African Tick Bite Fever: a multi-pronged approach for diagnostic evaluation

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Clinical Audit & Effectiveness

INTRODUCTION

African tick bite fever is an emerging spotted fever group rickettsial disease increasingly seen in international travellers returning from sub-Saharan Africa. It is characterised by an acute influenza-like illness with single or multiple inoculation eschars and associated regional lymphadenopathy. Diagnosis is usually confirmed through serology or tissue-based detection of rickettsiae from an eschar biopsy. Increasingly, eschar crust and swab samples have been used for PCR-based molecular detection of rickettsiae(1).

We present 2 cases of African tick bite fever in adults following foreign travel within sub-Saharan Africa. The first case involved a young Irish couple presenting with fevers, pruritic rash, and tender inguinal lymphadenopathy, following recent travel along the 'Garden route' of Cape Town, South Africa where they underwent a safari. The second case involved a young Irish male presenting with fevers, myalgia, and headache, following recent travel from a rural village in Uganda near Lake Victoria

Case 1

A young Irish couple presented to the Emergency Department following a recent trip to South Africa.

The 42-year-old male had a 4-day history of fevers, headache, myalgia, tender left inguinal lymphadenopathy, and a pruritic rash across his groin and lower limbs. His symptoms began 1 day after their return to Ireland.

The 40-year-old woman presented with a pruritic rash and bilateral tender inguinal lymphadenopathy. Her symptoms began In Kieraga, South Africa where she developed 2 pruritic rashes on her left shin which subsequently blistered and ulcerated. 5 days later, she developed diffuse rash and tender inguinal lymphadenopathy.

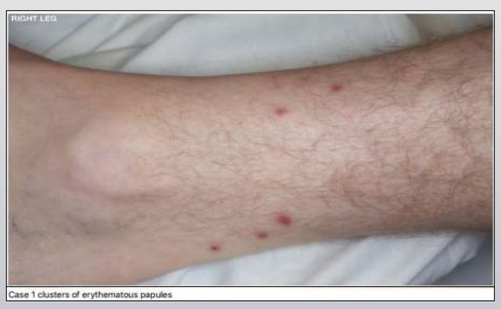
Travel History

The couple reported recent travel to Cape town, South Africa in August that year. They had spent 14 days visiting multiple destinations along the 'Garden route' of Cape town, a 200km coastline route from East to West Cape town provinces of South Africa. Notably, they had spent 4 days in Kariega where they had undergone a safari and had been in close proximity to an Impala antelope carcass. They denied any insect or animal bites.

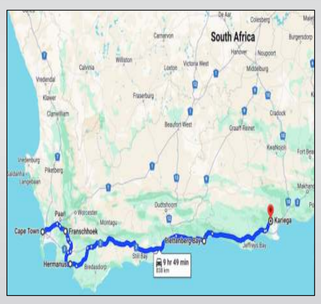
Physical exam and Key diagnostics

On examination, the man was febrile at 38.6 degree Celsius, but otherwise vitally stable. He had **a solitary 10mm x 10mm inoculation eschar at his left upper thigh with a surrounding annular erythematous halo** and associated tender left inguinal lymphadenopathy. He had **scattered clusters of erythematous papules on his bilateral lower legs and dorsal feet**

The eschar crust was **debrided and placed in a sterile universal specimen container. The base of the eschar was then dry swabbed. Both samples were sent for rickettsial DNA PCR** analysis with paired serology to the United Kingdom Rare and imported pathogens laboratory (RIPL). Punch biopsies of the erythematous papules were also performed for histopathology and tissue bacterial and fungal cultures



Case 1 clusters of erythematous papules



Stops of patients' journey on Garden Route, Cape Town (image from google Maps)

Results and Clinical Outcome

Histology showed papillary dermal oedema with a prominent superficial and deep dermal perivascular lymphocytic infiltrate with no evidence of vasculitis. Tissue cultures were negative for bacteria, fungi, and mycobacteria. Rickettsial serology was negative, however, the eschar sample was positive for rickettsia species DNA. Basic laboratory investigations were notable for an elevated CRP of 32mg/L and mild lymphopenia of 0.91 x10^9/L. All other investigations were unremarkable. The patient was treated with a 14-day course of doxycycline, 5-day course of meropenem (escalated due to persistent fevers) & 7-day course of ciprofloxacin with resolution of symptoms and lesions with residual scar at the eschar site.

His partner, who was systemically well with normal inflammatory markers, was diagnosed with a milder presentation of the disease and was not admitted. She was treated with 14-day course of Doxycycline and reviewed in the outpatient clinic. She had full resolution of her symptoms, with mild residual scarring and her Rickettsial serology test came back positive for Typhus group IgG.

