

Drug-induced lupus in a child after treatment with zafirlukast (Accolate)

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The incidence of drug-induced lupus (DIL) in the United States is 15,000 to 20,000 new cases per year, although this probably represents an underestimate. The common causes are procainamide and hydralazine, with at least 50 other drugs known to be associated. Symptoms of DIL may appear gradually, after institution of drug therapy, or with rapid onset. Here we report a child in whom DIL developed while she was receiving treatment with zafirlukast (Accolate) for mild asthma.

This 9-year-old white girl was diagnosed with asthma at 7 years of age. She was treated with inhaled bronchodilators until symptoms worsened. In October 1997, she began receiving zafirlukast at a dose of 20 mg twice daily. Her respiratory symptoms improved, but within 8 days she began having low-grade fevers (temperature, 99.6°F) associated with joint pain, muscle pain, fatigue, mouth sores, and headache but without frank joint swelling, skin rash, or cardiac or renal symptoms. She was evaluated serologically for collagen vascular disease, and concerns were raised about DIL. Zafirlukast was discontinued in January 1997 after 2 months of therapy. The low-grade fevers, myalgias, and fatigue gradually resolved, with only mild intermittent headache noted in March 1998, 2 months after discontinuation of zafirlukast.

At presentation in December 1997, results of physical examination were unremarkable except for tenderness to palpation of the deltoids and quadriceps bilaterally. Muscle strength was 5/5 in all muscle groups (per Medical Research Council of the UK grading, 5-normal power). There was no rash, synovitis, joint limitation of motion, or pain on range of motion.

Laboratory evaluation revealed a white blood cell count of 5200/mL with 1.7% eosinophils, hemoglobin of 14.9 g/dL, platelet count of 458,000/mL, urine protein of

Abbreviation used

DIL: Drug-induced lupus

2+, total bilirubin of 1.4 mg/dL, aspartate aminotransferase of 37 IU/L, normal creatine kinase and lactate dehydrogenase, and negative direct Coombs. The antinuclear antibody was positive at 1:1280, with a speckled and homogenous pattern. An unusual staining pattern was noted, with staining of late, but not early, mitotic figures. The ANA profile (anti-DNA, Smith, ribonuclear protein, Sjögren's syndrome A, and Sjögren's syndrome B antibodies) was negative. Antihistone antibodies were positive. In addition, IgG antibodies to H2A-H2B histone-DNA complex were positive at a value of 8 EIA units (negative, <5). In February 1998, with almost complete resolution of signs and symptoms, urinalysis showed only trace protein, and antibodies to H2A-H2B histone complex were negative. Urinary leukotrienes measured during the active phase of disease were within normal limits.

This child's initial symptoms of myalgia, arthralgia, and low-grade fever are typical of DIL.¹ Reactivity to H2A-H2B histone complex is found in more than 90% of patients with DIL caused by procainamide, in about 50% of patients with DIL caused by quinidine or hydralazine, and has been detected in individual patients with DIL caused by penicillamine, isoniazid, acebutolol, methyl-dopa, sulfasalazine, and ophthalmic timolol.² In patients with idiopathic lupus antihistone antibodies, the frequency of IgG antibodies to the H2A-H2B histone complex is 15% to 20%. However, the probability of coincidental onset of idiopathic lupus in this patient is doubtful because of her young age and lack of persistent arthralgias/arthritis, cytopenia, nephritis, or the rash seen in a majority of children at presentation.³ Exacerbation of preexisting lupus is also unlikely without supportive past medical history, with family history negative for lupus or other autoimmune disease, and with almost complete resolution of signs, symptoms, and abnormal laboratory parameters by 2 months after discontinuation of zafirlukast in the absence of therapy.

To the best of our knowledge, this is the first report of an association between zafirlukast, a potent leukotriene antagonist, and DIL, although zafirlukast has been associated with a clinical syndrome resembling Churg-Strauss vasculitis.⁴ It should be noted that zafirlukast is

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not approved for use in children less than 12 years of age, and dosage recommendations are not available.

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