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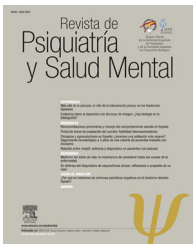

LETTERS TO THE EDITOR

## Clozapine-induced eosinophilia and serositis☆

### Eosinofilia y serositis inducida por clozapina

*Dear Editor,*

Clozapine is an atypical second-generation antipsychotic drug of choice in patients with: treatment-resistant schizophrenia, risk of suicide in patients with schizophrenia spectrum disorders, aggressiveness or violence in psychiatric patients, comorbid substance abuse, psychosis in Parkinson's disease and for prevention and treatment of tardive dyskinesia.[1,2] Despite its effectiveness in these settings, clozapine associated side effects pose a major concern during treatment: up to 76% of patients experience a side effect, with a rate of treatment withdrawal of 17%.[3] For this reason, a strict hematologic control is recommended.[4]

We report the case of a 46-year-old woman with a history of smoking, paranoid schizophrenia and bipolar disorder. She was treated with oxcarbazepine, quetiapine, aripiprazole and lorazepam. The patient was admitted to the Psychiatry ward with the diagnosis of psychotic decompensation.

During hospital admission treatment with oxcarbazepine, quetiapine and lorazepam was maintained. Additionally, venlafaxine and clorazepate dipotassium were added to the treatment. After 4 weeks of admission, oral clozapine treatment was started, initially at dose of 50 mg/day and gradually increasing the dose up to 200 mg/day.

On day 30 after the start of clozapine the patient presented with loose stools without blood or mucus in the absence of other associated symptoms. On physical examination, blood pressure was 105/74 mmHg, heart rate 62 bpm and temperature 36.4 °C. The abdomen was soft and non-tender. Blood analysis showed 23,600 leukocytes/μl (10,500 eosinophils microliter), C-reactive protein 0.1 mg/dl, creatinine 0.63 mg/dl. Peripheral blood smear disclosed eosinophilia at the expense of mature eosinophils and mature neutrophils with toxic granulation. IgE levels were 10.3 KU/L (reference range 0–114). A chest radiograph showed mild bilateral pleural effusion. Examination of feces for fecal parasites was negative. A transthoracic echocardiography was performed, in which no pericardial effusion was observed. Clozapine treatment was discontinued.

The subsequent evolution was favorable, with diarrhea disappearing within 48 h of clozapine withdrawal and with gradual return to normal levels of eosinophils. A chest radiograph performed four weeks later showed complete resolution of pleural effusion. The patient was discharged home after five months of admission.

Adverse reactions occur most frequently during the initiation of clozapine treatment and during the acute treatment and dose titration phases. Among the most frequent adverse effects of clozapine are agranulocytosis, seizures, hypersalivation, orthostasis, tachycardia, constipation and drowsiness.[2–5]

Clozapine-associated serositis is a serious and rare complication of clozapine treatment. Published literature suggests that this condition, in case it develops, often does so within 8–20 days of clozapine therapy initiation. Reports in the literature include cases of severe pericarditis and pericardial tamponade.[5] If polyserositis occurs, clozapine has to be discontinued inmediately.[6] In all reported cases, symptoms remitted upon discontinuation of clozapine.[6]

Clozapine-induced eosinophilia, seen in around 1% of clozapine-treated patients (up to 13% in some series), is a non-dose-dependent adverse effect. It occurs mostly in the initial 4 week-period of treatment.[7] In most cases, eosinophilia shows a transient course and spontaneous remission; however, in a few cases it has been reported to be associated with eosinophilic colitis, myocarditis, pancreatitis and toxic hepatitis.[8] As with other blood dyscrasias with clozapine, various mechanisms have been proposed to be responsible for clozapine associated eosinophilia. Clozapine-associated eosinophilia is understood as two different patterns: firstly, transient benign eosinophilia; and secondly, eosinophilia with end organ damage. Commonly proposed mechanisms include type-I hypersensitivity reaction, which is supported by evaluated IgE levels in few reports and stimulation of T-lymphocytes.[9]

The combination of clozapine-induced pleural effusion along with eosinophilia has only been described in a few case reports.[10,11] Patel et al. found eosinophilia after analysis of pleural fluid,[11] supporting the idea of eosinophilia as a causative agent of end organ damage.

Regarding management of clozapine induced eosinophilia, treatment withdrawal should be reserved to patients with eosinophilia-associated end organ damage, as clozapine induced eosinophilia is usually benign and transient. In patients with isolated eosinophilia, close

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monitoring for symptoms of end organ damage (including gastrointestinal symptoms, chest pain and dyspnea) is recommended, and clozapine should be withdrawn if end organ damage is suspected or confirmed.

