Azithromycin Therapy for Scrub Typhus During Pregnancy

Scrub typhus (tsutsugamushi disease) is a febrile disease that is endemic in Asian-Pacific areas. Therapy with tetracycline (doxycycline) or chloramphenicol is currently recommended for the treatment of scrub typhus [1]. Ciprofloxacin therapy has been used experimentally, but its efficacy has not yet been determined [2]. However, chloramphenicol and tetracycline, which are class D drugs according to the U.S. Food and Drug Administration (FDA) Fetal Risk Summary, should not be used to treat pregnant women [3]. The use of tetracycline or ciprofloxacin is contraindicated in children. Recently, azithromycin, a new macrolide antibiotic, has been proven to be more effective than doxycycline in an in vitro assay system against doxycycline-susceptible and -resistant strains of Orientia tsutsugamushi [4]. Moreover, there is no evidence that azithromycin causes harm to the developing fetus or to children [3]. On the basis of current in vivo testing that confirms the effectiveness of azithromycin, it may be the drug of choice for the treatment of scrub typhus in pregnant women and children.

We describe two pregnant patients with scrub typhus who were treated successfully with azithromycin without complications or relapse.

A 27-year-old pregnant woman, 19 weeks’ gestation, came to our hospital for evaluation of a 7-day history of high fever and headaches. Physical examination at admission to the hospital revealed a temperature of 39.4°C, a heart rate of 132/minute, and a macular skin rash involving the entire body. An eschar was found on the right posterior thigh. Laboratory evaluation revealed the following values: peripheral WBCs, 6,760/mm³; hematocrit, 26.5%; platelets, 143,000/mm³; aspartate aminotransferase (AST), 97 IU/L (normal, 8–40 IU/L); alanine aminotransferase (ALT), 87 IU/L (normal, 5–30 IU/L). A serology for O. tsutsugamushi (by use of passive hemagglutination test) was negative at that time. On the basis of a clinical diagnosis of scrub typhus, therapy with azithromycin was initiated. On the first day 1.0 g was given, and 500 mg was given on the second and the third days. The temperature decreased on the second day of drug administration, and the patient’s condition improved. A serology for O. tsutsugamushi performed the second week after discharge revealed positive conversion (titer, 1:320; normal, <1:80).

A 37-year-old pregnant woman, 24 weeks’ gestation, was admitted to the hospital because of a 6-day history of high-grade fever and skin rash. Physical examination at admission revealed a body temperature of 39.5°C; and eschar on the right breast; and a diffuse, erythematous, macular rash involving the entire body. A serology for antibodies to O. tsutsugamushi performed on the first...
day of admission was positive (titer, 1:80). The patient was treated with azithromycin, 500 mg q.d., on the first day, and then 250 mg q.d. for 2 additional days. Defervescence occurred within one day of therapy, and she recovered without complications. A second serology could not be performed because the patient did not visit the outpatient clinic after discharge.

Telephone follow-up 1 year after hospital admission indicated that both patients gave birth to healthy babies.

To determine the therapeutic dosage for the first patient, we referred to the treatment of chlamydial infection in pregnant women for which a single, 1.0-g dose of azithromycin was used successfully [5]. However, because the optimal dosage of azithromycin for the treatment of scrub typhus has not been determined, we added 500 mg of azithromycin for 2 additional days experimentally to reduce the risk of relapse or therapeutic failure. Because the result of treatment in the first patient was satisfactory, for the second patient, we reduced the therapeutic dose to 500 mg on the first day, and to 250 mg for 2 additional days. The result of this treatment was also successful.

Although this report of two cases provides only limited information, it suggests that azithromycin can be used in pregnant patients as therapy for scrub typhus. Further study is required to assess the effectiveness of azithromycin in the treatment of scrub typhus and to determine the appropriate dosage.

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References

Gynecomastia Associated with Indinavir Therapy

The syndrome of peripheral fat wasting (lipodystrophy) with central adiposity, hyperlipidemia, and insulin resistance has been associated with the use of HIV-1 protease inhibitors [1]. To date, the mechanisms of these effects have been only hypothesized [1, 2]. Two cases of breast hypertrophy in association with abdominal swelling and thinning of the thighs in women treated with indinavir have been reported [3, 4]. A proposed hypothesis explains breast hypertrophy in women as being secondary to the default accumulation of fat by more metabolically active breast adipocytes in the presence of estrogen [1]. We describe two HIV-1-infected men with normal testosterone and estrogen levels, in whom gynecomastia developed in association with indinavir therapy.

A 49-year-old patient with AIDS was started on lamivudine, stavudine, and indinavir therapy in November 1996 (case 1). He was also taking doxepin, famotidine, amitriptyline, and acetaminophen with codeine. Two months after the initiation of antiretroviral treatment, he noted redistribution of fatty tissue, and he also noted a nontender left breast lump, not associated with redness. Findings on physical examination included a 4-cm × 5-cm, non-tender, palpable mass in the left breast, increased abdominal girth, and thin limbs; no other abnormalities were noted. His last CD4 cell count was 640 cells/mm³, and the viral load was undetectable (<500 copies/mL).

A 65-year-old, asymptomatic, HIV-infected man had no history of opportunistic infections and had not received antiretroviral therapy (case 2). His CD4 cell count was 140/mm³ and he had a viral load of 72,985 RNA copies/mL. Therapy with zidovudine, lamivudine, and indinavir was initiated in standard doses, as well as trimethoprim-sulfamethoxazole three times per week. After 4 weeks, the viral load was undetectable (<500 RNA copies/mL). After 4 months of therapy, his CD4 cell count was 210 cells/mm³. Six months after the initiation of treatment, he noted bilateral nipple tenderness and painful enlargement of his left breast. Physical examination revealed a 4-cm × 3-cm area of palpable glandular tissue in that breast. The remainder of the physical examination findings were within normal limits.

For both patients, studies for evaluation of gynecomastia included serum prolactin, serum cortisol, human chorionic gonadotropin, testosterone, estradiol, and gonadotropin (luteinizing hormone, follicle stimulating hormone) levels; all were within normal limits. Results of renal, liver, and thyroid function tests were also within normal limits. Cholesterol levels were normal, and triglyceride levels were elevated (933 mg/dL) only for the first patient.

We describe two patients who developed gynecomastia 2 and 6 months after initiation of antiretroviral treatment. No other cause was found. The gynecomastia was not severe enough to warrant discontinuation of antiretroviral therapy, and after 4 months of follow-up the condition had remained unchanged in both patients.

Before the availability of protease inhibitors, gynecomastia in association with HIV infection was described for two patients [5], and in both cases the condition resolved within 6 months; neither of the two patients was receiving any medications. Case 1 (present report) was receiving other medications with which gynecomastia has been associated [6]; however, the patient had been taking those medications for >2 years, and it was after the initiation of antiretroviral therapy that gynecomastia developed. For both of the patients we described, therapy with nucleoside analogues and protease inhibitors was started simultaneously. Despite their exten-