Caso Clínico

Escaras de Inoculação e Febre: Um Caso de Febre da Carraça Africana

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RESUMO – A febre da carraça africana é causada pela bactéria intracelular *Rickettsia africae*. Esta bactéria é transmitida através da picada da carraça do género *Amblyomma*, com uma elevada taxa de infeção por *R. africae*. A febre da carraça africana é já a segunda causa mais frequente de febre em viajantes que regressam da África Subsariana.
Apresentamos o caso de um homem de 58 anos, em regresso da África do Sul, com história de febre, cefaleia generalizada e mialgias cervicais. Ao exame objetivo foram documentadas múltiplas escaras de inoculação e adenomegalias inguinais dolorosas. A histopatologia da biópsia cutânea foi compatível com *rickettsiose* e o diagnóstico de infeção por *R. africae* foi confirmado por reação em cadeia da polimerase (PCR).
O aumento global do turismo internacional, particularmente para áreas remotas, predispõe à picada de carraças. A febre da carraça africana deve ser considerada no diagnóstico diferencial de doentes febris com história de viagem recente a zonas endémicas.
PALAVRAS-CHAVE – África do Sul; Febre da Carraça; Infecções por Rickettsia; Viagem.

Inoculation Eschars and Fever: A Case of African Tick Bite Fever

ABSTRACT – *African tick bite fever is caused by the intracellular bacteria Rickettsia africae. This bacterium is transmitted through the bite of the Amblyomma tick, which carries a high rate of R. africae infection. African tick bite fever is the second most frequent cause of fever in travelers returning from sub-Saharan Africa.*
We present the case of a 58-year-old man, returning from South Africa, with a three-day history of fever, generalized headache and cervical myalgia. On physical examination multiple inoculation eschars and tender inguinal lymph nodes were documented. Histological examination of a skin lesion was compatible with spotted fever and the diagnosis of R. africae infection was confirmed through polymerase chain reaction analysis.
The global increase in international tourism, particularly to remote areas, predisposes to tick bites. In febrile tourists returning from endemic areas and after a thorough clinical examination, the diagnosis of African tick bite fever should be born in mind.
KEYWORDS – *Rickettsia Infections; South Africa; Tick-Borne Diseases; Travel.*

INTRODUCTION

African tick bite fever (ATBF) is a tickborne disease endemic in rural areas of sub-Saharan Africa and the West Indies caused by the Gram-negative intracellular bacteria *Rickettsia africae*.[1] Although the disease was first described in 1930, the causative agent was only isolated more than fifty years later in 1992.[2,3] This infection has been increasingly identified in European tourists returning from sub-Saharan Africa. Besides travelling to this endemic area, additional risk factors include game hunting, safaris and travel during rainy season (from November through April).[2,4] Fever, either isolated or associated with other symptoms and/or signs, is a common complaint observed in travelers. As such, a meticulous clinical history and physical examination are mandatory in order to achieve a final diagnosis. After malaria, *R. africae* infection is responsible for most cases of acute fever in tourists returning from Africa and, due to increasing international traveling, its frequency is likely to increase.[5,6]

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Physicians, including dermatologists need to be aware of ATBF in the differential diagnosis of febrile patients returning from this area, especially because it presents with characteristic cutaneous findings.[7] If the diagnosis is suspected, prompt treatment should be initiated. Herein, we present a case of ATBF with typical epidemiological, clinical and histopathologic features.

CASE REPORT

A previously healthy 58-year-old Caucasian man was seen in our emergency department with a three-day history of fever, generalized headache, cervical myalgia and multiple skin lesions. On the day of hospital admission, the patient had just returned from a trip to South Africa where he had visited Cape Town and several remote areas, on safari and hunting activities. One week prior to the onset of these symptoms, the patient reported contact with ungulate animals and hiking through the bushes during these activities. He first noticed small sized erythematous lesions on his legs, which he attributed to mosquito bites, and a few days later he developed fever, chills, headache and cervical myalgia.

On physical examination, the patient was febrile (tympanic temperature 38.3°C) with multiple centrally necrotic erythematous patches on the legs, abdomen and arms, some of them with central ulceration (Fig. 1) and bilateral tender inguinal lymphadenopathy.

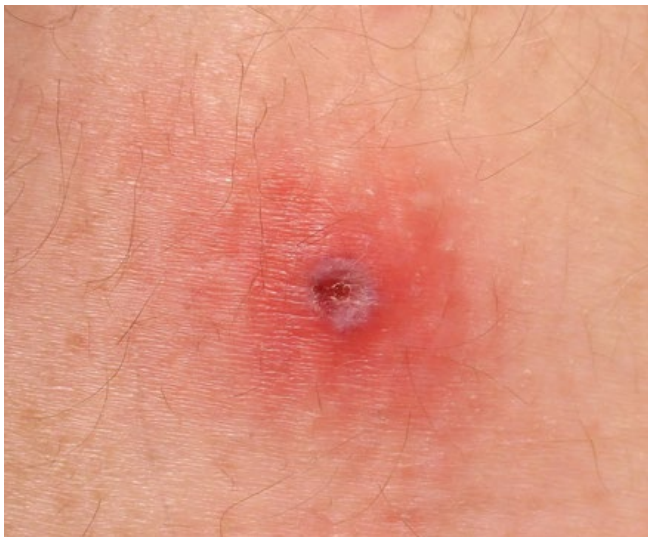

Figure 1 - Clinical picture: One of the multiple eschars of the patient, this one located on his left leg, showing a black, crusted ulcer with an erythematous halo.

