Minocycline induced organising pneumonia resolving without recourse to corticosteroids

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Summary
Minocycline is a tetracycline antibiotic used for the treatment of acne. Minocycline has been associated with a variety of pulmonary adverse effects, most notably organising pneumonia and pulmonary infiltrates with eosinophilia. Most cases of minocycline induced pneumonitis have required the cessation of minocycline coupled with the use of corticosteroids to effect a clinical cure. We present the case of a 21-year old woman who presented with a 2-month pneumonic illness who had been taking minocycline 100 mg per day for the previous 12 months for acne vulgaris. Radiology revealed multifocal consolidation with lung biopsy confirming organising pneumonia. Extensive investigation failed to reveal an alternative cause and minocycline cessation resulted in a complete radiological and clinical resolution within 6 weeks without recourse to corticosteroids. No signs of recurrence were present at follow up over an 8 month period.

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Introduction

Minocycline hydrochloride is a semi-synthetic derivative of tetracycline used in the UK as Minocin MR® to treat acne vulgaris. Minocycline can cause a variety of pulmonary adverse effects, most notably organising pneumonia and pulmonary infiltrates with eosinophilia. Minocycline has also been used to treat the organising pneumonia seen in rheumatoid arthritis. Nearly all the cases described have necessitated the use of corticosteroid therapy, although resolution after minocycline cessation only has been very rarely reported.

We report a case of minocycline induced organising pneumonia that rapidly resolved clinically and radiologically with minocycline cessation only.

Case report

A 21-year old Caucasian woman presented with a 2-month history of lethargy, progressive breathlessness, central chest pain and a cough productive of small amounts of...
yellow/green sputum without haemoptysis. She described loss of appetite with approximately 2 kg weight loss, associated with fever and sweats. She had been taking minocycline 100 mg/day (Minocin MR®) for the previous 12 months for acne vulgaris but was otherwise fit and well. She had no HIV risk factors, no symptoms suggestive of connective tissue disease and no exposure to organic/inorganic agents. She was an ex-smoker of only one pack year. Physical examination revealed increased vocal resonance in the right upper zone. Air entry and expansion were equal and normal with vesicular breath sounds. Pulse oximetry revealed oxygen saturation of 96% whilst breathing room air. Temperature spiked repeatedly up to 38.1°C.

Her chest radiograph (Fig. 1a) showed multiple patchy opacities in both lungs. Computed tomography (CT) confirmed multiple irregular foci of peripheral consolidation with air bronchograms predominantly in the upper lobes (Fig. 1b). Her eosinophil count was $0.3 \times 10^9/L$ and she had normal or negative serum angiotensin converting enzyme, immunoglobulins, HIV-1 and -2, rheumatoid factor, anti-neutrophil cytoplasmic antibodies (ANCA), antinuclear antibody (ANA) and extractable nuclear antigens. Sputum culture was negative as were tests for *Pneumococcus, Legionella and Mycoplasma*.

She was treated with intravenous flucloxacillin and augmentin with oral clarithromycin for ten days with no clinical improvement and no change in inflammatory markers (C-reactive protein varied between 60 and 70 mg/L). She therefore underwent fibreoptic bronchoscopy and bronchial lavage. No bacteria, fungi, or acid fast bacilli were identified or cultured. Cytology on bronchial washings revealed no malignant cells. Transbronchial lung biopsy revealed normal lung parenchyma. Video-assisted thoracoscopic surgical (VATS) lung biopsy was therefore performed, which showed acute inflammation and granulation tissue in bronchiolar lumens and alveolar spaces with some lymphocytic infiltration, compatible with organising pneumonia (Fig. 2a and b).

Minocycline was stopped immediately following the VATS biopsy but in view of the acne the patient was not keen to start corticosteroids. She was therefore closely observed in the clinic. Six weeks later the radiological abnormalities had completely resolved (Fig. 3) and she felt much better without the need to use corticosteroids. Eight months later she remained well with no sign of recurrence and interestingly no worsening of her acne.

**Discussion**

Our patient presented with the characteristic clinical features of organising pneumonia (OP) including dyspnoea and constitutional symptoms of fever, sweats, weight loss and loss of appetite. She had the typical radiological

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**Figure 1** (a) Chest radiograph showed multiple patchy opacities in both lungs. (b) Computed tomography (CT) scan showing multiple irregular foci of peripheral consolidation with air bronchograms.

**Figure 2** (a) VATS lung biopsy showing fibrinous exudate in alveoli (H&E, low power). (b) VATS lung biopsy showing organising pneumonia with Masson bodies (H&E, low power).
(patchy multifocal consolidation) and histological (fibrinous intra-alveolar exudate with Masson bodies) findings in OP. She had no other findings to suggest that the OP was anything other than secondary to minocycline therapy and the confirmatory feature was resolution of abnormalities on minocycline cessation alone. Furthermore, there was no relapse of OP on follow up whereas relapse of OP commonly occur in cryptogenic OP (COP), particularly on reducing or stopping corticosteroids.9

Previous reports of minocycline induced organising pneumonia have tended to show only a partial response to minocycline cessation with full resolution occurring only after using corticosteroids.2–6,9,10 This case is interesting because of the rapid and complete resolution on minocycline cessation only, without recourse to corticosteroids. Most previous reports are associated with eosinophilia3–6 but our patient had a normal peripheral blood eosinophil count. Neutrophilic alveolitis has also been described.10

In keeping with previous reports11 and given the severity of her adverse reaction she was not re-challenged with the drug. In a previous report, minocycline re-challenge has resulted in a recurrence of symptoms and hypoxaemia in a case where a preceding lymphocyte-stimulation test indicated an alternative drug was the cause of a patient’s drug induced OP.12 The lymphocyte-stimulation test for minocycline with peripheral blood lymphocytes is not believed to be useful for the diagnosis of minocycline induced OP.13

Curiously, minocycline has been used a treatment for OP in rheumatoid arthritis with significant improvements in arthritis, pulmonary function and CT findings.7

Conclusions

We present a case of minocycline induced organising pneumonia in an otherwise well young woman, which resolved rapidly and completely on minocycline cessation alone. Although this is a rare adverse effect we would still urge a cautious observation for the development of respiratory adverse effects when initiating treatment with minocycline. The absence of eosinophilia in this case may suggest a more benign prognosis. We would also like to emphasise that the development of respiratory symptoms can be delayed, and hence the need to consider drugs in new onset respiratory symptoms.

Learning points

- Organising pneumonia is a rare adverse effect of minocycline therapy.
- The onset of adverse effects from minocycline is not necessarily temporally related to the initiation of treatment.
- Organising pneumonia secondary to minocycline may completely resolve on drug cessation alone without recourse to corticosteroids.

Conflict of interest statement

No author has any conflict of interest in relation to any aspect of this manuscript.

References


