ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, May 1990, p. 904–905
0066-4804/90/050904-02$02.00/0

Vol. 34, No. 5

Serum Sickness-Like Illness Associated with Ciprofloxacin

THOMAS G. SLAMA

Infectious Disease Division, St. Vincent Hospital and Health Care Center, Indiana University School of Medicine, Indianapolis, Indiana 46260

Received 27 March 1989/Accepted 16 February 1990

Serum sickness is a systemic hypersensitivity reaction initially reported in children receiving horse serum. Drugs such as penicillins, cephalosporins, and sulfonamides are now noted to be the most common etiologic agents of serum sickness-like reactions. This case report describes a serum sickness-like reaction temporally related to ciprofloxacin, a previously unreported adverse effect of this drug or any of the other quinolones.

Serum sickness is a systemic hypersensitivity reaction initially described in children receiving horse serum containing diptheria antitoxin. These children presented with a clinical syndrome of fever, lymphadenopathy, cutaneous eruptions, arthralgias, and occasionally proteinuria. Since the initial description of serum sickness, the illness has been described following administration of horse antithymocyte globulin in bone marrow transplant patients (6).

Several drugs, including penicillins, cephalosporins, sulfonamides, tetracycline, isoniazid, thyroid preparations, barbiturates, phenytoin, nonsteroidal anti-inflammatory drugs, salicylates, captopril, propranolol, and hydralazine, have been reported to cause a clinical syndrome which is indistinguishable from true serum sickness (1, 7). These reports in both adults and children describe a clinical syndrome nearly identical to the originally reported serum sickness.

This case report describes a serum sickness-like illness temporally related to ciprofloxacin, to date an unreported adverse reaction to this fluoroquinolone or the other fluoroquinolones (4).

A 56-year-old male with a medical history of only degenerative joint disease presented to an immediate-care facility with coryza, myalgias, and low-grade fever (never over 100°F [37.8°C]) that had persisted for approximately 5 days despite acetaminophen (Tylenol) and non-aspirin-containing over-the-counter cold remedies. His physical examination was significant for a recorded oral temperature of 99°F (ca. 37.2°C) and no arthritis, rash, pharyngitis, or mucous membrane lesions. No laboratory or radiographic diagnostic studies were done, and he was given a prescription for ciprofloxacin (500 mg) to be taken twice daily.

Over the next 4 days, he noted no improvement in his original symptoms and also noted polyarthralgias despite continuing to take the ciprofloxacin as directed. On day 6 of ciprofloxacin therapy, his illness accelerated and was complicated by a fever of 104°F (40°C), a generalized urticarial eruption, and severe polyarthralgias and myalgias with definite joint effusions noted in the wrists, ankles, and knees bilaterally. Because of these worsening symptoms, he voluntarily stopped taking the ciprofloxacin on day 7. Because his fever, rash, polyarthralgias, and myalgias persisted and his arthritis worsened, he was admitted to the hospital 8 days after beginning the ciprofloxacin.

On admission to the hospital, his physical examination was significant for an oral temperature of 104°F, a generalized urticarial eruption, a soft II/VI systolic ejection murmur heard best at the pulmonic area, tender mobile anterior and posterior cervical and axillary lymphadenopathy, and massive effusions in the elbow, wrist, knee, and ankle joints bilaterally. There were no neurologic deficits, hepatosplenomegaly, vasculitic lesions, or peripheral manifestations of connective tissue disease or endocarditis. His myalgias were so severe that changing positions in bed was nearly impossible because of the pain.

Laboratory evaluations revealed a hemoglobin level of 12.3 g/dl, a hematocrit of 36%, and a total leukocyte count of 5,300/mm^3, including 58% polymorphonuclear leukocytes, 26% bands, 12% lymphocytes, and 4% monocytes. Two sets of blood cultures were sterile. The Westergen sedimentation rate was 69 mm/h. Urinalysis was remarkable only for 1+ proteinuria and 2+ ketones. Rheumatoid screen, hepatitis B surface antigen and antibody, hepatitis A antibody, or fungal immune diffusion tests for aspergilli, histoplasmosis, coccidioidomycosis, and blastomycosis were negative or nonreactive. Antinuclear antibody was reactive in a speckled pattern at 1:80. Serum CH50, C3, and C4 levels were normal.

Transient elevations of liver function tests have been reported with fluoroquinolones and were seen in this case, as measured by an alkaline phosphatase level of 128 to 178 mU/ml (normal level, 30 to 115 mU/ml), a lactic dehydrogenase level of 342 to 390 mU/ml (normal level, 60 to 200 mU/ml), a serum glutamic oxalacetic transaminase level of 67 to 190 mU/ml (normal level, 0 to 40 mU/ml), and a serum glutamic pyruvic transaminase level of 102 to 307 mU/ml (normal level, 0 to 45 mU/ml). All other blood chemistries measured were normal.