On laboratory evaluation an increased C-reactive protein level (4.18 mg/dL, N<0.5 mg/dL) was present, with a normal complete blood cell count and liver enzymes. Thick and thin blood smear studies did not reveal malaria parasites and HIV, hepatitis B virus (HBV) and hepatitis C virus (HCV) serologies were negative. A rickettsial spotted fever group titer was also negative. A skin biopsy of one of the eschars revealed epidermal and dermal necrosis with necrotizing vasculitis and a lymphocytic infiltrate suggestive of rickettsiosis (Fig. 2). Polymerase chain reaction (PCR) amplification of the genes encoding the 16S rRNA outer membrane proteins, rOmpA and rOmpB, performed on the biopsy specimen confirmed the diagnosis of *R. africae* infection.

The patient was treated with oral doxycycline 100 mg twice daily for 10 days with a complete clinical response and no documented side effects.

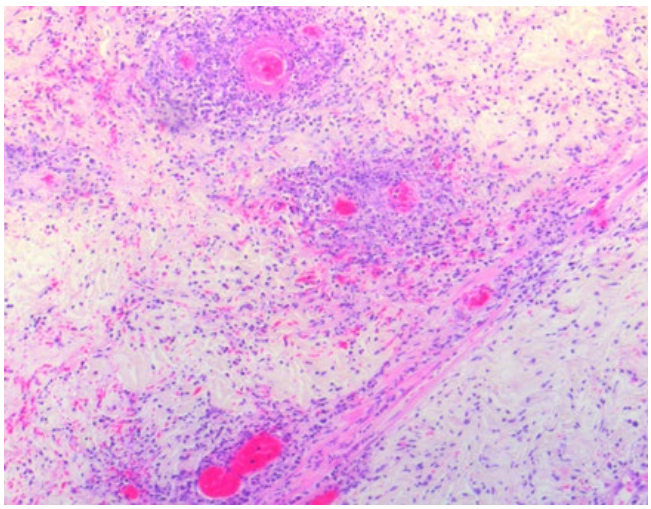

Figure 2 - Histopathological picture: Lymphocytic vasculitis with intravascular thrombi, extravasation of erythrocytes and perivascular and interstitial neutrophils (H&E, x100).

DISCUSSION

ATBF is an emerging rickettsiosis caused by *R. africae*, a small Gram-negative obligately intracellular bacteria, transmitted by *Amblyomma* ticks, endemic in sub-Saharan Africa.[7-9] Currently, in these areas, up to 100% of *Amblyomma* ticks are infected with *Rickettsia*.[8,9] These ticks are highly aggressive, and they actively converge on nearby hosts, which may be simultaneously bitten by many ticks. This behaviour explains why cases often occur within clusters of patients, presenting with multiple inoculation eschars.[3,7-9]

The incubation period before the onset of symptoms is six to seven days but it may be as long as ten days.[7,8,10] The typical clinical presentation of ATBF is fever, headache, multiple pathognomonic inoculation eschars and regional lymphadenopathy.[3,7-10] A skin rash is frequently absent.[3,7,10] It is worth noting that prominent neck muscle myalgia as well as aphthous stomatitis and lymphangitis may be present.[7] Complications like myocarditis and sub-acute neuropathy are uncommon but have been described, especially in elderly patients.[3,8,9]

The diagnosis is based on clinical and epidemiologic evaluation.[3,7-10] ATBF is the second most frequent cause of

fever, after malaria, in travellers returning from sub-Saharan African and it is especially common in patients who have either been on a safari or have visited rural areas.[3,7-9] Travel history together with clinical identification of an eschar should raise the suspicious of rickettsiosis and prompt treatment with doxycycline is mandatory. Laboratory tests may be useful to confirm the diagnosis - moderate lymphopenia, thrombocytopenia and elevated liver enzymes may be present during the first days of illness,[3,7,10] although these were not documented in our case.

Our patient presented with a classical epidemiological and clinical picture of ATBF, including the multiple inoculation eschars.[3,7] Serologies for *Rickettsia* were initially negative, which is line with a delayed increase in antibody titters following infection, frequently requiring more than two weeks after the onset of symptoms to become positive.[3,7,8,10] Skin biopsy showed a lymphohistiocytic vasculitis, the histopathological hallmark of rickettsial disease.[7] It is also worth noting that serological markers lack *Rickettsia* subspecies specificity due to antigenic cross-reactions[8-10] and histology is nonspecific. *Rickettsia* isolation requires cell cultures which are only available in reference laboratories.[7,8,10] PCR detection of *R. africae* in an eschar biopsy is a reliable method to achieve a correct diagnosis. Since *Rickettsiae* multiply in the inoculation site forming the eschar, it is the preferred location for a skin biopsy. Analysis of the eschar swab, eschar crust or blood may also be used.[3,7-10]

Doxycycline (100 mg twice a day for 10 days) is the treatment of choice for all spotted fever rickettsioses.[7-9] Alternatively, macrolide antibiotics and ciprofloxacin may be used.[7,8] It is worth noting that when typical signs of ATBF are encountered, treatment should be initiated before laboratory confirmation of the diagnosis, minimizing the risk of side effects.[3,7-9] Due to its potential increase from international tourism, physicians should promptly recognize this clinical entity when assessing patients returning from endemic areas, as described above. Prevention is also of extreme importance, and travellers with a significant risk of acquiring AFTB should be encouraged to wear protective clothes and tick repellent, both by topical application and impregnation of clothes.[7-9]

CONCLUSION

African tick bite fever is one of the most common causes of fever in travelers returning from sub-Saharan Africa. As such, and particularly after ruling out malaria, this diagnosis should always be considered when assessing febrile patients returning from endemic regions. Treatment initiation does not depend on any diagnostic tests and if there is a high clinical suspicion, prompt treatment with doxycycline is mandatory.

Note: This clinical report was presented as poster in the World Congress of Dermatology in Milan, Italy (from 10th to 15th June 2019).

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