



Colitis and bronchiolitis obliterans organising pneumonia— the treatment or the disease?

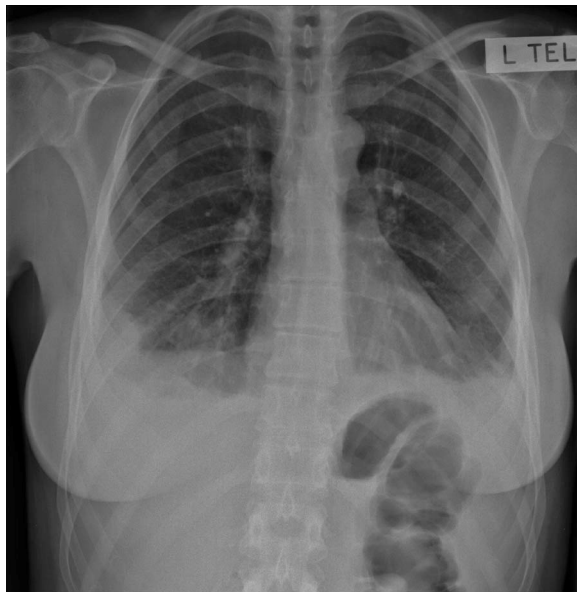
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A 31-year-old white female was admitted to hospital with a slight fever, bilateral chest pain, and dyspnoea, which had been gradually developing over the past 12 months. Of interest was a similar admission 3 months previously, when no cause for her symptoms had been found, but a CT pulmonary angiogram (CTPA) showed small areas of parenchymal air space opacity in both lower lobes but no pulmonary embolism.

Her past history included fertility problems but she was currently pregnant after *in vitro* fertilisation. Ulcerative colitis had been diagnosed 1 year ago and she had been on mesalazine (5-aminosalicylic acid) at a dose of 4 g daily since that time.

Her physical signs included bilateral basal chest dullness to percussion and a low-grade fever. A chest X-ray (Figure 1) showed bibasal pulmonary/pleural opacities, more marked on the right. Ultrasound of the chest revealed minimal pleural effusions.

Figure 1. X-ray showing bibasal pulmonary/pleural opacities suggestive of bronchiolitis obliterans organising pneumonia (BOOP)



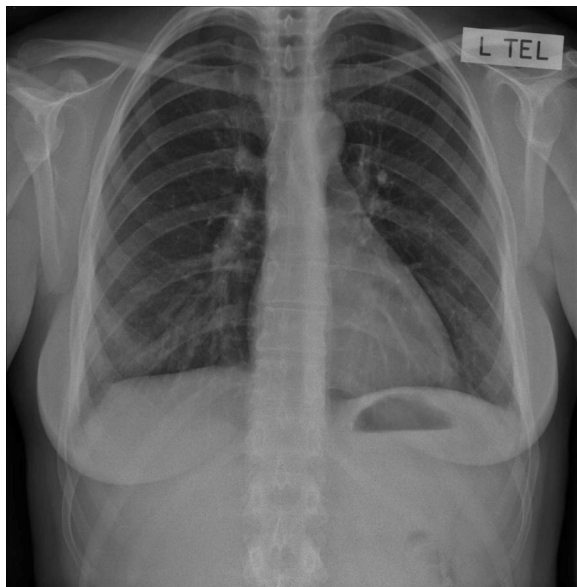
Blood screen: haemoglobin 106 g/L, white count $7.6 \times 10^9/L$ with normal differential, erythrocyte sedimentation rate (ESR) 35mm/hr. Serum sodium, potassium, creatinine, and liver function tests were all normal.

Lupus anticoagulant, anticardiolipin antibodies, and antineutrophil cytoplasmic antibodies (ANCA) were negative. Antinuclear antibody (ANA) was positive at >1280 with a diffuse, chromosome-positive pattern. ENA, DsDNA, and complement 3 and 4 were normal. Ultrasound of the abdomen and pelvis revealed no evidence of ovarian hyperstimulation syndrome.

As pulmonary embolism and ovarian hyperstimulation syndrome seemed unlikely, she was treated with amoxicillin, but with no improvement. A pulmonary complication of her inflammatory bowel disease was considered but this was felt to be less likely as her ulcerative colitis was well controlled.

Mesalazine was stopped and prednisone 40 mg daily was instituted. Within a few days her symptoms improved. One month later she had no symptoms and her X-ray showed considerable improvement. Three months later she had a normal chest X-ray (Figure 2) and had resumed all her usual activities, including vigorous exercise.

Figure 2. X-ray showing successful resolution of her symptoms



Sulphasalazine which has been used in the past to treat inflammatory bowel disease is known to occasionally cause infiltrative lung lesions. It has generally been considered that the sulpha component of sulphasalazine is responsible for this adverse reaction.¹ Mesalazine (5-aminosalicylic acid) is now more commonly used as it does not contain sulpha and is less likely to cause adverse reactions. However, there is a small literature suggesting that mesalazine can cause bronchiolitis obliterans organising pneumonia (BOOP).²

A similar case was reported by Swinburn et al in 1988, although these authors felt that the syndrome in their patient was probably unrelated to the mesalazine.³ Since that time there have been 20 or more case reports in the literature where mesalazine has been incriminated as a cause of BOOP.² In some of these cases, the exposure has been only for a few days (5 days in the case reported by LeGros),¹ but other cases have

been reported in which the exposure to the drug has been many months, or even years.²

The dose of mesalazine used has varied widely between 1 g and 4 g daily.² In all reported cases, withdrawal of the drug with or without steroid treatment has resulted in resolution of the pulmonary symptoms and x-ray abnormalities.²

Alternative diagnoses considered included diffuse interstitial pneumonia and systemic inflammatory response syndrome, but the timeline of her illness and its relationship to the inception and conclusion of her treatment with mesalazine made them unlikely. Inflammatory bowel disease may be associated with pulmonary manifestations such as our patient had, but the quiescence of the colitis over the entire symptomatic pulmonary disease process makes this alternative less likely.

Had this lady not been pregnant, further investigations such as high resolution computed tomography and/or transbronchial lung biopsy might have confirmed the diagnosis. Clearly these were not reasonable investigations in this case. Rechallenge with mesalazine was also not a sensible option.

The patient's respiratory symptoms commenced within days of the institution of mesalazine but intensified over the following year. Subsequently, the symptoms improved within days after the mesalazine was stopped. This sequence of events is highly suggestive that mesalazine was the underlying cause of the BOOP.

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2. Sossai P, Cappellato MG, Stefani S. Can a drug-induced pulmonary hypersensitivity reaction be dose-dependent? A case with mesalamine. *Mt Sinai J Med*. 2001;68:389-95.
3. Swinburn CR, Jackson GJ, Cobden I, et al. Bronchiolitis obliterans organising pneumonia in a patient with ulcerative colitis. *Thorax*. 1988;43:735-6.