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CASE STUDY

Bronchiolitis obliterans organizing pneumonia associated with minocycline therapy: a possible cause

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Bronchiolitis obliterans organizing pneumonia associated with minocycline therapy: a possible cause. D. Piperno, C. Donné, R. Loire, J-F. Cordier. ©ERS Journals Ltd 1995.
ABSTRACT: We report the case of a woman who presented with dyspnoea whilst taking minocycline for acne.

Imaging features of bilateral patchy alveolar opacities suggested a diagnosis of bronchiolitis obliterans organizing pneumonia, which was confirmed by lung biopsy. The patient improved, partially, after stopping minocycline, and then completely on treatment with corticosteroids, without relapse when these where stopped 8 weeks later.
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Bronchiolitis obliterans organizing pneumonia (BOOP) is a condition defined by the presence of intraluminal polyps of granulation tissue in the distal airspaces [1]. It may be idiopathic and associated with typical clinical and imaging features, or secondary to various causes, including reaction to different drugs [2].

Minocycline hydrochloride is a tetracycline derivative used for the treatment of various infections, and also used by dermatologists for the treatment of acne. Minocycline may induce pulmonary side-effects, consisting of pulmonary infiltrates frequently associated with blood and/or bronchoalveolar lavage eosinophilia [3].

We report a case where minocycline was probably the cause of bronchiolitis obliterans organizing pneumonia (BOOP).

Case report

A 20 year old woman presented in July 1993 with progressive mild dyspnoea. She had been treated for 3 months for inflammatory acne with minocycline hydrochloride (Mynocine ®), a drug which she had also received 3 yrs before for the same condition. She had no fever, or weight loss. Her physical examination was normal. Usual laboratory tests were unremarkable, except for increased erythrocyte sedimentation rate (90 $mm \cdot h^{-1}$). The white blood cell count was 8,500 $cells \cdot mm^{-3}$ ($8.5 \times 10^9 \cdot L^{-1}$) with 5% eosinophils (425 $cells \cdot mm^{-3}$ ($0.4 \times 10^9 \cdot L^{-1}$)).

The chest radiograph showed bilateral ill-defined alveolar opacities predominating in the upper lobes. Chest computed tomography (CT) scan confirmed the presence of patchy bilateral alveolar opacities, ranging from nodules to mass-like opacities with an air bronchogram (fig. 1).

Lung function tests showed a mild restrictive ventilatory defect: vital capacity 2.59 L (78% of predicted), with forced expiratory volume in one second 2.38 L (82% pred). Blood gases were: arterial oxygen tension (Pa,O_2) 10.4 kPa and arterial carbon dioxide tension (Pa,CO_2) 5.1 kPa, with pH at 7.38.

A transbronchial biopsy showed inflammatory alveolitis, with the presence of discrete buds of granulation tissue within alveoli. A lung specimen obtained by open lung biopsy showed numerous polyps of granulation tissue within the lumen of the alveoli and the bronchioles, together with a mild lymphocytic infiltration of some bronchioles (fig. 2).

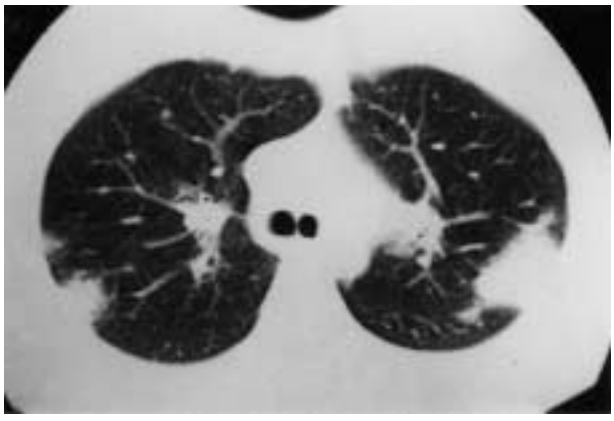

Fig. 1. – Patchy alveolar opacities typical of bronchiolitis obliterans organizing pneumonia (BOOP) on computed tomography (CT) scan.

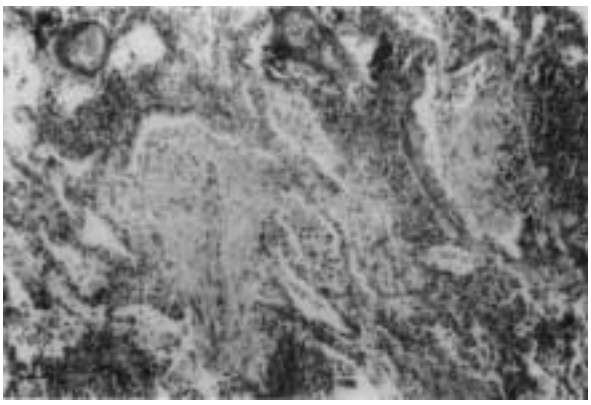

Fig. 2. – Buds of granulation tissue within the lumen of distal airspaces in the lung biopsy specimen. Mild lymphocytic infiltration of bronchiolar walls is present. (Original magnification ×100). (Scale bar = 50 μm).

