

## Case report

## Churg-Strauss syndrome associated with montelukast therapy

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## Abstract

**Churg-Strauss syndrome is a rare form of eosinophilic vasculitis associated with asthma. There have been several recent case reports of the condition in association with leukotriene antagonists and it has been speculated that the Churg-Strauss syndrome was unmasked when oral corticosteroids were withdrawn. We report a case of Churg-Strauss syndrome associated with montelukast therapy in an asthmatic patient in whom there had been no recent oral corticosteroid use. We believe that this is the first such reported case and would suggest that clinicians need to be vigilant in all patients who develop systemic symptoms when starting treatment with leukotriene antagonists.**

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**Keywords:** montelukast; pulmonary eosinophilia; Churg-Strauss syndrome

Churg-Strauss syndrome is a rare form of eosinophilic vasculitis associated with asthma. Recently there has been some concern that new cases have been associated with the use of anti-leukotriene drugs. There have been several published reports of eosinophilic conditions, including Churg-Strauss syndrome, associated with the use of zafirlukast.<sup>1-4</sup> In addition, there has been a recent case report documenting pulmonary eosinophilia in association with montelukast therapy, although there was no evidence of vasculitis in that patient.<sup>5</sup>

We report a case of Churg-Strauss syndrome in a patient with late onset asthma who developed clearcut eosinophilic vasculitis in association with worsening asthma which developed a few days after commencing montelukast. She had not been receiving continuous systemic corticosteroid previously. We believe that this is the first case of Churg-Strauss syndrome associated with montelukast in a patient not previously taking either continuous or multiple short courses of oral corticosteroids.

## Case report

A 72 year old woman was initially seen in August 1998 with a history of cough and wheeze over the previous few months. She was a lifelong non-smoker. She received a five day course of oral prednisolone from her general

practitioner with improvement in symptoms and a documented rise in peak expiratory flow (PEF) from 200 to 300 l/min (predicted 350 l/min). The patient was therefore started on regular inhaled beclomethasone and continued to improve. Her chest radiograph and full blood count including eosinophil count were normal. She was seen in the hospital outpatient department and spirometric tests at that stage showed a forced expiratory volume in one second (FEV<sub>1</sub>) of 1.56 l and forced vital capacity (FVC) of 2.04 l (predicted 2.2 l and 2.6 l, respectively). Peak flow was 280 l/min.

She elected to discontinue her inhaled beclomethasone. Three months later her symptoms of asthma returned and she required two further short courses of oral corticosteroids and inhaled beclomethasone was re-introduced. Her symptoms remained troublesome and she was changed to fluticasone 750 µg twice daily together with inhaled salmeterol 50 µg twice daily via a large volume spacer. Despite this, she remained symptomatic with peak flows varying between 250 and 350 l/min, although she did not require further systemic corticosteroid treatment.

In April 1999 she returned to her general practitioner with continuing symptoms of asthma. She was started on montelukast 10 mg daily (Singulair, Merck Sharp and Dohme, Hoddesdon, UK) and was referred back for further hospital assessment. She had not received any oral corticosteroids for at least three months.

Ten days after commencing montelukast she developed increasing cough and breathlessness, swollen ankles, polyarthralgia, and numbness over her fingers, toes and heels. This was associated with general malaise.

Four weeks after commencing montelukast she was seen in the outpatient department and noted to be generally unwell and very wheezy with a peak flow of 290 l/min and FEV<sub>1</sub>/FVC of 1.23/1.46 l/min. She had inspiratory crackles over both lung bases in addition to generalised expiratory wheeze. Admission was arranged to exclude other respiratory pathology. Following admission she was found to have a low grade temperature and she developed a vasculitic rash over both ankles with a painful peripheral neuropathy. Blood tests on admission showed C reactive protein (CRP) of 96 (normal <10), white cell count of  $28.7 \times 10^9/l$  with an absolute

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Figure 1 Chest radiograph showing bilateral basal infiltrates.

eosinophil count of 15.7 (54.7%), and a low albumin level (30 g/l). The chest radiograph showed bilateral basal infiltration (fig 1). Sputum culture and urine microscopy were unremarkable. Subsequently, rheumatoid factor was raised at 282 IU/ml (normal range 0–20). Antinuclear antibody and antineutrophil cytoplasmic antibody (ANCA) were both negative. *Aspergillus* precipitins and radioallergosorbent test (RAST) against *Aspergillus* were negative. The electrocardiogram and echocardiogram were both normal.

Treatment with montelukast and salmeterol was stopped and high dose oral prednisolone was commenced together with appropriate analgesia. The patient was also started on azathioprine (1 mg/kg). The cough and wheeze improved rapidly and there was resolution of the vasculitic rash. She was left with a painful peripheral neuropathy. All blood parameters including eosinophil count returned to normal within a few days of starting treatment.

On review one month later she continued to have numbness and pain over the metatarsophalangeal joints. She was still taking prednisolone 30 mg, azathioprine (1 mg/kg) daily, and fluticasone 500 µg twice daily. She was otherwise well and her peak flows were static between 300 and 350 l/min. Four months later both prednisolone and azathioprine were stopped. Her chest radiograph showed minimal residual infiltrate at the left base. The total eosinophil count was 0.13 (1.6%). Nerve conduction studies were not available until this time but were within normal limits. Two months after discontinuing immunosuppression she remained well and was maintained on only fluticasone 500 µg twice daily.

### Discussion

Montelukast is a potent leukotriene receptor antagonist which has been licensed in the UK for over a year for patients with asthma.<sup>6</sup> There has been some concern regarding the association between leukotriene antagonists and

Churg-Strauss syndrome.<sup>2–4</sup> In many cases this has been linked with the withdrawal of oral corticosteroids and previous authors have speculated that the Churg-Strauss syndrome was unmasked when oral steroids were withdrawn following the successful introduction of leukotriene receptor antagonists.<sup>2–7–8</sup> In other reports Churg-Strauss syndrome has been associated with zafirlukast and there has been no association with withdrawal of corticosteroids.<sup>3–4</sup> The Committee on Safety of Medicines (CSM) has received 12 reports of Churg-Strauss syndrome and one of pulmonary eosinophilia possibly associated with montelukast. Some of these patients had been on oral corticosteroids. Recovery after treatment occurred in most patients when the outcome was known to the CSM. There has also been a case of pulmonary eosinophilia associated with montelukast in which there was no association with corticosteroid withdrawal.<sup>5</sup> However, there has been no published case of documented Churg-Strauss syndrome following montelukast treatment in the absence of corticosteroid withdrawal.

The clear temporal relationship between the introduction of montelukast and the development of systemic symptoms of vasculitis in this case make an association very likely. Symptoms began within 10 days of commencing treatment when there had been no previous history of any systemic symptoms. Her asthma had not been well controlled just before starting montelukast, but this was not in association with a raised eosinophil count. There had been no use of oral corticosteroid for several months before the development of vasculitis and the only use of systemic steroids had been two short courses of prednisolone. The mechanism by which montelukast would appear to have played a direct causative role in the pathogenesis of this syndrome is unclear.

While anti-leukotriene drugs are generally safe and effective for most patients with asthma, clinicians need to be vigilant for pulmonary eosinophilia or Churg-Strauss syndrome in all patients who start treatment with leukotriene antagonists and develop systemic symptoms.

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