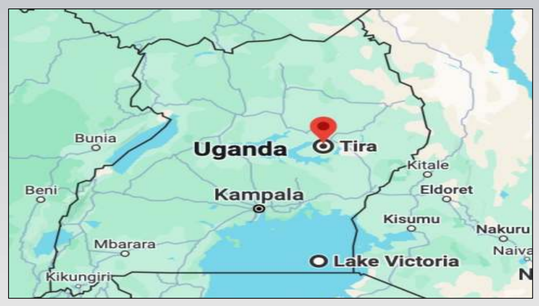
Case 2

A 71-year-old Irish male presented to the emergency department with a 10-day history of fevers, myalgia, night sweats and frontal-occipital headache with neck stiffness.

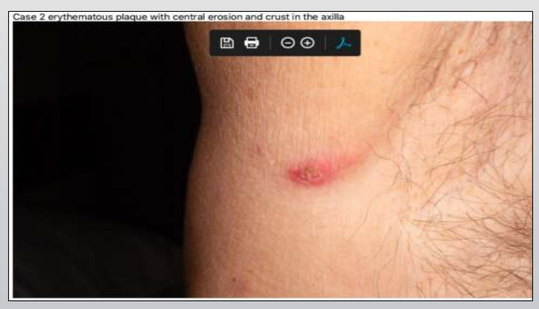
Travel History

He reported recent travel from Uganda 4 days prior to symptom onset. He had spent 2 weeks during the month of June carrying out charity-work in Tiira, a rural village in the South-East of Uganda near Lake Victoria.

He had been on malaria chemoprophylaxis with atovaquone-proguanil during his trip and denied any insect or animal bites. He consumed bottled water only and denied participation in water-based activities.



Tiira, South-East Uganda (image from google Maps)



Physical exam and Key diagnostics

On examination, he was febrile at 38.9 degree Celsius and tachycardic at 111beats per minute. He had a **1cm erythematous plaque with central crust/erosion in his right axilla with no eschar.** He also had **symmetrical erythematous maculo-papular lesions over his trunk and upper limbs.** He also bilateral cervical lymphadenopathy.

Punch biopsies of the axillary lesion were sent for tissue bacterial, fungal and tuberculosis cultures and the trunk lesions for histopathology. Ricketssial serology and DNA PCR testing was requested.

Results and Clinical Outcome

Histology showed orthokeratosis and focal parakeratosis, with a mild vacuolar interface dermatitis and mild superficial dermal perivascular lymphohistiocytic inflammation, without significant eosinophils. Within the clinical context, these histopathological features were most suggestive of a ricketssial disease. Tissue bacterial cultures grew staph epidermidis (non-contributory). Tissue fungal and mycobacteria cultures were negative.

Basic laboratory investigations were notable for an elevated CRP of 53mg/L and ESR of 19mm 1st hour. All other bloods were unremarkable. He had a lumbar puncture due to worsening headaches. Cerebrospinal fluid results showed 3 WCC/microL, and protein of 792 mg/L. Cerebrospinal fluid bacterial and viral testing were negative.

The patient received doxycycline for 2 weeks with clinical improvement and was discharged with outpatient clinic review. Ricketssial serology came back positive for Spotted Fever Group IgG, with an equivocal initial Lyme serology. However, repeat Lyme serology was negative.

Discussion

African tick bite fever is a spotted fever group rickettsial disease seen in travellers from sub-Saharan Africa with an incidence of up to 5.3% in endemic regions(2). Risk factors for transmission include safari tourism, game hunting, travel in the rainy season and travel to endemic areas in sub-Saharan Africa and the West Indies (3). The incubation period is 6-7 days(4). Typically a mild illness; however rare complications include subacute neuropathy and myocarditis(2).

Other important causes of eschar-forming include Tick-borne relapsing fever (Borreliosis), African trypanosomiasis, plague (Yersinia pestis), cutaneous anthrax and other spotted fever group rickettsioses endemic to the region such as Rickettsia conorii and Rickettsia massiliae (5,6)

Diagnosis is usually confirmed via serology or tissue-based detection of rickettsial DNA from an eschar biopsy. Increasingly, eschar crust and swab samples have been used for PCR-based molecular detection of rickettsiae.[5] Histological examination of the lesions play a primarily supportive role in the diagnosis. Reported cases have shown that eschars typically have features of perivasculitis with inflammatory cell infiltrates (7).

In the first case, a diagnosis was made using serology testing and clinical/epidemiological data. In the second case, the diagnosis was made using DNA PCR testing of both eschar crust and swab specimens. Additionally, both patients had undergone skin punch biopsies with histology, which showed typical features supportive of the diagnosis. Both cases were successfully treated with a two-week course of doxycycline.

CONCLUSION

This case series highlights the various supportive and confirmatory diagnostic tests available to reach a probable or definitive diagnosis of African tick bite fever, particularly the value of using combined eschar crust and swab specimens, which is a simple, non-invasive method with a high diagnostic yield that can be performed in a variety of clinical settings compared to traditional skin biopsy.

References

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