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Clozapine-Induced Cardiac Tamponade: A Rare Cause of Chest Pain

Yaşar Kapıcı[1*], Dilek Örüm[2], Sabri Abuş[3], Olga Bayar-Kapıcı[4]

[1]Department of Psychiatry, Faculty of Medicine, Adıyaman University, Adıyaman, Türkiye
[2]Department of Psychiatry, Elazığ Fethi Sekin City Hospital, Elazığ, Türkiye
[3]Department of Cardiology Faculty of Medicine, Adıyaman University, Adıyaman, Türkiye
[4]Department of Radiology, Seyhan State Hospital, Adana, Türkiye

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****Corresponding Author***
Yaşar Kapıcı
Department of Psychiatry
Faculty of Medicine
Adıyaman University
Adıyaman, Türkiye
Phone: +90 5301230290
E-mail: dryasarkapici@gmail.com

Doi:

Authors' ORCIDs
Yaşar Kapıcı
https://orcid.org/0000-0002-9248-9426
Dilek Örüm
https://orcid.org/0000-0001-8369-1553
Sabri Abuş
https://orcid.org/0000-0003-2464-4970
Olga Bayar-Kapıcı
https://orcid.org/0000-0003-0863-9127

Dear Editor,

Clozapine used in treatment-resistant schizophrenia can lead to life-threatening cardiovascular events such as dilated cardiomyopathy, myocarditis, and pericarditis [1]. Specifically, clozapine is associated with myocarditis and dilated cardiomyopathy with an estimated absolute risk of 0.01% to 0.19%. Mortality rate estimates (10%-46%) due to these rarely seen side effects are quite significant [2]. In this study, we discussed a case of cardiac tamponade that occurred during clozapine titration and resolved after discontinuation of the medication.

A 35-year-old single male patient living in Adiyaman/Turkey was admitted to the emergency department of a training and research hospital with complaints such as chest pain, shortness of breath, and sweating. The patient had been diagnosed with schizophrenia approximately 10 years ago and had a history of being managed with medications such as olanzapine, risperidone, quetiapine, and haloperidol. Despite using risperidone 8 mg/day and olanzapine 20 mg/day regularly for last six months, the patient, whose positive psychotic symptoms persisted, was started on clozapine 25 mg/day five weeks ago and the clozapine dose was increased by cross-titration method while the dose of olanzapine and risperidone was decreased. At the end of four weeks, olanzapine and risperidone were completely stopped and the clozapine dose was increased to 300 mg/day. On the 7th day of increasing the clozapine dose to 300 mg/day (five weeks after starting clozapine), the above symptoms suddenly appeared with chest pain and the patient was admitted to the emergency department. The patient's blood pressure was 78/37 mmHg, pulse was 135 per minute, respiratory rate was 25 per minute, and oxygen saturation was 90. The patient's physical examination revealed bilateral jugular venous distension. The patient also had cold sweats. The patient's eating habits did not change in recent days. The patient reported no history of alcohol, illicit substance use, or other medical conditions. There were no signs or symptoms suggestive of infection. No history of animal bites or similar was reported. The only medication the patient used was clozapine, and the patient did not use herbal formulations. The patient was evaluated by an emergency medicine specialist, consulted by a cardiologist, and had blood analysis, electrocardiography, thoracic computed tomography (CT) angiography (Figure 1), and echocardiography (Figure 2). In the thorax CT angiography performed to exclude pulmonary embolism, there is pericardial

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effusion in axial sections and pleural effusion in the left hemithorax. No pulmonary embolism was detected (Figure 1). In the echocardiography pericardial effusion was detected (Figure 2). In addition, echocardiography showed collapse in the right heart chambers. The patient was diagnosed with cardiac tamponade. The patient was hospitalized in the cardiology intensive care unit after undergoing pericardiocentesis. It was decided that the current side effect was caused by clozapine and the medication was discontinued. The patient's hemodynamic parameters reached equilibrium within 24 hours. The patient was started on olanzapine 5 mg/day and it was planned to gradually increase the dose. No similar side effect was observed again during outpatient follow-up. The patient and his relatives were warned about the cardiac side effect associated with the use of clozapine, and informed consent was obtained from the patient for the publication of his data. The patient's Naranjo Adverse Drug Reaction Probability Scale (NADRPS) score was 6 [3].

