

The information in this column is not intended as a definitive treatment strategy but as a suggested approach for clinicians treating patients with similar histories. Individual cases may vary and should be evaluated carefully before treatment is provided. The patient described in this column gave informed consent for the publication of the column.

Myoclonus as an indicator of infection in patients with schizophrenia treated with clozapine

Clozapine is the treatment of choice for refractory schizophrenia. However, a retrospective analysis indicated that death was a common cause of ceasing clozapine treatment.¹ In another study that investigated the reasons for discontinuing clozapine, pneumonia was the primary cause of death in about 24% of patients.² Therefore, the relation between the risk of pneumonia and clozapine has raised clinical concerns.

Asymptomatic or subclinical illnesses such as pancreatitis³ have been reported in patients with schizophrenia treated with clozapine. Accordingly, awareness of a silent infection is extremely important to patient safety. Here, we present a patient with schizophrenia treated with clozapine whose occurrence of myoclonus was an indicator of asymptomatic pneumonia.

In April 2010, a 60-year-old Chinese woman presented because of a 2-day history of paroxysmal unstable gait due to leg folding. The patient had a 35-year history of schizophrenia, which had been well controlled with a clozapine dosage of 350 mg/day. The family reported no prior history of physical illness or substance abuse.

On examination, this patient was afebrile and had stable vital signs. There was no evidence of focal neurologic deficit. Laboratory tests showed leukocytosis ($12.700 \times 10^9/L$) and a high concentration of C-reactive protein (201.15 nmol/L). The patient had experienced benign reversible leukocytosis 12 times in the past 2 years. A chest radiograph (lateral view) re-

vealed a huge retrocardiac mass shadow in the left lower lobe of the lung. Given the patient's substantial weight loss (20.5 lbs) in the past 8 months and the lack of symptoms or signs of infection, we performed a more thorough work-up, including computed tomography of her chest, bronchoscopy (cytology and biopsy), cerebral magnetic resonance imaging, electroencephalography, bone scan, tuberculosis culture, acid-fast stain, thyroid screen, tumour marker analysis, comprehensive metabolic panel, blood culture, sputum culture, urinalysis and stool analysis. None of these examinations provided any evidence of cancer. The patient's leg folding improved after the clozapine dosage was tapered to 200 mg/day. Surprisingly, the patch lesion on the chest radiograph resolved after 20 days of treatment with empiric antibiotics (augmentin and clarithromycin). As such, we discarded a suspected diagnosis of cancer in favour of asymptomatic pneumonia in the left lower lobe of the lung. By July 2010, she was well, and the chest radiograph and additional laboratory tests were unremarkable.

This patient's case demonstrates myoclonus associated with clozapine heralding silent pneumonia. Positive and negative myoclonus have been reported to be dose-dependent adverse effects of clozapine.^{4,5} Positive myoclonus presents as a jerking movement, whereas negative myoclonus presents as knee buckling or leg folding, which may stem from a brief lapse of muscle activity. Evidence has suggested that infection could substantially increase the serum concentrations of clozapine to toxic levels via the cytokine sup-

pression of cytochrome P450 1A2.⁵ Thus, our patient's silent pneumonia may have led to an increase in serum clozapine levels to the point of toxicity, which subsequently resulted in paroxysmal negative myoclonus. Although the serum clozapine levels were not monitored, the rapid improvement of leg folding when the clozapine dosage was decreased could support the causal inference.

Notably, the patient did not display any symptoms of pneumonia even though a chest radiograph revealed a large pneumonic patch over the left lower lobe of the lung. In schizophrenia, a reduction in sensation and pain responsiveness, as well as an altered perception of symptom awareness, have been linked to poor treatment outcomes of pneumonia,⁶ implying that a diagnosis of pneumonia can be easily delayed or even missed.

Patients with schizophrenia do not always present typical clinical features of infections. Therefore, clinicians must pay particular attention to signs of clozapine toxicity, including sedation, myoclonus and seizures,⁷ which may be indicators of an underlying infection. Our patient's case reminds us that silent pneumonia may develop in patients with schizophrenia treated with clozapine. Moreover, myoclonus may signal undiagnosed pneumonia.

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References

1. Atkinson JM, Douglas-Hall P, Fischetti C, et al. Outcome following clozapine discontinuation: a retrospective analysis. *J Clin Psychiatry* 2007;68:1027-30.
2. Taylor DM, Douglas-Hall P, Olofinjana B, et al. Reasons for discontinuing clozapine: matched, case-control comparison with risperidone long-acting injection. *Br J Psychiatry* 2009;194:165-7.
3. Bergemann N, Ehrig C, Diebold K, et al. Asymptomatic pancreatitis associated with clozapine. *Pharmacopsychiatry* 1999;32:78-80.
4. Praharaj SK, Venkatesh BG, Sarkhel S, et al. Clozapine-induced myoclonus: a case study and brief review. *Prog Neuropsychopharmacol Biol Psychiatry* 2010;34:242-3.
5. de Leon J, Diaz FJ. Serious respiratory infections can increase clozapine levels and contribute to side effects: a case report. *Prog Neuropsychopharmacol Biol Psychiatry* 2003;27:1059-63.
6. Chen YH, Lin HC, Lin HC. Poor clinical outcomes among pneumonia patients with schizophrenia. *Schizophr Bull* 2010 Mar 25. [Epub ahead of print]
7. de Leon J. Respiratory infections rather than antibiotics may increase clozapine levels: a critical review of the literature. *J Clin Psychiatry* 2004;65:1144-5.