Because of the profound arthritis, diagnostic arthrocenteses were performed on the left knee on hospital days 1 and 2. The joint fluid was yellow and contained 15 to 80 erythrocytes per mm^3 and 23 to 500 mononuclear leukocytes per mm^3. Joint fluid glucose levels varied between 88 and 133 mg/dl, with a corresponding blood glucose level of 158 to 179 mg/dl. Examination for crystals was negative on both occasions. Gram stain analysis did not reveal any microorganisms, and subsequent cultures were all sterile. These results were considered suggestive of a nonspecific reactive arthritis.

During the initial day of hospitalization, the patient was started on vancomycin and tobramycin for suspected bacteremia. Forty-eight hours into the hospitalization, when blood and joint aspiration cultures were known to be sterile, none of the other diagnostic studies were suggestive of a bacterial infection, and he had shown no clinical improvement, all antibiotics were discontinued and therapy with hydrocortisone (250 mg given intravenously every 6 h) was started.

Within 24 h of the institution of steroid therapy, the patient became afebrile and noted a marked resolution of his myalgias, arthritis, lymphadenopathy, and rash. Two days later, the steroid therapy was converted to an oral regimen and rapidly tapered over the next 7 days without any recurrence of myalgias, lymphadenopathy, arthritis, or rash. At the same time that steroid therapy was discontinued, the patient returned to work and remains asymptomatic 5 months later.

Although true serum sickness has been reported for years, serum sickness-like reactions are now seen more frequently following therapy with a variety of medications and are most frequently noted with the beta-lactam antibiotics (9; National Disease and Therapeutics Index [Database], 1985).

This case report describes the temporal relationship between a serum sickness-like illness in an adult and ciprofloxacin. The onset of clinical signs and symptoms correlated only with ciprofloxacin administration. No other medications reported to cause this syndrome were used, and all diagnostic studies failed to reveal any other cause for the illness.

To date, only norfloxacin and ciprofloxacin are available for use in the United States, although clinical investigations are ongoing with many other fluoroquinolones, including ofloxacin, enoxacin, fleroxacin, and perfloxacin.

Although a series of 15 cases of anaphylactoid reactions (3) and 3 cases of acute renal failure (5) have recently been reported to be associated with ciprofloxacin, the most frequent adverse reactions to the fluoroquinolones have been gastrointestinal and cutaneous, with no cases of serum sickness-like reactions reported to date (2, 4, 8).

Although uncommon, serum sickness-like reactions must now be considered a possible adverse reaction to ciprofloxacin and watched for with the other fluoroquinolones.

LITERATURE CITED

1. **Alanis, A., and A. V. Weinstein.** 1983. Adverse reactions associated with the use of oral penicillins and cephalosporins. Med. Clin. North Am. **67**:113–129.
2. **Choe, V., B. Rothchild, and L. Laitman.** 1989. Ciprofloxacin induced vasculitis. N. Engl. J. Med. **320**:257–258.
3. **Davis, H., E. McGoodwin, and T. Reed.** 1989. Anaphylactoid reactions reported after treatment with ciprofloxacin. Ann. Intern. Med. **111**:1041–1043.
4. **Hooper, D. C., and J. S. Wolfson.** 1985. The fluoroquinolones: pharmacology, clinical uses, and toxicities in humans. Antimicrob. Agents Chemother. **28**:716–721.
5. **Hootkins, R., A. Z. Fenves, and M. K. Stephens.** 1989. Acute renal failure secondary to oral ciprofloxacin therapy: a presentation of three cases and a review of the literature. Clin. Nephrol. **32**:75–78.
6. **Lawley, T. J., L. Bielory, P. Gascon, K. Yancey, N. Young, and M. Frank.** 1984. A prospective clinical and immunologic analysis of patients with serum sickness. N. Engl. J. Med. **311**:1407–1413.
7. **Lin, R. Y.** 1986. Serum sickness syndrome. Am. Fam. Physician **157**:157–162.
8. **Neu, H.** 1989. New oral and parenteral quinolones. Am. J. Med. **87**(Suppl. 5A):283–287.
9. **Platt, R., M. W. Dreis, D. L. Kennedy, and J. N. Kuritsky.** 1988. Serum sickness-like reactions to amoxicillin, cefaclor, cephalexin, and trimethoprim-sulfamethoxazole. J. Infect. Dis. **158**: 474–477.