This case report was evaluated as reversible cardiac tamponade plus pericardial effusion associated with clozapine because there was a temporal relationship between them. Other possible causes of the cardiac tamponade, such as drugs, diet, illicit substance, animal bite, and infection, were excluded. Drug-related side effect severity was determined by NADPRS, indicating a possible relationship between clozapine use and cardiac side effect [3].

The most frequently reported cardiac side effect of clozapine is myocarditis, however cardiac tamponade and pericardial effusion are rarely observed. Clozapine-induced polyserositis can result in ascites, pericardial effusion, and pleural effusion. A rare (less than 1 in 10,000) and dangerous side effect of clozapine is pericardial effusion. Pericardial effusion may occur as soon as one week following the initiation of clozapine medication. There have also been documented instances of delayed cardiac symptoms that develop months or years after the start of clozapine therapy [4]. Bath et al. reported a 20-year-old female patient with schizophrenia who developed cardiac tamponade plus pericardial effusion after 10 months of clozapine use [4]. Murko et al. reported a 43-year-old male patient with schizophrenia who had been using clozapine for seven years and was mentally stable, with cardiac tamponade plus pericardial effusion [5]. In the present case, the side effect occurred after five weeks of clozapine use. Clozapine-induced cardiac tamponade has been explained by a number of mechanisms, including direct toxicity and immune-mediated toxicity [1]. However, the pathogenesis of clozapine-associated cardiac tamponade and pericardial effusion is remains unclear. As a result, clozapine can present with life-threatening cardiac tamponade and pericardial effusion. A detailed medical history and physical examination should be performed before initiating clozapine therapy. In patients receiving clozapine, cardiac signs such as chest pain, dyspnoea, and tachycardia should be promptly evaluated for cardiac conditions. Pericardiocentesis and discontinuation of clozapine use are the main interventions. More studies are needed to elucidate the mechanisms of occurrence of clozapine-induced cardiac tamponade.

