Introduction

Antileukotriene drugs are therapeutic agents with known efficacy in mild to moderate asthma [1]. Zafirlukast is a potent and selective cysteinyl leukotriene type 1 receptor (CysLT1) antagonist which is being used for the treatment of chronic asthma, allergic rhinitis and nasal polyps [2,3].

Churg-Strauss syndrome, a systemic vasculitis characterised by necrotizing angiitis with eosinophilic infiltration, has been described in small numbers of patients receiving CysLT1 antagonists. It is unclear if this effect is directly related to the administration of antileukotrienes or if the corticosteroid-sparing effect of antileukotrienes unmask a Churg-Strauss syndrome [4]. We report a case of a patient with Samter syndrome who developed hypereosinophilia while receiving zafirlukast therapy.

Case report

A 63-year-old man with a history of more than 20 years of severe asthma associated with nasal polyps and nonsteroidal antiinflammatory drug (NSAID) intolerance received treatment with inhaled salmeterol, fluticasone and tiotropium as well as nasal budesonide. Despite good adherence to therapy, he developed frequent exacerbations of asthma and rhinitis, which were treated with short courses of 30 mg of either prednisone or deflazacort by oral route. Zafirlukast was introduced in December 2003 to reduce the need for corticosteroid therapy and achieve greater control of asthma. After eight weeks of treatment with 20 mg of zafirlukast twice a day, the patient complained of malaise, anorexia, weight loss of 3 kg, impotence and mesogastric abdominal pain elicited by food ingestion which did not improve with the addition of antacid and anticholinergic drugs. Several years before he had suffered from a transient episode of impotence which was attributed to the administration of montelukast. On physical examination, there were no cutaneous lesions, arthritis or neuropathy. Laboratory findings included a leukocyte count: 34.7 x 10^9 cells/L with 69% eosinophils, erythrocyte sedimentation rate: 39 mm/h, C reactive protein level: 35.8 µg/ml, rheumathoid factor: 116.1 IU/
The result of a test for perinuclear antineutrophil cytoplasmatic antibodies (p-ANCA) was negative. Eosinophil cationic protein (ECP) reached 92 μg/L. A specimen of arterial blood, drawn while the patient was breathing room air, showed pH: 7.46, PaO2 78.4 mmHg and PaCO2 34.9 mmHg. Parasites in stools and sputum were not observed. A chest radiography, an electrocardiogram, an echocardiogram and an abdominal echography were normal. A bone marrow smear showed eosinophilia of 44%.

Zafirlukast therapy was discontinued and treatment with intravenous methylprednisolone (20 mg three times a day) was prescribed. The abdominal pain and constitutional syndrome resolved rapidly and the patient was released from the hospital after six days. Eosinophil counts returned to baseline values after five days. The patient has been followed for 18 months. He controls the symptomatology of asthma and nasal polyps with inhaled fluticasone, salmeterol and tiotropium and nasal budesonide at the same doses as before the above described episode.

Discussion

Churg-Strauss syndrome is characterised by asthma, mononeuropathy or polyneuropathy, paranasal sinus abnormalities, pulmonary infiltrates, eosinophilia and a biopsy specimen containing a blood vessel with extravascular eosinophils. According to the American College of Rheumatology [5], four criteria are necessary for diagnosis. In our case, the patient’s diagnosis was chronic asthma associated with nasal polyps and NSAID intolerance. This condition is known as the Samter syndrome [6], and is usually associated with high counts of eosinophils [7]. Our patient showed an eosinophil baseline count of 800/mm3 during treatment with inhaled bronchodilators and corticosteroids. The administration of zafirlukast was clearly associated with an increase in eosinophil counts without the appearance of other signs or symptoms of necrotizing vasculitis. In these circumstances, he did not fulfil the criteria to be diagnosed with Churg-Strauss syndrome. Neither did the patient fulfil criteria for hypereosinophilic syndrome.

The episode could not be attributed to the administration of lower inhaled and systemic asthma therapy, as has been proposed by a recent NIH workshop on the possible relationship between leukotriene antagonists and Churg-Strauss syndrome [8].

The patient complained of impotence related to the administration of zafirlukast and montelukast. There are no reports of this adverse effect related to the use of antileukotrienes and nor has this symptom been described as a part of Churg-Strauss syndrome.

Carriers of the variant C allele of LTC4 synthase show a better response to leukotriene receptor antagonists [9, 10]. In order to detect the potential response to antileukotriene drugs in asthma, future pharmacogenomic studies are necessary.

References