

CASE REPORT

Imported Relapsing Fever in European Tourists

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Two 'imported' cases of relapsing fever after a trip through Senegal are described. Two women developed a tick-borne relapsing fever after having slept outdoors on a terrace in Zinguichor, Senegal. The first patient was rapidly cured after a course of doxycycline. The second patient initially received erythromycin, but despite this treatment she developed neurological symptoms and *Borrelia* persisted in the thick-smear examination. After treatment with doxycycline she developed a Jarish-Herxheimer reaction. Treatment with doxycycline was continued and finally all symptoms disappeared within 36 hours after starting this treatment. A diagnosis of relapsing fever should be considered in all patients returning from the tropics with recurrent fever, especially if no malaria parasites are found.

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INTRODUCTION

Relapsing fever is an infectious disease caused by arthropod-borne spirochetes of the genus *Borrelia* and is clinically characterized by recurrent febrile episodes. There are two forms of relapsing fever: louse-borne and tick-borne relapsing fever. The former is caused by *B. recurrentis* and is transmitted only among humans by the human body louse. Louse-borne relapsing fever usually occurs in epidemics which are often associated with catastrophic events such as war or famine. Tick-borne relapsing fever is caused by several species of *Borrelia* and is transmitted to men by ticks of the genus *Ornithodoros*. Many rodents and small animals serve as a natural reservoir for these *Borrelia*. Tick-borne relapsing fever is endemic in disseminated foci around the world where *Ornithodoros* ticks are present (1). We recently observed 2 imported cases of tick-borne relapsing fever in Belgian women who returned from a holiday trip to Senegal.

CASE REPORTS

In July 1991, 5 Belgian women made a trip through Senegal. Two of them developed tick-borne relapsing fever. Both women had slept outdoors during a night in Zinguichor, capital of the Casamance province. They had slept on the floor of a terrace, while the others had slept inside. Three days later both developed high-grade fever (40°C).

Case 1

A 42-year-old woman, who was initially treated with quinine, continued to present fever for 3 days. Nine days later she developed a second fever episode lasting 2 days. Five days later, back in Belgium, she developed a third fever episode; a thick smear showed the presence of *Borrelia* spirochetes 0.5/field (10 × 100 mm).

Doxycycline was started and the fever disappeared. No relapse occurred during a 6-month follow-up.

Case 2

A 47-year-old woman, who was initially treated with quinine and pyrimethamine-sulfadoxine, continued to present fever for 4 days. 11 days later the fever recurred and she again received pyrimethamine-sulfadoxine. Fever persisted for another 4 days. Three days after the second episode of fever she developed diarrhea. Two days later she developed a third episode of fever lasting 2 days. Because *Campylobacter jejuni* was grown from stools and because *Borrelia* spirochetes were found in the thick smear (0.2/field) (10×100 mm), she was treated with erythromycin 500 mg QID. Initially some improvement was obtained. However, despite 12 days of erythromycin treatment she developed profound weakness, anorexia, nausea, lost 6 kg of body weight and developed diarrhea again. Four days after erythromycin had been stopped, she was hospitalized because of profound weakness, vertigo, headache and difficulty in concentrating and finding words. The day after admission she developed a fever. A thick smear still showed presence of 2 *Borrelia* spirochetes. There was a moderate degree of hyponatremia (126 mmol/l) but a stool culture failed to reveal any pathogens. Doxycycline 100 mg/day was started. One hour after the first dose she developed chills and the fever increased to 38.7°C. She became agitated and confused. The difficulty in concentrating and finding words suddenly became worse. There was no focal neurological deficit. No abnormality was shown on a CT scan of the brain. Fundoscopy was normal. 24 h later the fever abated. Minor concentration problems persisted for 48 h. Doxycycline treatment was continued for 10 days. Less than 36 h after starting the doxycycline medication she felt completely restored. There was no recurrence of fever during a 6-month follow-up period.

DISCUSSION

'Imported' relapsing fever is very uncommon in Europe (2). The 2 patients described in this report acquired their relapsing fever in Senegal. In Senegal, relapsing fever is endemic and is thought to be caused by *Borrelia crociduræ* transmitted by the tick *Alectrorobius sonrai* (formerly *Ornithodoros erraticus sonrai*) (3–6).

