Pulmonary fibrosis associated with nabumetone

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Summary: A patient is described who developed a rapid onset of pulmonary fibrosis following treatment with a new non-steroidal anti-inflammatory drug, nabumetone. Resolution of symptoms, physical signs and radiographic changes followed drug withdrawal and steroid therapy.

Introduction

Pulmonary infiltration and fibrosis have been described with a number of non-steroidal anti-inflammatory agents.¹ We report a case where an unusual radiographic appearance of pulmonary infiltration was associated with drug therapy.

Case report

A 68 year old woman with osteoarthritis and osteoporosis was treated with paracetamol and dextropropoxyphene (Co-proxamol), ibuprofen 1,200 mg/day and calcium lactate gluconate (Sandocal) for 4 years. Tiaprofenic acid 600 mg/day was added but gastric disturbance lead to a change in her analgesia to nabumetone 1500 mg/day. Two weeks later she developed shortness of breath and a dry cough. Breathlessness increased over 6 weeks until she was short of breath on minimal exertion. She was a non-smoker without recognized risk factors for fibrotic lung disease.

On examination there was no cyanosis or clubbing and no signs of cardiac failure or pulmonary hypertension. Crepitations were heard over both lung bases and deep inspiration provoked explosive coughing.

Full blood count and biochemical screening were normal, but ESR was elevated at 48 mm/hour. Auto-antibody screen and rheumatoid factor were negative. Blood gases revealed mild hypoxaemia Po2 9.1 kPa, O₂ saturation 94%. Chest X-ray showed ill-defined reticular nodular shadowing affecting both lower and mid zones bilaterally. Chest computed tomographic scan (Figure 1) demonstrated bizarre pulmonary shadowing predominantly in the lower zones, without subpleural bias or evidence of bronchiectasis and with sparing of the lung apices. Forced expiratory volume in the first second (FEV₁) (predicted) was 1.2 litres (1.7–2.5) and forced vital capacity (FVC) 1.4 litres (2.2–3.1). Transfer factor was reduced [KCO 1.3 (1.7–2.1)]. Fibreoptic bronchoscopy revealed no endobronchial abnormality but transbronchial lung biopsy showed interstitial inflammation with eosinophils and alveolar cell hyperplasia which was confirmed at open lung biopsy. In addition, open biopsy showed fibrous organization of intra-alveolar exudate, lymphoid follicles and frequent histiocytes, some multinucleated. Bronchioles showed mucus plugging and inflammation and there was intimal and medial thickening of pulmonary arterial branches.

Nabumetone was stopped and prednisolone 50 mg/day commenced with a rapid resolution of symptoms and an improvement in physical signs. Prednisolone was gradually tailed off and 18 months after presentation FVC was 2.2 litres and

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Chest X-ray at this time revealed resolution of reticular shadowing although some ill defined opacities remained at both lung bases.

Discussion

A clear temporal relationship between the change in analgesic treatment and the onset of breathlessness caused our patient to ascribe her symptoms to nabumetone. The unusual radiographic findings of central rather than peripheral shadowing without the ill-defined nodules and streaking of fibrosing alveolitis led us to consider unusual causes of lung fibrosis. Although bilateral diffuse reticular nodular shadowing has been described with several non-steroidal anti-inflammatory agents such as sulindac, tolfenamic acid, naproxen and azaproazone, the changes seen in our patient are not typical of either drug-induced or other known causes of pulmonary fibrosis.

The histological features were those of an active interstitial pneumonitis with bronchiolitis and were non-specific in appearance. Eosinophils were focally very prominent in the lymphohistiocytic background. There was no alveolar cell dysplasia. The appearances share some of the features with nitrofurantoin-induced pneumonitis.

The history and unusual features of our case led us to believe that nabumetone may have been responsible for our patient’s pulmonary fibrosis. Enquiry to the Committee of Safety in Medicine revealed that there have been two other cases of pulmonary fibrosis associated with nabumetone therapy.

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References

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