African Tick Bite Fever

A Not-So-Uncommon Illness in International Travelers

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Background: African tick bite fever is a rickettsial illness that has recently emerged as a significant disease among international travelers. The vector is the Amblyomma tick, which is endemic to sub-Saharan Africa and parts of the eastern Caribbean.

Observations: We describe a middle-aged woman who returned from a mission trip to Zimbabwe with an influenzalike illness and inoculation eschar; she also had a history of travel to a game farm. Biopsy revealed a histopathologic pattern consistent with an infectious pathogenesis. Immunohistochemical staining confirmed the presence of rickettsial organisms. In light of the patient’s history, the clinical constellation of signs and symptoms, and the results of ancillary laboratory testing, a diagnosis of African tick bite fever was made. The patient was treated with doxycycline hydrochloride and had an uncomplicated course.

Conclusions: This report further highlights the epidemiological and clinical features of African tick bite fever. With the increase in international travel, it is important to recognize the illness in those who have been to endemic countries and to counsel patients regarding preventive measures for planned travel.

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African Tick Bite Fever (ATBF) is an acute, influenzalike illness that is frequently characterized by fever, regional lymphadenopathy, and inoculation eschars. The causative agent of ATBF is Rickettsia africae, an intracellular gram-negative bacillus that is classified in the spotted fever group of rickettsial bacteria transmitted by infected ticks of the Amblyomma genus, which parasitize cattle and wild ungulates.

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Report of a Case

A 48-year-old woman who was referred for the evaluation of an eschar on her left hip had tender lymphadenopathy, fever, fatigue, headache, dizziness, and anorexia for 2 weeks after returning from a 13-day trip to Zimbabwe, where she had spent time at a game farm. She noticed a “pink sore” the day after her return to the United States. The referring physician had ordered basic blood tests and prescribed oral ciprofloxacin (1 g twice daily).

Cutaneous examination revealed no abnormalities except for a 3.5 × 2.0-cm, deeply erythematous, nontender nodule with a central eschar on the patient’s left hip (Figure 1). Tender, left inguinal lymphadenopathy was present. A punch biopsy specimen obtained adjacent to the eschar demonstrated epidermal necrosis with a subadjacent superficial and deep mixed inflammatory cell infiltrate with a suppurative granulomatous component. Inflammation was present in a perivascular, periappendageal, and nodular interstitial distribution. A lymphocytic vasculitis with reactive atypical lymphocytes and vascular fibrin deposition was also noted (Figure 2A and B). Stains were negative for organisms, and bacterial, fungal, and mycobacterial cultures demonstrated no growth. Tissue sent to the Centers for Disease Control and Prevention for immunohistochemical testing revealed the presence of spotted fever group rickettsial organisms in the endothelium (Figure 2C). The results of serologic testing by polymerase chain reaction (PCR) were negative. A presumptive diagnosis of ATBF was made; the ciprofloxacin therapy was discontinued; and the patient began a 2-week course of oral doxycycline hydrochloride (100 mg twice daily). Complete resolution occurred within 3 weeks, with only a residual scar at the inoculation site.
The incidence of ATBF has been estimated to be up to 5.3% in travelers to endemic regions, which is likely an underestimation owing to the large number of travelers who do not seek treatment for their “flu-like” illness. Risk factors include game hunting, safari tourism, travel in the rainy season (November through April), and travel to southern Africa. The illness often occurs in clusters, affecting a group of persons on the same trip. An incubation period of 6 to 10 days from the presumed tick bite to the onset of an abrupt influenza-like syndrome with fever, fatigue, headache, and myalgia is typical. The inoculation eschar, single or multiple, occurs most commonly on the legs and is accompanied by tender lymphadenopathy of the draining nodes. A generalized cutaneous rash is seen in 15% to 46% of patients. The causative agent of ATBF is *R. africae*, which is transmitted by *Amblyomma* genus ticks that feed on cattle and wild game. The feeding strategy of *Amblyomma* ticks is for several ticks to attack simultaneously, resulting in clustering of cases and multiple inoculation eschars.

Laboratory diagnosis of ATBF may be made with non-PCR serologic tests; however, other rickettsial species cross-react, and the results are not positive until 3 weeks after the onset of symptoms. Polymerase chain reaction–based methods are sensitive and specific for the identification of *R. africae* in serum or tissue specimens. The results of serologic testing by PCR were negative in our patient, probably because she had previously undergone 1 week of ciprofloxacin therapy. Immunohistochemical analysis is a sensitive method for diagnosis early in the disease course; however, cross-reactivity can occur among the different rickettsial species.

With the increased mobility of the population, it is important to recognize the signs of diseases that are localized to a particular geographic area. African tick bite fever was virtually unknown outside of endemic regions...
as recently as 1 decade ago but is now considered the most important rickettsial infection that occurs in international travelers.6 After the abolition of apartheid in the early 1990s, international tourism rates to South Africa, where 80% of ATBF cases are acquired, increased 6-fold.4-6 African tick bite fever is also endemic in Zimbabwe, Botswana, Tanzania, Kenya, Zambia, and some parts of the eastern Caribbean.4 Prevention for persons traveling to endemic areas involves the application of lotions containing 20% N,N-diethyl-3-methylbenzamide (DEET).7 If ATBF is suspected, a skin biopsy specimen should be obtained from the site of an inoculation eschar for immunohistochemical analysis. Also, blood and tissue samples should be sent to a reference laboratory for PCR-based genomic detection. Therapy should be initiated with doxycycline (100 mg twice daily for 7 days).

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REFERENCES