African Tick Bite Fever in a Returned Traveler

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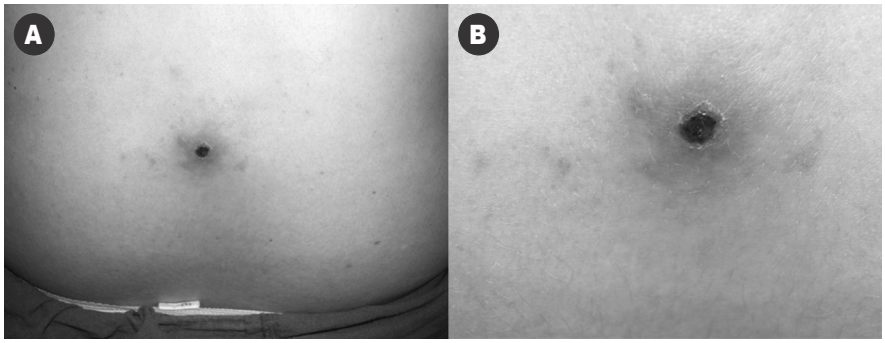
The frequency of international travel today has enabled infectious agents to cross boundaries much faster than in the past. The growing trend of adventure travel enhances this phenomenon. Travelers often visit developing countries, stay in rural areas and therefore expose themselves intensely to various pathogens and vectors. We describe here a case of spotted fever in a returned traveler.

Patient Description

A 25 year old female was admitted to our department with a 3 day history of fever and headache. Two days prior to her admission she returned from a 4 month trip to southern Africa, where she stayed mostly in rural regions of Swaziland, Malawi and South Africa. Before leaving Israel she consulted a geographic medicine clinic and was vaccinated according to international guidelines. However, she took malaria prophylaxis only for the first few days of her trip and did not adhere to other precautions regarding clothing, swimming in rivers and lakes, etc.

The patient felt well during her entire trip but 2 days after returning to Israel she developed fever, accompanied by severe malaise and headache. She noticed two nodules on her waist and a small ulcer in the center of her back. She could not recall animal contact specifically.

Physical examination on admission was unremarkable except for a single ulcerative lesion, approximately 20x10 mm, in the center of the patient's back, covered by a dry black eschar [Figure]. Two small, slightly tender subcutaneous nodules were palpated in the left side of her back and small discrete papules were found on her back as well.



[A] Eschar (tache noire) in the center of the patient's back. **[B]** Enlarged photo of the same lesion.

The patient's laboratory tests were normal. Malaria antigen test and a blood film for malaria parasites were negative. Serologic tests for dengue fever and Rickettsiae were negative as well. The patient was treated with doxycycline followed by a rapid convalescence. It took several more weeks for asthenia and weakness to resolve. A second serum sample taken 10 days after her admission showed seroconversion for rickettsial antibodies, confirmed by the National Laboratory for Rickettsial Diseases in Ness Ziona. Western blot with cross-adsorption studies performed at the Unité des Rickettsies, Marseille, France, confirmed the diagnosis of R. *africae*.

Comment

Rickettsial diseases are zoonoses caused by a group of obligate intracellular Gram-negative bacteria, transmitted to humans by various vectors. Several rickettsial diseases have been described in Israel. By far the most common one is Mediterranean spotted fever, caused by the tick-borne bacteria R. *conorii* [1]. The Israeli variant of Mediterranean spotted fever, named Israeli spotted fever, is a relatively severe and sometimes life-threatening illness compared with other variants of Mediterranean spotted fever such as Astrakhan spotted fever and others.

The clinical presentation of Israeli spotted fever is ambiguous. Most patients complain of fever and chills, headache and/or myalgia and only a minority present with a typical rash. The black crusted eschar (tache noire) at the site of inoculation is rare in Israeli spotted fever and a history of exposure to animals is obtained in a minority of cases. The non-specific findings and the lack of a reliable and immediate laboratory test are often an obstacle for rapid diagnosis and many cases are probably missed. One should keep a high index of suspicion for this potentially lethal infection, especially during summer months when tick activity is high.

Rickettsioses have been extensively

reported in the literature over the past two decades as a cause for significant morbidity and mortality among travelers. African tick bite fever is the most frequently encountered rickettsiosis in this population, with over 350 cases reported to date [2]. According to a recently published analysis of 17,353 ill returned travelers, it is the second most common identified etiology for fever in returning travelers from sub-Saharan Africa, malaria being the first [3]. Most of the cases are associated with safari or game hunting and some are diagnosed in clusters. About 80% of the cases seen worldwide originate in South Africa.

African tick bite fever is caused by *Rickettsia africae*. The principal vectors for its transfer are hard ticks of the *Amblyomma* genus and the disease is endemic in sub-Saharan Africa and the French West Indies. Several clinical manifestations are unique for this type of spotted fever and may help with the diagnosis [4]. Fever appears in 81–92% of cases and a rash is present only in 42–50%, however local lymphadenopathy (like the one our patient had on her back) is common (49–57%). An eschar is found in 53–98% and in over half of the cases several lesions coexist due to multiple tick bites by this notoriously aggressive type of tick. The eschar of African tick bite fever needs to be distinguished from the eschar of anthrax, which progresses from papule to vesicular or bullous lesion with surrounding non-pitting edema and then to central black painless eschar. Fatal cases of African tick bite fever have been described but the case-fatality rate is unknown.

Diagnosis of African tick bite fever like most rickettsial diseases is made clinically, and treatment is given empirically in order to avoid the associated mortality and morbidity. Serological testing for acute-phase serum samples is usually negative and the diagnosis has to be confirmed by a second convalescent-phase sample. The National Center for Rickettsial Diseases in Ness Ziona uses the immunofluorescent antibody test and enzyme-linked immunosorbent assay for detecting antibodies to R. *conorii* [1]. However, we should emphasize that routine serological testing is not species specific and there is cross-reactivity between different species of Rickettsiae. Highly specific antibody tests are available at reference laboratories such as the Unité des Rickettsies in Marseille, where we sent our patient's sera. These tests are used primarily for epidemiological studies and are rarely indicated for diagnostic purposes. In the case presented here, the patient's serum reacted in the commonly used test for R. *conorii* and the diagnosis of African tick bite fever was based on the typical clinical manifestations and the recent history of travel to endemic areas. While variants of Mediterranean spotted fever exist in parts of Africa, data gathered in Didier Raoult's laboratory in Marseille indicate that over 95% of spotted fever cases acquired in South Africa are caused by R. *africae* (D. Raoult, personal communications). Considering that the mean incubation period for rickettsial diseases is 6–7 days (range 3–18) and that our patient had classic symptoms that appeared 2 days after her return, the diagnosis of African tick bite fever was inevitable. Our suspicion was later confirmed by the results from the reference lab in Marseille.

Guidelines for the diagnosis of rickettsial diseases state that the antibody response in African tick bite fever may be delayed, as compared to other rickettsioses, and early treatment has been shown to abolish the serological response [4]. Other tools for specific diagnosis, used primarily for research purposes, include tissue cell cultures and molecular biology techniques such as polymerase chain reaction. A skin biopsy, especially if taken directly from the "tache noire," is a useful specimen for diagnosis using these methods.

African tick bite fever, like any other spotted fever, should be promptly treated with antibiotics to prevent clinical deterioration and possibly death. Studies have shown that patients who recover from severe spotted fever may have significant long-term morbidities, mostly neurological deficits such as paresis, hearing loss and neuropathy [5]. This case illustrates the importance of interrogating any febrile patient about recent travel, bearing in mind the potential of life-threatening illnesses in returned travelers.

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