Case report

Olanzapine-induced eosinophilic pleuritis

Matthew Evison a, b, *, Jayne Holme a, Mohamed Alaloul a, Helen Doran c, Paul Bishop c, Richard Booton a, b, Nauman Chaudhry a

a North West Lung Centre, University Hospital of South Manchester, Southmoor Road, Wythenshawe, M23 9LT, UK
b The Institute of Inflammation and Repair, The University of Manchester, UK
c Department of Thoracic Pathology, University Hospital of South Manchester, Southmoor Road, Wythenshawe, M23 9LT, UK

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ABSTRACT

An elderly patient, with a history of depression with psychosis, presented with breathlessness, a right exudative pleural effusion and a peripheral eosinophilia. The pleural fluid was eosinophil-rich (10% of leucocytes). Olanzapine therapy had been commenced 12 months previously. There was a family history of TB and the patient was of African origin. A full diagnostic work-up ensued including computed tomography of the thorax and local anaesthetic thoracoscopy. The pleura was unremarkable on CT and displayed bland smooth thickening at visual inspection during thoracoscopy. Pleural biopsies demonstrated chronic inflammation with eosinophils but no evidence of granulomatous inflammation or malignancy. Pleural tissue culture did not yield mycobacteria. A diagnosis of olanzapine-induced eosinophilic pleuritis was suspected and the pleural disease resolved with withdrawal of olanzapine.

Eosinophilic pleural fluid is not a marker of non-malignant aetiology and eosinophilic pleural effusions require a careful and systematic diagnostic work-up. This is the second case report to identify olanzapine as a causative agent in eosinophilic pleural effusion.

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Case report

An elderly patient presented with progressive breathlessness and a dull ache in the lateral right chest wall. Past medical history included cerebrovascular disease and recurrent depression with psychosis. 12 months previously treatment with olanzapine had been commenced and the dose progressively titrated. The patient was born in Africa and had lived in the United Kingdom (UK) for several decades. Occupational history revealed no relevant exposures. The patient was a lifelong non-smoker. There was a family history of tuberculosis. The patient was WHO performance status 2. Examination revealed reduced breath sounds and dullness to percussion in the right chest, confirmed as a pleural effusion on chest X-ray (CXR). This effusion was not present on CXR two years previously (Fig. 1). Routine laboratory blood tests revealed a peripheral eosinophilia (1.27 × 10^9/L). Pleural aspiration was undertaken and biochemical analysis classified the effusion as an exudate (fluid protein 56 g/L, serum protein 82 g/L, fluid LDH 522 U/L and serum LDH 385 U/L). However there was no bacterial or mycobacterial growth on culture. Fluid cytology revealed an excess of eosinophils (10% of leucocytes) and reactive mesothelial cells. Computed Tomography (CT) of the thorax demonstrated a moderate-sized unilateral pleural effusion with an unremarkable appearance of the pleura, including no mediastinal pleural thickening. There was, however, a calcified granuloma in the left lower lobe. A differential diagnosis of tuberculous pleuritis, malignancy or drug-induced pleuritis was made and the patient underwent local anaesthetic thoracoscopy (Figs. 2–4).

Visual inspection of the pleura revealed bland, smooth pleural thickening without nodularity or plaques. Pleural biopsy demonstrated mesothelial proliferation and chronic inflammation with eosinophils. There was no evidence of granulomatous inflammation or malignancy. Pleural tissue sent for culture failed to yield any growth of mycobacteria. A diagnosis of olanzapine-induced eosinophilic pleuritis was made with subsequent withdrawal of the medication. The pleural fluid did not re-accumulate following thoracoscopy and the CXR 6 months later revealed no evidence of pleural disease.

* Corresponding author. North West Lung Centre, University Hospital of South Manchester, Southmoor Road, Wythenshawe M23 9LT, UK. Tel.: +44 161 291 2721; fax: +44 (0)161 291 2919.
E-mail addresses: matthewevison@hotmail.co.uk, matthew.evison@uhsm.nhs.uk (M. Evison).

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Discussion

In the largest single centre cohort analysis of patients with pleural effusions 7% (135/1868) were classified as eosinophilic pleural effusions, defined as ≥10% eosinophils [1]. Within this cohort of eosinophilic pleural effusions an underlying cause was found in 85%. The commonest identified causes were malignancy (35%), infection (20%) and chest wall trauma (12%). An eosinophilic effusion is not, therefore, a marker of non-malignant aetiology. Interesting, the risk of malignancy seems to be inversely proportional to the percentage of eosinophils both in the study described above by Krenke et al. and in meta-analysis [1,2].

Drug-induced pleural effusions are an additional cause of eosinophilic pleural effusions and, given the simple intervention of drug withdrawal will lead to resolution in the majority of cases, an important aetiology to consider in all pleural effusions. Our knowledge of drug-induced eosinophilic pleural effusions stems almost entirely from case reports [3]. Neurological agents (sodium valproate, clozapine, dantrolene and fluoxetine), cardiological agents (warfarin, diltiazem, simvastatin) and antibiotics (nitrofurantoin) have all been implicated [3]. There has been only one previous report of olanzapine-induced eosinophilic pleural effusion [4] and one case involving combined therapy with clozapine and olanzapine [5].

Fig. 1. CXR series: (A) CXR 2 years prior to presentation and prior to olanzapine therapy, (B) CXR at presentation, (C) CXR 6 months after olanzapine withdrawal.

Fig. 2. Computed tomography of the thorax demonstrating a small to moderate right sided pleural effusion with unremarkable pleura, and a left lower lobe calcified granuloma.

Fig. 3. Papanicolaou stained cyto spin demonstrating eosinophil-rich pleural fluid (cells with bi-lobed nuclei with brown granules). An eosinophilic effusion is defined as ≥10% eosinophils. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Fig. 4. Pleural biopsy taken during pleuroscopy demonstrating a chronic inflammatory cell infiltrate and eosinophils.
In conclusion, eosinophilic pleural effusions require a systematic diagnostic work-up as per non-eosinophilic pleural effusions. They are not a marker of non-malignant aetiology. A careful medication history is vital in all patients with pleural disease. This is the second case to report olanzapine as the causative agent of eosinophilic pleuritis. Resolution of the pleural disease occurred with discontinuation of the medication.

Contributorship statement

ME wrote the manuscript with all authors providing review and editing. NC is responsible for the overall content as guarantor.

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