Sulfasalazine has been reported to induce pulmonary eosinophilia and hypersensitivity with symptoms of dyspnea and fever. We present the results of bronchoalveolar lavage in a patient with acute sulfasalazine-induced hypersensitivity pneumonitis. The lavage specimen showed a significant influx of eosinophils.

Sulfasalazine is a chemical combination of 5-aminosalicylic acid, a salicylate analogue, and sulfapyridine, a sulfonamide, linked by an azo bond. It is primarily used as an oral agent in the treatment of inflammatory bowel disease. Adverse reactions with sulfasalazine are common, occurring in approximately 20 percent of patients taking the drug. Pulmonary hypersensitivity reactions, however, seldom have been reported. We describe a case of sulfasalazine-induced hypersensitivity pneumonitis in a patient taking the drug for inflammatory bowel disease associated with reactive arthritis. Bronchoalveolar lavage (BAL) demonstrated a marked increase in the percentage of eosinophils and a slight increase in the number of lymphocytes.

Case Report

A 40-year-old non-smoking man had a three-year history of arthralgia of the left knee joint. Rheumatologic investigations, including arthroscopy and ileocoloscopy with removal of specimens for biopsy, revealed the diagnosis of a reactive arthritis with chronic synovitis associated with the bowel disease. He never experienced, however, any gastrointestinal complaints. At that time, the chest radiograph was normal. Treatment with sulfasalazine was initiated in a dosage of 500 mg twice a day for four days and subsequently increased to 1,000 mg twice a day. Ten days later, the patient developed malaise, lethargy, loss of energy and anorexia, followed by an irritating dry cough, dyspnea on exertion, chest tightness, night sweats and fever up to 38.5°C. On admission, his body temperature was 37.9°C, the pulse was regular at 88 beats/min, and the blood pressure was 115/70 mm Hg. There were no abnormal auscultatory findings on examination of the chest.

Laboratory values included a white blood cell count of 11.300/μm, with 51 percent neutrophils, 31 percent lymphocytes, 13 percent monocytes and 5 percent eosinophils. The total eosinophil count was 916/μm (normally 50 to 250/μm). The erythrocyte sedimentation rate (ESR) was 38 mm in 1 h. Skin prick tests with the most common inhalant allergens were positive for Dermatophagoides pteronyssinus and Alternaria tenuis. Total IgE was 11 IU/ml. No precipitating antibodies to common antigens causing hypersensitivity pneumonitis could be demonstrated. There was no rise in antibody titer to common respiratory viruses. Boentengrams of the chest showed bilateral acinar infiltrates, principally in both lung apices, bilateral pleural reaction with obliteration of the costodiaphragmatic sinus on both sides, and accentuation of interstitial markings with Kerley-B lines.

Pulmonary function tests revealed a moderate restrictive reduction in lung volumes with a single-breath carbon monoxide diffusing capacity of 82 percent of predicted value. Capillary blood gas analysis revealed a pH of 7.36, a PO2 of 58 mm Hg and a PCO2 of 40 mm Hg. Fiberoptic bronchoscopy, performed on the day of admission showed moderate bronchial inflammation. Bronchoalveolar lavage (five times a 50-ml aliquot of sterile saline solution) was performed in the right middle lobe. The total cell count was 2.56 × 107 cells/100 ml lavage fluid. Differential cell analysis of the pooled liquid from the last four washings revealed 37 percent eosinophils, 38 percent alveolar macrophages, 10 percent neutrophils, 1 percent basophils and 14 percent lymphocytes (88 percent T-lymphocytes, 5 percent B-lymphocytes, and an OKT4:OKT8 ratio of 2.32).

Discontinuation of the sulfasalazine therapy promptly was followed by a marked symptomatic improvement and a disappearance of all radiographic and functional abnormalities within one week. The eosinophil count remained elevated at 430/μm.

Discussion

Although sulfasalazine treatment commonly is used in inflammatory bowel disease, and a high incidence of non-respiratory side effects is observed, only ten well documented cases of pulmonary injury due to sulfasalazine treatment have been reported. Fibrosing alveolitis is the most severe pulmonary complication and has been reported twice, including one patient with a fatal outcome, the other also showing bronchiolitis obliterans.