In short, we present the case of a young female who developed pleural effusion and hypereosinophilia 4 weeks after the initiation of clozapine therapy, with associated gastrointestinal symptoms. Symptoms remitted shortly upon discontinuation of clozapine. The elevated numbers of eosinophils in peripheral blood are thought to play a role in the pathogenesis of clozapine induced polyserositis.

## References


1. Alvarez de Morales Gómez-Moreno E, Muquebil Ali Al Shaban Rodríguez OW, Fernández Fernández J, Fresno García C. Flexibilization in controlling the use of clozapine: a great opportunity. Rev Psiquiatr Salud Ment. 2018;11:255–6.
2. Iglesias García C, Iglesias Alonso A, Bobes J. Concentrations in plasma clozapine levels in schizophrenic and schizoaffective patients. Rev Psiquiatr Salud Ment. 2017;10:192–6.
3. Mouaffak F, Gaillard R, Burgess E, Zaki H, Olie JP, Krebs MO. Clozapine-induced serositis: review of its clinical features, pathophysiology and management strategies. Clin Neuropharmacol. 2009;32:219–23.
4. Pons A, Undurruga J, Batalla A, Bernando M. Clozapine and agranulocytosis in Spain: do we have a safer population? A 5-year hematologic follow-up. Rev Psiquiatr Salud Ment. 2012;5:37–42.
5. Bhatti MA, Zander J, Reeve E. Clozapine-induced pericarditis, pericardial tamponade, polyserositis, and rash. J Clin Psychiatry. 2005;66:1490–1.
6. Branik E, Nitschke M. Pericarditis and polyserositis as a side effect of clozapine in an adolescent girl. J Child Adolesc Psychopharmacol. 2004;14:311–4.
7. Chatterton R. Eosinophilia after commencement of clozapine treatment. Aust N Z J Psychiatry. 1997;31:874–6.
8. Karmacharya R, Mino M, Pirl WF. Clozapine-induced eosinophilic colitis. Am J Psychiatry. 2005;162:1386–7.
9. Lucht MJ, Rietschel M. Clozapine-induced eosinophilia: subsequent neutropenia and corresponding allergic mechanisms. J Clin Psychiatry. 1998;59:195–7.
10. Thompson J, Chengappa KN, Good CB, Baker RW, Kiewe RP, Bezner J, et al. Hepatitis, hyperglycemia, pleural effusion, eosinophilia, hematuria and proteinuria occurring early in clozapine treatment. Int Clin Psychopharmacol. 1998;13:95–8.
11. Patel JJ, Lisi PA, Lathara Z, Lipchik RJ. Clozapine-induced peripheral and pleural fluid eosinophilia. Ann Pharmacother. 2012;46:e4.



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# Psychosis as debut of sporadic Creutzfeldt–Jakob disease☆

## Psicosis como inicio de enfermedad de Creutzfeldt-Jakob esporádica

*Dear Editor,*

Creutzfeldt–Jakob disease (CJD) is a neurodegenerative pathology belonging to the group of prion diseases or transmissible spongiform encephalopathies. It is caused by the central nervous system deposit of a pathological isoform of the normal prion protein (PrPc) present in all mammals. The mechanism by which this conformational change is produced is unknown. The accumulation of the pathological prion protein (PrPsc) gives rise to a neural degeneration that provokes a rapidly progressive fatal neurological deterioration.

There are three forms of CJD: sporadic (sCJD), familial and acquired. The sporadic form represents 85% of the cases, with greater incidence in individuals approximately 60 years old; and 90% of the patients die within a year of symptom onset, with a mean survival of 6 months.[1]

The classic clinical presentation of sCJD includes rapidly progressive dementia, myoclonus, and pyramidal, extrapyramidal and cerebellar signs. Although it is less frequent, the disease can begin with non-specific psychiatric signs and symptoms such as personality changes, behavioural changes, anxiety, depression and even as a psychotic condition, which can make initial diagnosis more difficult.[2–11]

Diagnosis is based on the clinical features and the neurological examination findings, together with the presence of alterations in the diffusion-weighted sequences (DWI) or brain magnetic resonance imaging (MRI) scan using fluid-attenuated inversion recovery (FLAIR) in the caudate nucleus and putamen or in at least two cortical regions,[12] an electroencephalogram (EEG) showing periodic sharp wave complexes superimposed on a slow background rhythm,[13] and/or cerebrospinal fluid positive for 14-3-3 protein.[1] Nevertheless, these findings are not pathognomonic and their normality does not rule out the disease. Definitive diagnosis is established using pathological studies that show spongiform degeneration, neuron loss and gliosis.[1] There is currently no cure, with treatment being merely symptomatic.

We present the case of a 53-year-old Columbian female, divorced, having a 20-year-old son. The patient had no other

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