

## Letters to the Editor

### Pericardial and bilateral pleural effusion associated with clozapine treatment

Sir,

We are aware of seven published reports that described pleural or pericardial effusion associated with clozapine [1–3,5–8]. We report a case of a patient who at first presented with flu-like symptoms, but developed bilateral pleural and pericardial effusion 6 weeks after initiating clozapine therapy.

#### 1. Case report

Mr. A was a 21-year old white man transferred to our hospital with the diagnosis of paranoid schizophrenia, according to DSM-IV criteria. He was treated with zuclopentixol, which we stopped because of extrapyramidal side effects. We started olanzapine. Despite 8 weeks of treatment (maximum 20 mg/day) his psychotic symptoms did not resolve completely. Clozapine was initiated and titrated upward, while olanzapine was tapered to discontinuation. After 10 days (clozapine 150 mg/day, olanzapine 15 mg/day) he developed flu-like symptoms. His temperature was 39.4 °C and he noted generalized malaise, headache and anorexia. Total white blood count (WBC) was normal. The next day he was afebrile. On day 14 his temperature spiked to 39.0 °C. He complained of generalized malaise, anorexia, nausea, a dry cough and some pleuritic-type chest pain. Physical examination revealed no abnormalities. WBC was  $10.7 \times 10^9/l$  (normal range 4.6–10.6). We assumed he had an upper respiratory infection. The temperature remained elevated. On day 16 (clozapine 200 mg/day, olanzapine 10 mg/day) the erythrocyte sedimentation rate (ESR) was 71. WBC and a chest X-ray were normal. We decided not to increase the dosage of clozapine. Within a few days his clinical status improved, so we again increased the clozapine. On day 35 amitriptyline (50 mg/day) was added because of hypersalivation. The patient was no longer psychotic. From day 43 (clozapine 300 mg/day) he began experiencing breathlessness and complained about pain in his shoulders with deep inspiration. He had a respiratory rate of 22/min and a heart rate of 120/min. The ESR was 84. Chest X-ray showed an enlarged cardiac silhouette and bilateral pleural effusion. An echocardiogram revealed pericardial and pleural effusion with no compromise of cardiac function. A rheumatologic work-up was non-diagnostic. Clozapine and amitriptyline were discontinued and olanzapine was restarted (10 mg/day). A chest X-ray on day 55 revealed partial resolution of the pleural effusion and reduction of the enlargement of the cardiac silhouette. On day 57 the patient noted pleuritic chest pain again, probably as a result of resolution of the pleural effusion with

increasing irritation of the pleura. (Both perfusion as well as ventilation lung scan were normal). All symptoms resolved within 2 weeks. On day 89, after excessive physical exertion, he mentioned chest pain once more (olanzapine 20 mg/day). A chest X-ray showed left sided shadowing posterobasal and an enlarged cardiac silhouette. The patient refused to discontinue olanzapine. Over the next 2 weeks all his symptoms abated with normalization of the chest X-ray and laboratory results. He continued to receive olanzapine and was discharged on day 144 without any complaints.

#### 2. Discussion

This case joins previous reports [1,3,4,8] suggesting polyserositis may be a complication in clozapine treatment. Although we cannot demonstrate a direct link with certainty, the relation between onset and end of the symptoms with clozapine is high. The lack of evidence of other etiologies and the previously reported cases suggest clozapine was the cause.

#### References

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Erik Boot  
Lieuwe de Haan \*  
Yener Guzelcan  
Willem F. Scholte  
Hanneke Assies

*Department of Psychiatry, Academic Medical Center,  
University of Amsterdam, P.O. Box 22700,  
1100 DE Amsterdam, The Netherlands*

\* Corresponding author.

*E-mail address:* [l.dehaan@AMC.UVA.NL](mailto:l.dehaan@AMC.UVA.NL) (L. de Haan).