LETTERS

Histological appearances of putative montelukast related Churg–Strauss syndrome

Leukotriene receptor antagonists (LTRA) are widely used in the treatment of asthma. Over the years, case reports have suggested a possible link between their introduction and the development of Churg–Strauss syndrome. The case we describe highlights a strong temporal relationship between the initiation of montelukast and appearance of features suggestive of Churg–Strauss syndrome; our patient went on to have a lung biopsy which confirmed the diagnosis. We speculate that the slightly atypical histological features observed (airway involvement by necrotising granulomas) could indicate changes caused by LTRA induced disease per se.

LTRAs have emerged as useful oral therapeutic adjuncts in the management of persistent asthma.[1] These drugs are usually well tolerated[2] although some reports have suggested a link between LTRAs and the development of Churg–Strauss syndrome. Most (although not all) of these cases have occurred where concomitant prescription of an LTRA has allowed a reduction in corticosteroid dose or corticosteroid withdrawal, in turn indicating that latent Churg–Strauss syndrome may have been unmasked by a decrease in anti-inflammatory therapy.[3]

A non-smoking 40-year-old patient with lifelong atopic asthma presented to the chest clinic with 3 months of very gradually deteriorating asthma control despite regular use of twice daily fluticasone 125 μg/salmeterol 25 μg through an Evohaler plus spacer for well over a year. There was nothing of note in his past medical, occupational or social histories, and he was using no other medication. There were no other symptoms and clinical examination revealed faint bilateral expiratory wheeze alone. At this point his forced expiratory volume in 1 second (FEV_1) was 2.5 litres, forced expiratory volume (FVC) 3.8 litres and peak expiratory flow (PEF) 400 l/min. He was started on montelukast 10 mg/day and prescribed 2 puffs twice daily of fluticasone 250 μg/salmeterol 25 μg through an Evohaler plus spacer. Over the next 3–4 weeks, he experienced a dramatic worsening of respiratory symptoms and developed a florid maculopapular rash mainly in the upper body; no other systemic features were present. His lung function had also deteriorated with FEV_1 being 2 litres, FVC 3.1 litres and PEF 370 l/min. At this time, the chest radiograph showed widespread bilateral infiltrates, and full blood count showed a raised eosinophil count of 11×10^9/l, having been 2×10^9/l just before institution of montelukast; renal function was normal, and antineutrophil cytoplasmic antibodies (taken approximately 3–4 weeks after initiation of montelukast) and aspergillus serology were negative. A high resolution CT showed widespread airspace opacification predominantly around smaller airways. He was started on high dose oral corticosteroids, advised to continue with fluticasone/salmeterol and montelukast was discontinued, all which resulted in a marked improvement in clinical, laboratory and radiological features. A video assisted thoracoscopic lung biopsy (while using daily prednisolone 30 mg) several weeks later showed a number of abnormalities consistent with Churg–Strauss syndrome. These included patchy eosinophilic pneumonia and scattered necrotising granulomas with eosinophils involving the pulmonary parenchyma, pulmonary arteries and veins, but unusually, similar granulomas involved several bronchioles with crescentic zones of necrobiotic tissue with eosinophils lining the partial circumference of airways, surrounded by epithelioid histiocytes and occasional giant cells (fig 1). Other airways demonstrated peribronchiolar metaplasia and mucous plugging.

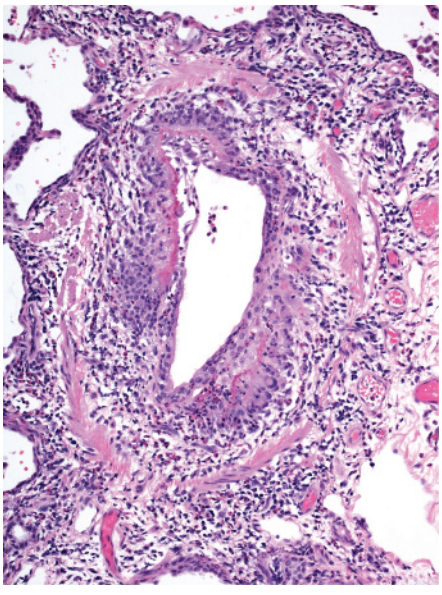

Figure 1 Open lung biopsy specimen showing features of presumed montelukast related Churg–Strauss syndrome.

In contrast with most other published reports, our case highlights the appearance of Churg–Strauss syndrome shortly after initiation of montelukast despite a concomitant increase in inhaled corticosteroid dose. It is impossible to be certain that montelukast was responsible although the striking temporal relationship between its introduction and dramatic deterioration in asthma control supports the notion that this drug was probably implicated. It is important to be aware that although fluticasone/salmeterol has also been implicated in Churg–Strauss syndrome, we feel it is unlikely to be responsible in this case, as our patient had been using this combination product for well over a year without adverse effect and in fact improved despite its continuation.

Although clinical features of Churg–Strauss syndrome, whether associated with montelukast or not, are similar, it is conceivable that the slightly atypical histological features (airway involvement by necrotising granulomas) described above may represent changes caused by LTRA induced disease per se. It is important to be aware that there is ongoing uncertainty as to whether LTRAs unmask an already present syndrome or play a more direct causative role by an unknown mechanism.[4] However, when initiating LTRAs, clinicians should remain vigilant in terms of clinical, laboratory and radiological features which may necessitate drug withdrawal and consideration of possible Churg–Strauss syndrome. This report adds to the published literature surrounding the putative association between leukotriene receptor antagonists and development of Churg–Strauss syndrome and in distinction to most other reports, highlights its histological features.

G P Currie,[1] L McKinlay,[1] K M Kerr[2]

[1] Department of Respiratory Medicine, Aberdeen Royal Infirmary, Aberdeen, UK; [2] Department of Pathology, Aberdeen Royal Infirmary, Aberdeen, UK

Correspondence to: Dr G P Currie, Department of Respiratory Medicine, Aberdeen Royal Infirmary, Foresterhill, Aberdeen AB25 2ZD, UK; graeme.currie@nhs.net

Competing interests: GPC has received funding from MSD and AstraZeneca for attending postgraduate conferences and giving talks, both of whom manufacture LTRAs.

Accepted 13 July 2008

Thorax 2008;**63**:1120. doi:10.1136/thx.2008.102566

REFERENCES

1. **Currie GP,** McLaughlin K. The expanding role of leukotriene receptor antagonists in chronic asthma. *Ann Allergy Asthma Immunol* 2006;**97**:731–41.
2. **Storms W,** Michele TM, Knorr B, *et al*. Clinical safety and tolerability of montelukast, a leukotriene receptor antagonist, in controlled clinical trials in patients aged ⩾6 years. *Clin Exp Allergy* 2001;**31**:77–87.
3. **Wechsler ME,** Pauwels R, Drazen JM. Leukotriene modifiers and Churg–Strauss syndrome: adverse effect or response to corticosteroid withdrawal? *Drug Saf* 1999;**21**:241–51.
4. **Lipworth BJ,** Wilson AM. Montelukast and Churg–Strauss syndrome. *Thorax* 2001;**56**:244.

Optimal treatment for idiopathic pulmonary fibrosis

The recent review series on interstitial lung disease has created a great deal of interest. However, the review by Williams and Wilson of novel treatments and lung transplantation in pulmonary fibrosis[1] does not reflect recent developments in clinical and translational research in idiopathic pulmonary fibrosis (IPF).

The belief that inflammation is the primary driver of fibrosis in IPF has been superseded by newer pathogenetic paradigms that emphasise