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Ulcerative colitis following introduction of zafirlukast and corticosteroid withdrawal in severe atopic asthma

To the Editor:

The leukotriene (LT) receptor antagonist accolate (zafirlukast) has recently been approved for use in the US and most European countries as an oral preventative, as well as a chronic treatment, for asthma in both adults and children aged ≥12 yrs [1, 2]. The drug specifically blocks the docking of LT molecules to the cysteinyl leukotriene ($CysLT_1$) receptor subtype on airway smooth muscle cells and represents the first really new class of anti-asthmatic drugs to be introduced in 20 yrs [3]. Although LT receptor antagonists are generally well tolerated and side-effects associated with these drugs are rare, several cases of an eosinophilic disorder reminiscent of the Churg-Strauss syndrome have been reported in patients taking zafirlukast [4, 5] and montelukast (post-marketing informational letter). Characteristically, these patients were on a high-dose of inhaled or oral corticosteroid therapy, and were able to reduce the dose as a beneficial consequence of the effects of the LT antagonists. However, it is unclear whether the Churg-Strauss syndrome is a result of the reduction of corticosteroid dose or an idiosyncratic effect of LT agonists.

This article reports the case of a 65 yr old male Caucasian patient with severe atopic asthma, who experienced an exacerbation of ulcerative colitis after initiation of zafirlukast treatment. The patient presented with a 25-yr history of ulcerative colitis, that was in remission for >10 yrs. In addition, in 1972, he was diagnosed with severe atopic asthma, for which he had been receiving a daily dose of 5–15 mg prednisolone during the past 6 yrs. He also used inhaled beclomethasone diproprionate (BDP; 500 μg *b.i.d.*), oral theophylline (375 mg *b.i.d.*) and ketotifen (1 mg at night), as well as inhaled fenoterol on demand. The patient was seeking medical advice since he was concerned about the potential side effects of long-term oral steroid therapy.

On examination, the patient was comfortable at rest but a reduced breath sound and prolonged expiratory wheeze were heard over both lungs. He had a normal erythrocyte sedimentation rate (10 $mm \cdot h^{-1}$) and total leukocyte count ($cells \cdot \mu L^{-1}$), and peripheral eosinophilia (8% of leukocytes). Sputum cultures were negative. Total serum immunoglobulin (Ig)E levels were elevated to 1,640 $IU \cdot L^{-1}$ (<100 $IU \cdot L^{-1}$), and specific IgE directed against common allergens, including grass pollen, birch pollen, and house dust mite, were detected. His chest radiograph revealed moderate hyperinflation, while a high-resolution computed tomographic scan of the lung was normal. Lung function testing revealed an obstructive defect, with an increased residual volume of 152% of predicted, reduced forced expiratory volume in one second (FEV_1) (44.6% pred), and a mean forced mid-expiratory flow ($FEF_{25–75\%}$) <10% pred, consistent with obstruction of the small airways. Diffusion capacity for carbon monoxide ($D_{L,CO}$) was normal.

A treatment with zafirlukast (20 mg), in combination with inhaled formeterol (24 μg) and fluticasone (500 μg) twice daily, resulted in an alleviation of the asthma symptoms. Mean peak expiratory flow improved from 300 to 440 $L \cdot min^{-1}$. The stable clinical condition allowed a gradual reduction of oral prednisolone, which could be discontinued 8 weeks after the initiation of zafirlukast. Thirteen days following discontinuation of corticosteroid treatment, the patient began experiencing lower abdominal cramps accompanied by up to 10 attacks of bloody diarrhoea per day. A colonoscopy confirmed the clinically-suspected diagnosis, and revealed an exacerbation of the ulcerative colitis. Consequently, while zafirlukast therapy was continued, resumption of the oral prednisolone therapy (5–7.5 mg) led to a gradual resolution of his bowel symptoms.

To the authors knowledge, this is the first report of an inflammatory bowel disease deteriorating under treatment with zafirlukast. A small number of cases of the Churg-Strauss syndrome have recently been reported among patients with severe asthma, in whom corticosteroids were either reduced or discontinued [4, 5]. The case reported herein parallels these reports, in as much as the discontinuation of chronic steroid therapy in a patient with severe atopic asthma res-ulted in the recurrence of a co-existing immunologic disorder, which previously may have been controlled by the anti-inflammatory asthma treatment. While the underlying pathomechanism of zafirlukast-associated exacerbation of ulcerative colitis remains to be elucidated, this observation has important clinical implications for physicians prescribing zafirlukast, and possibly other leukotriene receptor antagonists, to paients with corticosteroid-dependent asthma.

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