofen 600 mg three times a day during treatment. On the second day of hospitalization in the intensive care unit, troponin decreased to 5420 pg/ml and CK-MB to 9,49ng/ml. The complaints of shortness of breath and chest pain were vanished, though palpitations occurred occasionally. The treatment of the patient was completed in the intensive care unit for ten days. During this time, the patient's symptoms improved. After the resorption of the edema in the lung base on the chest X-ray and the ECG findings improved, the patient was taken to the internal medicine service. The patient, whose treatment continued in the service for ten days, was discharged with full recovery at the end of this period.

Discussion

Quetiapine is a dibenzothiazepine derivative second generation antipsychotic agent. Clozapine, a structurally similar dibenzodiazepine derivative second-generation antipsychotic, is similar to quetiapine in terms of its mechanism of action and side effects, including cardiac adverse event [6,7]. It has been found that approximately 1-3% of patients treated with clozapine developed myocarditis [8,9]. In comparison, cases of quetiapine-induced myocarditis are much rarer.

The patient's symptoms and signs indicated a cardiac disorder. In the ECG, the increase in the blood levels of cardiac markers accompanied by the elevation of the ST segment in the D1-aVL leads indicated that the heart muscle is damaged. The absence of myocardial infarction findings in coronary angiography and the decrease in ejection fraction in ECHO revealed that there is another pathology that impairs the pump function of the heart other than ischemic damage. No narrowing or occlusion of the coronary arteries was found on angiography. Thus, the diagnosis of the patient was confirmed as myocarditis.

The patient did not have flu-like symptoms or symptoms suggestive of viral diarrhea during the two weeks prior to admission to the Hospital. Therefore, the possibility of viral myocarditis was ruled out.

Getting a score of 7 in the evaluation of the case according to the Naranjo scale, which is used to determine whether any pathological findings occurred on the patients due to an adverse reaction is, indicating a strongly possible adverse drug reaction[10]. As a result, myocarditis due to quetiapine overdose was diagnosed.

In the literature, there are three cases of myocarditis associated with the use of quetiapine to date. In one of these cases, quetiapine was used alone, in the other cases combined with lithium or methylphenidate [4,5,7]. We present the second case of myocarditis related to quetiapine treatment alone.

Although the underlying mechanism has not been fully elucidated, it is thought that drug-induced myocarditis may occur by one of two different mechanisms:The first one is the direct toxic effect of the drug on the cardiac muscle; the other one is hypersensitivity. Hypersensitivity seems to be the primary underlying mechanism in cases of olanzapine and clozapine-associated myocarditis [11-13]. Nonetheless, it seems difficult to make the same definition for quetiapine-induced myocarditis cases. Eosinophilia and morbilliform rash were

present in the case where quetiapine was used in combination with Lithium. However, there was no other finding suggestive of hypersensitivity such as eosinophilia in the other two case reports and our case. Since it is known that lithium can cause morbilliform eruptions, considering the presence of morbilliform rash in the first case, it can be thought that the hypersensitivity reaction was caused by lithium[14,15]. In the light of this knowledge, it is more likely that the direct toxic effect of quetiapine on the heart muscle played a role in the development of myocarditis. However, examination with biopsy or other methods is necessary to reveal this possibility. It should be noted that the limitation of this study is that myocardial biopsy and cardiac MRI could not be performed because the patient did not accept them. However, the findings described above depict that the case was an idiosyncratic reaction or a direct toxic effect due to quetiapine.

Drug-induced myocarditis is a rare but potentially fatal adverse effect. Psychiatrists should be alert that when symptoms suggestive of cardiac pathologies such as palpitations, fatigue, chest pain, and shortness of breath develop in patients using second-generation antipsychotic drugs such as quetiapine, drug-induced myocarditis may be an underlying factor, among other reasons.

References

1. Kelleni MT, Abdelbasset M. Drug Induced Cardiotoxicity: Mechanism, Prevention and Management. In: Tan W editor. Cardiotoxicity. London: Intechopen press;2018. pp.127-137.
2. Enger C, Weatherby L, Reynolds RF, Glasser DB, Walker AM. Serious cardiovascular events and mortality among patients with schizophrenia. *Journal of Nervous and Mental Disease*. 2014; 192(1): 19–27.
3. Feinstein RE. Cardiovascular effects of novel antipsychotic medications. *Heart Disease*. 2002; 4(3):184–190.
4. Roesch-Ely D, Van Einsiedel R, Kathöfer S, Schwaninger M, Weisbrod M. Myocarditis With Quetiapine. *American Journal of Psychiatry*. 2002; 159(9): 1607-1608.
5. Wassef N, Khan N, Munir S. Quetiapine-induced myocarditis presenting as acute STEMI. BMJ Case Rep. 2015;2015:bcr2014207151.
6. Bush A, Burgess C. Fatal cardiomyopathy due to quetiapine. *N Z Med J*. 2008; 121(1268): U2909.
7. Bhogal S, Ladia V, Paul TK. Quetiapine-Associated Myopericarditis. Am J Ther. 2018;25(5):e578-e579.
8. Khasawneh FT and Shankar GS. Minimizing Cardiovascular Adverse Effects of Atypical Antipsychotic Drugs in Patients with Schizophrenia. Cardiol Res Pract. 2014;2014:273060.
9. Ronaldson KJ, Fitzgerald PB, Mc Neil JJ. Clozapine-induced myocarditis, widely overlooked adverse reaction. *Acta Psychiatr Scand*. 2015;132:231–240.
10. Naranjo CA, Busto U, Sellers Em, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. *Clinical Pharmacology & Therapeutics*. 1981; *30*(2), 239-245.
11. Raz A, Bergman R, Eilam O, Yungerman T Hayek T. A case report of olanzapine-induced hypersensitivity syndrome. *Am J Med Sci*. 2001;321:156–158.
12. Sahpaz A, Pehlivan S, Turkkan D, Kara DO, Alkan HA. Eosinophilic Myocarditis in Long Term Use of Antipsychotics: Case Series and Review of the Literature. Bulletin of Clinical Psychopharmacology. 2016; 26(4):417-21.
13. Vang T, Rosenzweig M, Bruhn CH, Polcwiartek C, Kanters JK, Nielsen J. Eosinophilic myocarditis during treatment with olanzapine - report of two possible cases. BMC Psychiatry. 2016; 16:70.
14. Shreedhar KB, Madhukara J, Jessy J, Manohari SM, Srinivasan K. Drug hypersensitivity syndrome with lithium. Indian J Dermatol Venereol Leprol. 2010;76(4):426-427.
15. Jafferany M. Lithium and skin: dermatologic manifestations of lithium therapy. International Journal of Dermatology. 2008; 47(11):1101–1111.