Individuals living in endemic areas develop a certain degree of immunity against *Borrelia* infection. This explains why the highest incidence of *Borrelia* infection is observed in children and why travellers are particularly at risk of acquiring such infections. Ticks live in crevices of walls and floors, in animal burrows and in caves. They bite at night (1). Probably our 2 patients were bitten by ticks during the night they slept outdoors. Because such bites are painless, patients are usually not aware that they have been bitten.

Relapsing fever has a variable clinical presentation. Except for the recurrent nature of the illness, there are no pathognomonic signs. The incubation time of tick-borne relapsing fever varies between 3 and 18 days. The initial attack usually starts abruptly, with shivering, and high fever. Often patients may complain of headache, backache, muscle pain, arthralgia, nausea, diarrhea, cough, dizziness and epistaxis. The spleen and liver may become enlarged and jaundice may develop. Patients may also develop neurologic manifestations such as lethargy, sometimes delirium and agitation. About 8% of the patients will develop neurological manifestations such as meningitis, focal deficits, cranial nerve palsies, hemiplegia, paraplegia, epilepsy and paresthesias. Ocular manifestations include uveitis and iridocyclitis. The initial attack averages 3 days and is generally followed by a 9-day fever-free period. During the afebrile interval often malaise and other symptoms observed during the initial attack may persist. Exceptionally an initial attack of tick-borne relapsing fever may be fulminant, leading to coma and death. After an untreated initial attack the patient may develop recurrent episodes of fever. A progressive decline in the general condition, with weakness and weight loss, occurs if adequate treatment is not given.

The periodic rise and fall of the fever in patients with *Borrelia* infection is explained by the ability of the *Borrelia* to change surface antigens when challenged by antibody (7).

Relapsing fever is often misdiagnosed as malaria. This was also the case in our patients, who were initially treated with quinine and pyrimethamine-sulfadoxine.

The diagnosis of tick-borne relapsing fever is made by demonstrating the presence of spirochetes in a thick or thin smear. Some cases with mild spirochetemia are only diagnosed

with animal inoculation or concentration methods. Due to the antigenic variation of *Borrelia* strains and the cross-reactivity between different *Borrelia* species, serological tests have no or little diagnostic value (1).

Tetracycline or doxycycline for about 5 days is the treatment of choice for relapsing fever (1). Doxycycline was effective in curing our 2 patients. However, in analogy with *B. burgdorferi* infection it is worth questioning the efficacy of tetracycline and doxycycline in patients with relapsing fever with neurological complications. Indeed tetracycline and doxycycline, in contrast to third generation cephalosporins, do not attain the concentrations within the cerebrospinal fluid that are needed to inhibit *B. burgdorferi* in vitro (8). For the treatment of late Lyme borreliosis the superiority of ceftriaxone over penicillin treatment has been demonstrated (9). Ceftriaxone has also cured a patient with relapsing fever with neurological involvement and who did not respond to penicillin (6).

Erythromycin is generally considered to be effective against *Borrelia* infections and has been recommended on this indication in small children and pregnant women (1, 10, 11). However, treatment failure with erythromycin as in our second patient has been reported previously (1, 10). Therefore more studies are needed concerning the efficacy of third generation cephalosporins in children and pregnant women with relapsing fever. For the developing countries, however, these third generation cephalosporins are too expensive. In these countries, penicillin should remain the drug of choice for the treatment of relapsing fever in children and pregnant women as well as in patients with relapsing fever with neurological involvement.

Our second patient probably developed a Jarish-Herxheimer (JHR) reaction shortly after starting doxycycline treatment. Such reactions have been observed in other patients with relapsing fever, especially during tetracycline treatment. The pathogenesis of this reaction remains incompletely understood (14). The typical JHR starts about one hour after treatment with rigors and a sudden rise in temperature, pulse rate, breathing and blood pressure. Soon thereafter a phase of flushing, profuse sweating and fall in blood pressure is seen. Sometimes this may lead to cardiovascular collapse and death. With tetracycline, a JHR was observed in 61 (59%) of 104 patients with a *B. duttonii* tick-borne relapsing fever (15) but in none of 23 patients with *B. crociduræ* relapsing fever (4). A JHR is usually more severe in relapsing fever than in syphilis.

With the increase of traveling in the tropical regions, where relapsing fever is endemic, more imported cases of relapsing fever can be expected in the future. Relapsing fever should be considered in all patients returning from the tropics with recurring fever, especially if no malaria parasites are detected.

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