# Letter to the Editor

## A Case of Cardiac Arrest and Pulmonary Embolism After Clozapine Titration

**To the Editor:** We describe a case in which a patient was started on clozapine treatment and subsequently developed pericardial tamponade and cardiac arrest complicated by pulmonary embolism.

***Case report.*** Mr A, a 52-year-old man with a history of severe, treatment-resistant schizophrenia (*DSM-IV* criteria), was hospitalized in 2010 to start a clozapine trial. Medical assessment revealed no abnormalities upon physical examination, laboratory values within normal limits, and no abnormalities in vital signs. At the time of his admission, he was treated with divalproex sodium 1,500 mg and perphenazine 16 mg daily and risperidone 50 mg every 2 weeks via depot injection. Past medical history included mild obesity, hyperlipidemia, well-controlled hypertension, and benign prostatic hypertrophy. Nonpsychiatric medications included simvastatin 80 mg, furosemide 20 mg, finasteride 5 mg, and tamsulosin 0.4 mg daily; the patient had remained medically stable for over 1 year prior to admission. Clozapine was started at 12.5 mg and increased daily in 12.5-25–mg increments up to 300 mg/d in divided doses, as perphenazine was tapered off. Divalproex sodium was continued at the same dose.

Fifteen days after initiation of clozapine treatment, Mr A developed a fever of 102.5°F and tachycardia and was transferred to the medical unit with a pulse rate ranging from 110 to over 120 bpm. Laboratory investigations for neuroleptic malignant syndrome and infectious etiologies were negative. On the 17th day after clozapine initiation, the patient experienced respiratory depression, hypoxia, and hypotension. Chest computed tomography (CT) and echocardiogram revealed large pericardial effusion. The patient was scheduled for right heart catheterization to evaluate for cardiac tamponade and was emergently intubated due to progressive hypoxemia of 85% $O_2$ saturation.

At the time of intubation, the patient went into pulseless electrical activity and was resuscitated after administration of 1 mg of epinephrine. Subsequently, right heart catheterization was performed with a Swan-Ganz inguinal catheter. Thoracocentesis obtained 750 mL of serosanguineous liquid that was negative for infectious, malignant, or immunologic etiology; however, pericardial biopsy revealed inflammatory cells. After the diagnosis of pericarditis was made, clozapine was discontinued. On the second day after thoracocentesis, Mr A became progressively hypoxemic and hypotensive while continuing to have mild fever of unknown origin. Subsequent chest CT revealed a large right pulmonary embolism and bilateral pleural effusions. Risperidone injections ceased following this diagnosis. At that time, the patient was continued on mechanical ventilation and started on intravenous heparin, and the Swan-Ganz catheter was removed. This slowly resulted in hemodynamic stabilization. Mr A was started on broad-spectrum antibiotic coverage, although the extensive work-up continued to be negative. His temperature normalized 7 days after stopping clozapine, and he improved further.

This patient developed severe cardiopulmonary symptoms leading to cardiac arrest shortly after initiation of clozapine treatment. Multiple etiologies can be implicated in the pathogenesis of pericarditis, including infections, malignancy, autoimmunity, and uremia. Rapid development of cardiac tamponade leading to cardiac arrest combined with the extensive negative baseline workup coincides with the initiation of clozapine treatment and is consistent with previously described cases of clozapine-related cardiopulmonary complications that include polyserositis.[1,2]

What makes this case unique, however, is the severity and lethality of symptoms and the development of pulmonary embolism. Inguinal catheterization could be a potential source of emboli, although in this case several other risk factors could contribute to their development, including obesity, hypertension, and hyperlipidemia. In addition, clozapine could be an independent risk factor for development of pulmonary embolism,[3] but to what degree is unclear. Although the patient presented with some heart disease–related risk factors, these were not contraindications for initiation of clozapine treatment.

### References


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