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Case Report

Churg-Strauss syndrome associated with leukotriene receptor antagonists

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CASE REPORT A 46-year-old man presented with a three-year history of rhinitis treated with intranasal corticosteroids. In July 1998 he attended his general practitioner with wheeze and was diagnosed as suffering from asthma. Treatment with inhaled salbutamol and beclomethasone 200 mcg twice daily was commenced in September 1998 and he improved. In January 1999 he presented with recurrent wheeze and non-productive cough; chest examination showed bilateral rhonchi. Chest radiograph showed obvious airspace consolidation in the left midzone, with a smaller area in the right midzone and possibly a further area at the right apex (Figure 1). He was commenced on zafirlukast 20 mg twice daily. Although he had improved at review 8 weeks later, it was noted he had developed a petechial rash over the lower pretibial area of both legs. He was changed from zafirlukast to montelukast. Chest radiograph two weeks following this review showed resolution of the previous areas of consolidation but new consolidation was noted at the left base and right mid zone (Figure 2). Eosinophil count was noted to be elevated at 16.9 x 10^9/1 (72% eosinophilia). The platelet count was normal. There had been no reduction in the dose of inhaled corticosteroids over this period. He was thought to have pulmonary eosinophilia and was commenced on prednisolone 40 mg daily for one week with symptomatic improvement including resolution of the petechial rash. At review two weeks following completion of prednisolone, he was again noted to have a petechial rash, again in a similar distribution. He complained of diarrhoea five days later and montelukast was stopped. He continued to complain of dyspnoea, wheeze and non-productive cough. At review two weeks later, he complained of increasing exertional dyspnoea and he was commenced on prednisolone 30 mg daily for one week. Again he symptomatically improved and the petechial rash resolved. Again, one week following completion of prednisolone, he continued to complain of dyspnoea, wheeze and cough and was commenced on prednisolone 30 mg daily for five days.

He was initially seen at the Chest clinic six weeks later, two days after completing a further five-day course of prednisolone 30 mg for increasing dyspnoea. He still complained of dyspnoea and non-productive cough. There was no other significant history and in particular there was no history of any inhaled allergens. Chest radiograph was normal. He was commenced on fluticasone 1000 mcg twice daily. At review, four weeks later, his symptoms had improved, but he complained of recurrence of the rash over both lower limbs. On examination he was thin. He had a purpuric rash, which was more extensive than previously, over both lower limbs and particularly pretibially. The nasal mucosa was reddened and inflamed and nasal polyps were noted. Respiratory rate was 15. Chest examination was normal. There was no other abnormality on examination. Spirometry showed an FEV1 of 3.941 (108% predicted) and a FVC of 4.731 (104% predicted). Residual volume was 126% predicted; total lung capacity was 108% predicted and residual volume/total lung capacity ratio was 110% predicted. Transfer factor was 72% predicted.

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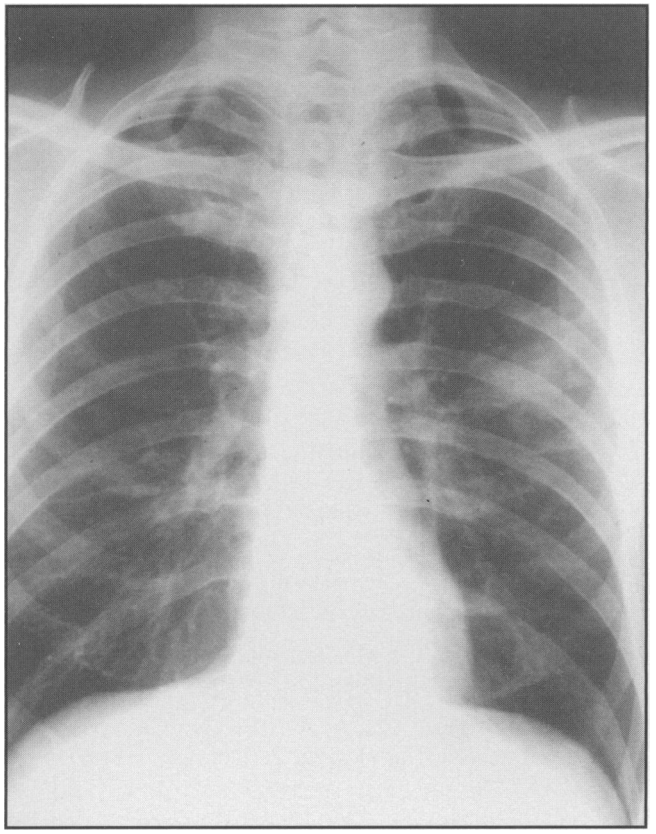

Fig 1. Chest radiograph showing obvious airspace consolidation in the left midzone, with a smaller area in the right midzone and possibly at the right apex.

Chest radiograph showed peripheral ill-defined streaky infiltrates with septal thickening. CT chest showed bilateral peripheral pulmonary infiltrates, more prominent on the right. C reactive protein was 31. Eosinophil count was 15.0 x 10^9/l (69% eosinophilia). Platelet count was normal. IgE was 1003 IU/1. pANCA was 1:20 however myeloperoxidase (MPO) was negative indicating this was a false positive and not significant. The remainder of the vasculitic and autoimmune screen was normal. Skin biopsy showed evidence of necrotising small vessel vasculitis with eosinophilic infiltration.

