

Cefuroxime-Induced Lupus

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Drug-induced lupus erythematosus (DILE) is a syndrome that shares symptoms and laboratory characteristics with idiopathic systemic lupus erythematosus. Recognition of DILE is important because it usually reverts within a few weeks after stopping the offending drug. Antibiotics are uncommonly associated with DILE, and cefuroxime has never been incriminated as a cause. We present herein the first case of DILE induced by cefuroxime. Although this is the first report of cefuroxime-induced DILE, we should be aware of this occurrence.

Key words: drugs ■ lupus

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INTRODUCTION

Cefuroxime is a broad-spectrum, β -lactamase-stable cephalosporin that kills a wide variety of bacteria that cause most commonly occurring infections. It is used to treat infections of the upper and lower airways, ears, nose, throat, skin and soft tissue. It may also be used to treat urinary tract infections, certain sexually transmitted infections and Lyme disease.¹ Like many other medicines, cefuroxime may cause some side effects. The most commonly reported side effects are dry mouth, headache, abdominal pain and mild diarrhea. If they occur, they are most likely to be mild and temporary; however, some may be serious and need medical attention.²

In this report, we present a case that developed a lupus erythematosus (LE)-like reaction in the course of cefuroxime axetil treatment. This association has not been reported in any previously published report.

CASE REPORT

A 54-year-old woman was admitted to the chest outpatient clinic with fever, cough, dyspnea and exhaustion for 10 days. She was commenced on cefuroxime axetil (1 g/day per oral in two divided doses) when a diagnosis

of pneumonia was entertained. After cefuroxime therapy, complaints of the patient were relieved. On the tenth day of cefuroxime treatment, the patient was readmitted to the chest outpatient clinic with malaise, widespread arthralgia and myalgia. She also had bilateral conjunctival hemorrhage and malar rash. Then she was referred to our general internal medicine outpatient clinic and hospitalized.

On physical examination, her body temperature was 38.5°C (101.3°F), heart rate was 73 beats/min and arterial blood pressure was 110/80 mmHg. Bilateral palpebral and conjunctival edema was observed. Skin examination revealed pruritic, erythematous, macular skin rashes, distributed in a generalized fashion over her body, including her palms and soles. She had arthralgia but did not have any sign of arthritis (e.g., hyperemia, warmth or swelling) in any joint. Other physical findings were normal.

The white blood cell count was 15,000/mm³, with 94% polymorphonuclear leukocytes (12% band forms) and 6% lymphocytes at the first admission to the chest clinic. Laboratory test results were as follows on admission to our clinic: white blood cell count 6,200 with 58% polymorphonuclear leukocytes and 38% lymphocytes, hematocrit 39.7%, platelet count 118,000/mm³, blood urea nitrogen 21 mg/dL, serum creatinine 0.6 mg/dL, glucose 98 mg/dL, alanine amino transferase 24 IU/L and aspartate amino transferase 28 IU/L. The prothrombin and partial-thromboplastin times were normal, and erythrocyte sedimentation rate (ESR) was 80 mm/h. Urine analysis and other biochemical parameters were normal. The antinuclear antibody (ANA) test was positive (1/100 titer) with a homogeneous pattern, and anti-histone antibody was positive. Antibody tests for double-stranded DNA (ds-DNA), extractable nuclear antigens and rheumatoid factor (RF) were negative.

Cefuroxime was suspected as the etiologic agent of the patient's skin and mucosal reaction, and it was stopped. We did not give any other antibiotic, as the patient's pneumonia relieved. The patient's complaints persisted after three days from cessation of cefuroxime. Therefore, 1 mg/kg/day methyl prednisolone was started. Eruptions were noted to fade and arthralgia mostly

resolved on the third day of steroid therapy. The dose of steroid therapy was decreased gradually. All clinical findings subsided completely within 10 days, and steroid therapy was eventually discontinued at the end of two weeks. She remained asymptomatic, and ESR decreased to 18 mm/h six months later.

DISCUSSION

LE is an autoimmune disease of the connective tissue, whose specific causes are unknown. It is estimated that up to 10% of the cases with systemic LE are DILE.³ In the last 40 years, many drugs and other chemical agents have been reported to cause a syndrome similar to systemic LE (SLE). Some drugs such as procainamide and hydralazine have a high propensity to cause DILE. Other drugs such as betaxolol, acebutolol, propylthiouracil valproate and sulfasalazine are the subject of case reports. Some antibiotics like minocycline, vancomycin and nafcillin were also reported as a cause of DILE.^{5,8-10,12,13}

There is no consensus regarding the diagnostic criteria, but some authors have suggested that the following be used: adequate exposure to a medication, no previous history of idiopathic SLE, detection of positivity of autoantibodies with ≥1 clinical sign of SLE, and rapid improvement in clinical and serological markers after withdrawal of suspicious medication.^{5,6,9}

The clinical and laboratory manifestations of DILE are similar to those of mild form of idiopathic SLE.⁴ Clinical manifestations of DILE include symmetrical, nondeforming arthralgias, myalgias, serositis, fever and weight loss. Pulmonary involvement, with pleuritis, pleural effusion or pulmonary infiltration, can also be seen. Pericardial involvement is less common. Hepatomegaly, splenomegaly, renal involvement and neuropsychiatric disorders are also unusual in DILE. The typical manifestations for SLE—butterfly rash, alopecia, discoid lesions and mucosal ulcers—are usually absent in DILE.⁶⁻⁸ Recognition of DILE is important because it usually reverts within a few weeks after stopping the offending drug.⁴

Laboratory findings usually include a positive ANA, negative antibodies to ds-DNA and positive tests for antihistone antibodies. Hypocomplementemia is not seen in DILE. Mild anemia and thrombocytopenia can be seen, as well as elevated ESR and C-reactive protein levels.^{9,11,14}

The fundamentals of treatment of DILE are discontinuation of the offending medication and appropriate clinical management of symptoms. Most clinical signs and symptoms are self-limited and resolve within several weeks of cessation of medication. Nonsteroidal anti-inflammatory drugs can be used for milder symptoms. However, steroid therapy may occasionally be necessary for severe symptoms. If there is end-organ damage, it should be treated as in idiopathic SLE.

Our patient is the first reported case of cefuroxime-induced lupus. Her symptoms had a rapid onset with the beginning of cefuroxime treatment and resolved after the discontinuation of the drug as in previously reported cases of DILE.^{7,12} She had neither central nervous system nor renal involvement. The elevated ESR and ANA titers, as well as the presence of antihistone antibodies and the absence of anti-ds-DNA antibodies, helped us differentiate this diagnosis from that of idiopathic SLE. Six months after discontinuation of cefuroxime, the sedimentation rate fell to 18 mm/h and ANA to negative titers.

In conclusion, we present the first drug-induced LE case associated with cefuroxime. Clinicians should be aware of DILE as a possible complication of cefuroxime therapy, and patients with stigmata of LE should be questioned for cefuroxime therapy.

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