Diagnosis of African Tick-bite Fever

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Background

*R. africae* is the etiological agent for African tick-bite fever (ATBF), the most common tick-borne bacterial zoonosis.[1] There are two known vectors of the disease: the *Amblyomma variegatum* ticks found in Sub-Saharan Africa and West Indies, and the *Amblyomma hebraeum* ticks found specifically in Southern Africa.[2,3]

Unlike other ticks that passively infect their host, *Amblyomma hebraeum* ticks uniquely attract other ticks to the host. Studies have shown that male ticks that are feeding on a non-human host (usually cattle) can emit an aggression-attachment pheromone that attracts other unfed ticks to the host. The presence of the pheromone allows unfed ticks to actively discriminate between hosts on which these parasites have fed successfully (suitable hosts) and those on which they have not.[4] The aggressive hunting nature of the *A. hebraeum* ticks explains the clinical presentation of having multiple eschars and affecting large groups of exposed travellers such as soldiers, leisure safari tourists, game hunters, and foreign aid workers.[2] Another South African spotted fever group *Rickettsia* has been estimated to have a very high prevalence in *Amblyomma* ticks (95.2%) and *R. conorii* in southern African ticks found in Sub-Saharan Africa.[5,6] The incidence of ATBF is now one of the most common rickettsial infections in Africa.[12,13] Accordingly, it is incredibly important for travelers to utilize repellents containing at least 19.5% diethyl-3-methylbenzamide (DEET) as a preventative measure when traveling to endemic areas.[14]

ATBF is highly sensitive to doxycycline and the early exposure to the drug prevented the development of detectable titers of reactive antibodies, thus producing a negative serology test.[10] In our patient’s case, early exposure to doxycycline explains his negative serology tests.

Due to *R. africae*-carrying tick’s aggressive hunting nature, they are associated with multiple eschars and tend to affect a groups of people, especially in rural areas.[4,5] The infection presents with a maculopapular or papulovesicular rash, fatigue, headache, myalgia, and regional lymphadenopathy. The inoculation eschar, single or multiple, commonly presents on the legs and is accompanied by tender lymphadenopathy of the draining nodes.[7] More severe symptoms such as, myocarditis and subacute neuropathy have been reported in elderly patients.[8]

Case Report

A 77-year old male presented with a pruritic maculopapular and papulovesicular rash distributed over his upper and lower extremities bilaterally that started 3 weeks prior. He noted he was on a 12-day mission trip in Limpopo, the northernmost province of South Africa, where he was constructing and installing safe toilets to replace areas using dangerous toilet pits. The patient believed he had been bitten by ticks and noted an eschar on his left lower leg on the third day of the trip. He also noted that he developed a sudden, persistent, and pruritic rash 10 days after inoculation by an infected tick.[7] Clinical signs include fever, generalized maculopapular or papulovesicular rash, fatigue, headache, myalgia, and regional lymphadenopathy. The inoculation eschar, single or multiple, commonly presents on the legs and is accompanied by tender lymphadenopathy of the draining nodes.[1] More severe symptoms such as, myocarditis and subacute neuropathy have been reported in elderly patients.[8]

Biospies were taken from the right shin, left volar forearm, and right fourth finger, all of which revealed histologic findings consistent with a bullous arthropod reaction without any evidence of a vasculitis. Aerobic and anaerobic bacterial cultures taken from the right shin showed no growth.

Ten days after the initial biospies, serum samples and eschar swabs were collected and sent then to the Center for Disease Control and Prevention for further testing. The serum Spotted Fever Group IgG IFA (Rocky Mountain Spotted Fever) and African Tick-bite Fever antibodies were negative. However, the cultures from the eschar swab came back positive for *R. africae*.

The patient was given triamcinolone 0.1% cream to apply BID to pruritic lesions for up to two days and an additional 7-day course of doxycycline monohydrate 100mg PO BID was given. The skin lesions had fully resolved without scar 7 days after treatment was given.

Key Points

- African tick-bite fever (ATBF) is one of the most common tick-borne bacterial zoonoses.
- ATBF should be considered in those with exposure to rural area of Southern Africa in the preceding 2 weeks, particularly when presenting with multiple eschar sites
- The *R. africae*-carrying ticks are unique, given their ability to actively attract and hunt their non-human hosts via an aggression-attachment pheromone
- Laboratory diagnosis of ATBF can be challenging due to its high cross-reactivity with *R. conorii* in serological testing and it’s delay in seroconversion

Discussion

Diagnosis of rickettsiosis can occur through serology testing, in which presence of disease-specific antibodies are detected via indirect immunofluorescence assay (IFA) using disease-specific antigens. Antigens from *R. rickettsii* (Rocky Mountain Spotted Fever), *R. conorii* (MSF), and *R. africae (ATBF)* are commercially available for the diagnosis of rickettsiosis.

Unfortunately, antigens from *R. conorii* exhibit cross-reactivity with *R. africae*, which can confound the diagnosis.[1,11] Another diagnostic dilemma is that serology IFA tests can be less sensitive when done after the initiation of antibacterial treatment. The current hypothesis is that *R. africae* is highly sensitive to doxycycline and the early exposure to the drug prevented the development of detectable titers of reactive antibodies, thus producing a negative serology test.[10] In our patient’s case, early exposure to doxycycline explains his negative serology tests.

References


Figure 1. African tick-bites distributed over the right ankle

Figure 2. Early eschar forming over the left lower leg

Figure 3. Early eschar sites mediated of host