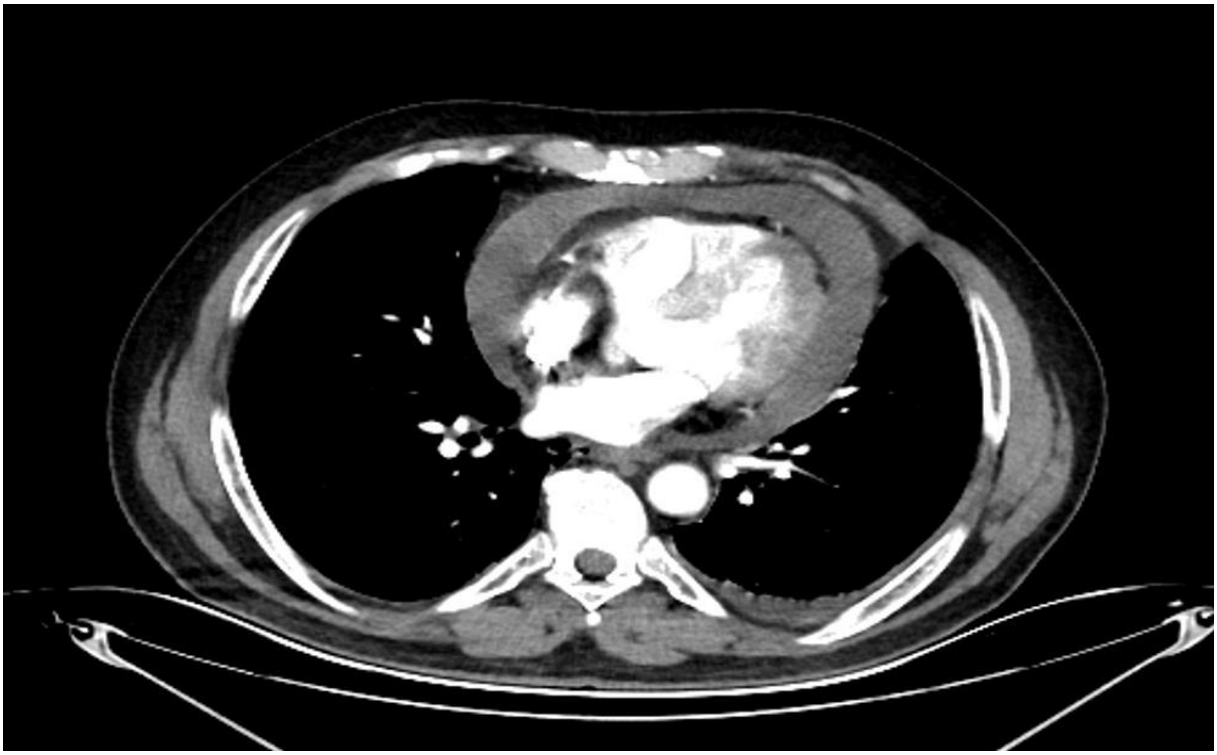

Figure 1: Thoracic Computed Tomography.

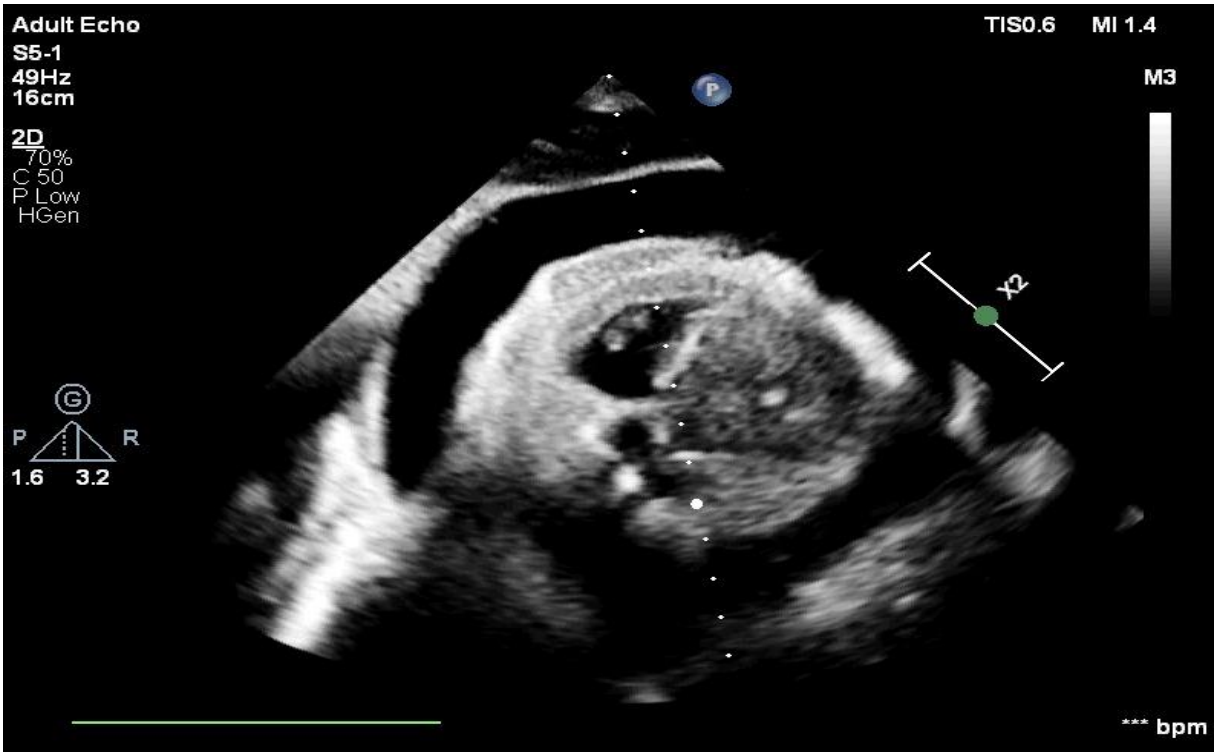

Figure 2: Echocardiogram.

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Conflict of Interests
There is no conflict of interest declared by the authors.

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Ethical Approval
There is no need ethical approval for this letter.

Data sharing statement
None.

Consent to participate
Informed consent was obtained from the patient and his/her relative.

Informed Statement
No informed statement is required for this study.

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