Hypersensitivity pneumonitis is the most common pulmonary
nary injury induced by sulfasalazine, eight cases being reported in the English-language literature. 11 The onset usually is acute and unrelated to cumulative dose of the drug or to duration of therapy. 12 Symptoms of the syndrome include dyspnea, cough, chest tightness and chest pain, night sweats and fever, frequently without significant auscultatory chest findings. 13,14 Usually there is peripheral eosinophilia and an elevated ESR. 15 Chest radiography reveals bilateral patchy acinar or reticular infiltrates, mainly peripheral. 16 The most common abnormality of pulmonary function is an obstructive pattern with decreased carbon monoxide transfer factor. 17 Challenge tests demonstrated that the sulfapyridine portion of sulfasalazine causes the hypersensitivity reaction. 18 The prognosis of sulfasalazine-induced hypersensitivity pneumonitis is generally excellent with complete recovery on discontinuation of the drug. 19 Corticosteroids may hasten the recovery but are seldom indicated.

The only published report of transbronchial lung biopsy performed in a patient with sulfasalazine-induced hypersensitivity pneumonitis showed interstitial pneumonitis and slight fibrosis but no tissue eosinophilia. 8

To our knowledge, our study is the first report of bronchoalveolar lavage in sulfasalazine-induced hypersensitivity pneumonitis. Bronchoalveolar lavage analysis showed a marked influx of eosinophils and a moderate increase in the numbers of the lymphocytes and basophils. These findings support an immunologic pathogenesis of the disease, rather than direct toxicity of the drug. A predominantly eosinophilic pattern of BAL fluid points to eosinophilic lung disease. However, the exact immunologic mechanisms by which sulfasalazine induces eosinophilic pneumonia remain unknown. The association of the acute respiratory disease with the intake of sulfasalazine and the complete disappearance of all respiratory abnormalities after cessation of the drug provides evidence that the eosinophilic lung infiltrate in our patient should be regarded as a hypersensitivity reaction to sulfasalazine.

REFERENCES


**Flecainide-Induced Sustained Ventricular Tachycardia Successfully Treated with Lidocaine**

Jerry L. Bauman, Pharm. D.; Jose Gallastegui, M.D.; Seth R. Tanenbaum, M.D.; and Robert J. Hariman, M.D.

A 69-year-old man had new sustained ventricular tachycardia caused by flecainide which promptly responded to intravenous lidocaine therapy. Discontinuation of the lidocaine infusion resulted in the reappearance of ventricular tachycardia which again immediately terminated after lidocaine was given. In this case, lidocaine effectively reversed the proarrhythmic effects of flecainide.

In addition to successfully suppressing arrhythmogenic foci, antiarrhythmic drugs may also paradoxically precipitate new rhythm disturbances or worsen existing arrhythmias. 15,16 Indeed, antiarrhythmic agents have been causally related to out-of-hospital cardiac arrest in patients who do not have underlying sustained ventricular tachycardia or ventricular fibrillation. 17 Flecainide is a new type IC antiarrhythmic agent recently approved for the treatment of serious ventricular arrhythmias. The proarrhythmic potential of flecainide has received considerable attention in the medical literature. 18 However, there is little information regarding the therapeutic approach to patients with flecainide-induced arrhythmias. We report a case of new sustained ventricular tachycardia related to flecainide therapy which terminated immediately after intravenous administration of lidocaine.

**CASE REPORT**

A 69-year-old black man was admitted to the University of Illinois Hospital for numerous episodes of palpitations associated with mild dizziness. An ambulatory Holter recording prior to admission showed sinus bradycardia with preexcited ventricular complexes and occasional episodes of a slightly irregular rhythm with wide QRS complexes (rate 120 bpm, 9 beats maximum).

On admission, physical examination was not remarkable. Blood pressure was 146/90 mm Hg. Laboratory examination revealed normal findings except for a blood urea nitrogen value of 31 mg/dl and a serum creatinine concentration of 2.2 mg/dl. Chest roentgenogram revealed a normal heart size. Ejection fraction by gated nuclear angiography was 51 percent. Twelve-lead ECG showed sinus bradycardia (rate 56 bpm) with evidence of ventricular preexcitation.

Electrocardiographic monitoring for 48 hours revealed occasional premature ventricular complexes and several episodes of a self-terminating wide QRS tachycardia (four to nine beats) (Fig 1A). Intravenous and oral procainamide failed to suppress recurrences of this rhythm, and the patient was subsequently taken to the electrophysiology laboratory.

During this study, nonsustained ventricular tachycardia was confirmed as the cause of the wide QRS tachycardia (Fig 2A) and the effective refractory period of the accessory atrioventricular pathway was determined to be 200 ms.

Oral flecainide, 100 mg twice daily, was started (48 hours after the

*From the Departments of Pharmacy Practice and Medicine, Section of Cardiology, University of Illinois at Chicago.

Reprint requests: Dr. Bauman, University of Illinois College of Pharmacy, 933 Wood Street, Chicago, 60612

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