Nerve conduction studies showed that peripheral nerve conduction was within normal limits. Transthoracic echocardiographic examination was normal. Direct urine microscopy showed an inactive sediment. Renal function was normal. Churg-Strauss syndrome was diagnosed and the patient was commenced on prednisolone 60 mg daily. Within one week he was clinically well, his symptoms and the vasculitic rash had resolved completely. C reactive protein was 5, eosinophil count was 0.1 x 10^9/l (1% eosinophilia) and chest radiograph was normal.

DISCUSSION

Churg-Strauss syndrome is an eosinophilic necrotising vasculitis. The presence of four of six defined criteria (asthma, paranasal sinus abnormalities, mononeuropathy or polyneuropathy, non-fixed radiographic pulmonary infiltrates, eosinophilia > 10% and biopsy containing blood vessels with extravascular eosinophils) establishes the diagnosis with a sensitivity of 85% and a specificity of 99.7%.[1] The differential diagnosis of hypereosinophilia and systemic vasculitis is beyond the scope of this case report; however this has previously been comprehensively reviewed.[2] Recent reports have described Churg-Strauss syndrome in asthma patients being treated with leukotriene receptor antagonists. The Committee on Safety of Medicines has received 63 reports of Churg-Strauss syndrome since 1963, 59 since the start of 1998. Of these, 90% were associated with drugs used to treat asthma, mainly leukotriene receptor antagonists.[3] It has been suggested that these patients had formes fruste Churg-Strauss syndrome which was unmasked following

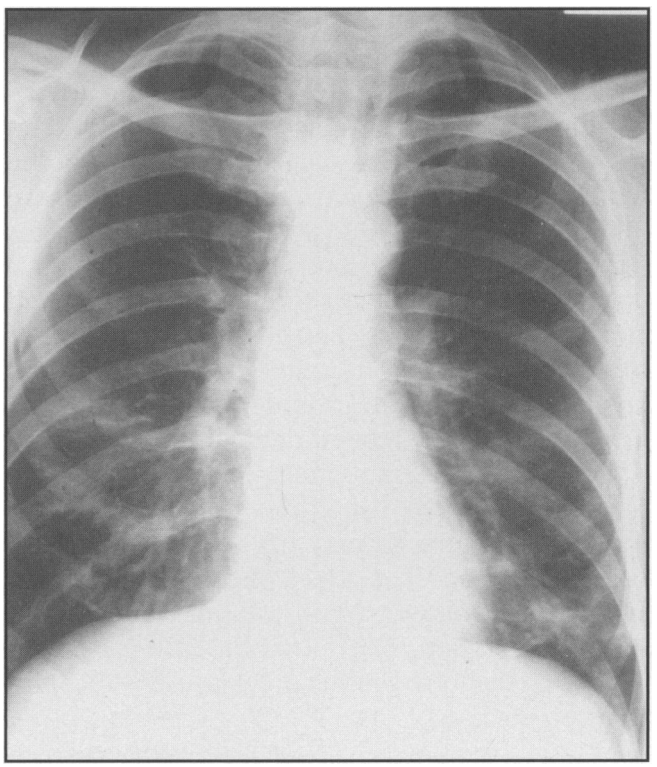

Fig 2. Chest radiograph showing resolution of the previous areas of consolidation but new consolidation at the left base and right mid zone.

corticosteroid withdrawal facilitated by the use of the leukotriene receptor antagonists .[4] Churg-Strauss syndrome has also been reported in patients who have not received maintenance systemic corticosteroids.[4-9] However in all but one of these reports the patients had received recent intermittent systemic corticosteroids.[9]

It is likely that this patient already had Churg-Strauss syndrome at the time of initial presentation. At that stage three of the four required American College of Rheumatology criteria for the diagnosis of Churg-Strauss syndrome were present (rhinitis, asthma and pulmonary infiltrates) but the eosinophil count was not measured. The skin vasculitis appeared following the introduction of zafirlukast. Whilst the onset of the skin vasculitis could have been coincidental, the clear temporal relationship would also be consistent with the hypothesis that leukotriene receptor antagonists accelerated the disease process. This patient had not previously received any systemic corticosteroids. Furthermore the dose of inhaled and intranasal corticosteroid used is lower than that recognised to have a systemic effect. The mechanism by which leukotriene receptor antagonists cause Churg-Strauss syndrome is uncertain. It has been postulated that leukotriene receptor blockade which does not inhibit the eosinophilic chemotactant, leukotriene B4, may result in a state of eosinophilic activation leading to the development of Churg-Strauss syndrome. However, the fact that Churg-Strauss syndrome has been reported with the 5-lipoxygtrase inhibitors, which also block leukotriene B4, makes this possibility less likely. Alternatively it is possible Churg-Strauss syndrome may represent an idiosyncratic or hypersensitivity reaction to leukotriene receptor antagonist exposure. In conclusion this report provides evidence that the use of leukotriene receptor antagonists may play a part in accelerating Churg-Strauss syndrome. This case report illustrates that leukotriene receptor antagonists may trigger Churg-Strauss syndrome, and that this condition should be suspected in patients with asthma who develop marked eosinophilia or other vasculitic features following the introduction of leukotriene receptor antagonists.

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