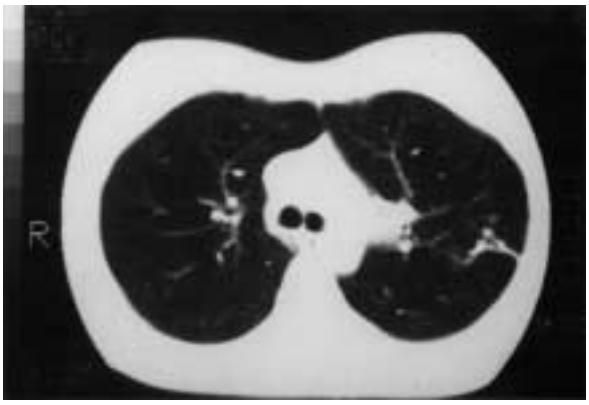

Fig. 3. – Computed tomography (CT) scan, performed 4 months after stopping corticosteroids, shows the clearing of pulmonary opacities, with only mild sequelae of the pulmonary biopsy on the left.

Minocycline treatment was interrupted at the beginning of diagnostic investigations, and a chest radiograph 3 weeks later showed partial improvement. Corticosteroids were then prescribed after pathological diagnosis was obtained, beginning with prednisolone 1 $mg \cdot kg^{-1}$ daily for 10 days, which was then progressively reduced for a total duration of treatment of 8 weeks. At the end of treatment, the patient was asymptomatic and her chest radiographic abnormalities had cleared. Vital capacity was 2.79 L (84% pred) with forced expiratory volume in one second 2.58 L (89% pred). CT scans performed 1 month and 4 months after stopping treatment showed almost complete clearing, except for a mild sequelae of pulmonary biopsy (fig. 3).

Discussion

Our patient presented with dyspnoea and the typical imaging features of BOOP, consisting of bilateral patchy alveolar opacities with ill-defined limits, but she lacked the flu-like initial symptoms commonly present in idiopathic BOOP (also termed cryptogenic organizing pneumonitis) [4]. However, her erythrocyte sedimentation rate was markedly increased, as seen in idiopathic BOOP. The diagnosis of BOOP was suggested by transbronchial biopsies, and then assessed by open lung biopsy (retrospectively, we feel that the open lung biopsy might have been avoided).

We consider that in our patient BOOP was related to minocycline uptake for several reasons. The patient had no other condition usually associated with BOOP, which developed whilst taking the drug and partially regressed spontaneously when the patient was undergoing diagnostic investigations. Furthermore, her BOOP did not relapse after a rather short course of corticosteroids, whereas relapse on reducing or stopping corticosteroids is very common in idiopathic BOOP, which classically requires a more prolonged treatment (sometimes more than one year).

Drug reaction is a well identified cause of BOOP, and several types of drugs have been incriminated: anti-inflammatory and immunomodulatory (gold, mesalazine, methotrexate, naproxen, sulphasalazine, sulphamethoxypyridazine, sulindac); antimicrobial (amphotericin B, cephalosporin); cardiovascular (acebutolol, amiodarone); cytotoxic (bleomycin, mitomycin-C); and illicit (free-base cocaine) [5, 6]. The clinical and imaging presentation of drug-induced BOOP is similar to that of idiopathic BOOP in most cases [6].

Pneumonitis is now well-recognized as a side-effect of minocycline treatment [3]. Patients present with dyspnoea, which may be severe, during treatment with the drug. Pulmonary abnormalities on chest radiograph or CT scan are alveolar or diffuse infiltrative opacities with a wide range of distribution. Blood eosinophilia is common but not constant, and bronchoalveolar lavage usually shows eosinophilia and/or lymphocytosis, suggesting a hypersensitivity mechanism [3, 7]. No eosinophilia was present in the blood or the lung biopsy specimen in our patient, but we cannot exclude its presence at the beginning of her pulmonary symptoms.

The occurrence of either eosinophilic pneumonitis or BOOP as a pulmonary reaction to minocycline is a further argument for the relationship between these two disorders, as has been suggested previously for their idiopathic forms [4, 8, 9]. Overlap between eosinophilic pneumonia and BOOP may also be observed in patients developing pneumonitis after bleomycin treatment [8, 10].

In conclusion, we have reported a novel case of drug-induced BOOP. The fact that minocycline may be responsible for either eosinophilic pneumonia or BOOP suggests that both conditions may share common pathogenic mechanisms.

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