Secondary organizing pneumonia (bronchiolitis obliterans with organizing pneumonia) associated with adalimumab for treatment of chronic plaque psoriasis

PermnaLink
https://escholarship.org/uc/item/7m04d30g

Journal
Dermatology Online Journal, 25(10)

Authors
Doolan, Brent J
Cranwell, William C
Nicolopoulos, Jenny
et al.

Publication Date
2019

License
CC BY-NC-ND 4.0
Secondary organizing pneumonia (bronchiolitis obliterans with organizing pneumonia) associated with adalimumab for treatment of chronic plaque psoriasis

Brent J Doolan, BSc MBBS MPH&TM, William C Cranwell MBBS(Hons) BMedSc(Hons) MPH&TM, Jenny Nicolopoulos, MBBS FACD, Con Dolianitis, BA MBBS Mmed FACD

Affiliations: Department of Dermatology, The Royal Melbourne Hospital, Melbourne, Victoria, Australia

Corresponding Author: Brent J Doolan, The Royal Melbourne Hospital, Melbourne, Victoria, Australia 3050, Tel: 61-3 9342 4531, Email: brentjamesdoolan@gmail.com

Abstract
Organizing pneumonia is defined histopathologically by intra-alveolar buds of granulation tissue, consisting of intermixed myofibroblasts and connective tissue. The pathological pattern of organizing pneumonia may be idiopathic or related to a determined cause, termed secondary organizing pneumonia. We report a 68-year-old woman with a longstanding history of chronic plaque psoriasis, treated with the tumor necrosis factor (TNF) inhibitor, adalimumab. After 8 years of treatment, she developed a gradual-onset, non-productive cough with associated generalized fatigue and mild dyspnea. Radiological investigations demonstrated ground-glass opacities in the left lower lobe and bronchoscopy revealed a fibroinflammatory process consistent with organizing pneumonia. Her biologic treatment was ceased and corticosteroid treatment commenced, with resolution of both her symptoms and the radiological findings. Given the increasing incidence of biologic treatment in the management of dermatological conditions, clinicians should be aware of secondary organizing pneumonia as a possible side effect of TNF inhibitor therapy.

Keywords: secondary organizing pneumonia, adalimumab, biologics, psoriasis, bronchiolitis obliterans with organizing pneumonia

Introduction
Organizing pneumonia (formerly bronchiolitis obliterans with organizing pneumonia) is defined histopathologically by intra-alveolar buds of granulation tissue, consisting of intermixed myofibroblasts and connective tissue [1]. The pathological pattern of organizing pneumonia may be idiopathic (cryptogenic organizing pneumonia) or due to a determined cause (secondary organizing pneumonia), including connective tissue disorders, infectious diseases, parasitic infection, organ transplantation and drugs [2]. Drugs used commonly in dermatology implicated in the pathogenesis of secondary organizing pneumonia include sirolimus, minocycline, rituximab, tacrolimus, thalidomide, and methotrexate [2]. If left untreated, organizing pneumonia can progress to pulmonary fibrosis, with a mortality rate between 5-27% [2]. We report a case of drug-induced secondary organizing pneumonia in a patient on the tumor necrosis factor inhibitor, adalimumab, for chronic plaque psoriasis.

Case Synopsis
We report a 68-year-old woman with a longstanding history of chronic plaque psoriasis. Medical history was significant for aortic incompetence, hypercholesterolaemia, paroxysmal atrial fibrillation, and hypertension. Regular medications included atorvastatin, atenolol, and apixaban. She was commenced on adalimumab 40mg subcutaneous every two weeks and after four months of treatment had a significant reduction in her psoriasis (Psoriasis Area Severity Index score decrease from 17.1 to 1.2). After 8 years of treatment she complained of a gradual-onset, non-productive cough with associated generalized fatigue and mild dyspnea. A computed tomography (CT) scan was performed to investigate abdominal discomfort and this incidentally revealed consolidation with linear inter-
and intra-lobular septal thickening in the lower lobe. A dedicated high resolution high resolution CT (HRCT) demonstrated ground-glass opacities in the left lower lobe with ongoing thickening of the interlobular septa bi-basally, along with a 2.5mm sub-pleural nodule. There was preserved lung architecture and no pathological lymphadenopathy.

All blood tests including full blood examination, inflammatory markers, antinuclear antibodies, and QuantiFERON-TB Gold were all within normal range. Bronchoscopy revealed a fibroinflammatory process consistent with organizing pneumonia, without necrosis or vasculitis. Bronchoalveolar lavage yielded a lymphocytosis of 85% of returned cells, excluding infection, with no cytological evidence of malignancy. She was diagnosed with organizing pneumonia secondary to adalimumab and biologic treatment was discontinued. She was commenced on prednisolone 50mg daily, which was tapered over 6 weeks. Repeat HRCT at 9 weeks revealed significant improvement in pulmonary pathology and resolution of her symptoms.

**Case Discussion**

Tumor necrosis factor is a cytokine that has been implicated as both a pro- and anti-fibrotic agent involved in the pathophysiology of pulmonary fibrosis [3]. Tumor necrosis factor has been shown to promote pulmonary tissue repair, eliminating inflammatory cells by inducing apoptosis and preventing the development of fibrosis [3]. It has also been shown to play a pro-fibrotic role by upregulating messenger pathways that activate extracellular regulated kinase-specific pathways in fibroblasts [4]. Specifically, by upregulating the expression of transforming growth factor β1 in the lungs, TNF increase in the expression and DNA binding of the activator protein-1, and regulation of p21, a cyclin-dependent kinase inhibitor that plays a key role in regulating cell cycle progression and apoptosis [4]. Therefore, TNF inhibitors including adalimumab have been postulated as a potential therapeutic pathway for interstitial lung disease [5]. However, there are an increasing number of cases of drug-induced lung disease by these agents [5], especially in those that have factors associated with increased risk of interstitial lung disease, such as smoking, autoimmunity disease, and concomitant therapies such as methotrexate, azathioprine, and cyclophosphamide [4]. Thus, a careful clinical evaluation including assessment of previous pulmonary disease, respiratory radiological findings, and risk factors for interstitial lung disease should be undertaken when considering biologic therapy.

**Conclusion**

Given the increasing incidence of biologic treatment in the management of dermatological conditions, clinicians should be aware of secondary organizing pneumonia as a possible side effect of TNF inhibitor therapy.

**Potential conflicts of interest**

The authors declare no conflicts of interests.

**References**


