A Fatal Case of Rickettsiosis from South Africa

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Abstract

We present a case of fatal Rickettsiosis from South Africa.

Keywords: Forensic medicine, forensic pathology; rickettsiosis, tick bite fever, eschar

CASE REPORT

A 59-year-old White man died suddenly and unexpectedly at his home in Pretoria, South Africa. According to the available history, he became aware of a bite of unknown origin (initially suspected to be a spider bite) on the posterior aspect of his neck 7 days before his death. He never removed or witnessed an insect. There was a report of a nonspecific headache before death, but no other complaints were noted. There was no report of seeking medical help during this time, and no hospitalization or medical records were available. His body was referred for medicolegal investigation in accordance with the South African Inquests Act 58 of 1959.[1]

The body was that of an adult White man who was thin with poor/average nutrition (height, 1.85 m; weight, 80 kg). Approximately 6 cm superior from C7 was an eschar, which measured 1.5 × 1.2 cm in size (Fig. 1). This wound showed signs of healing. Approximately 4 cm to the right of the eschar was a 0.5 cm in diameter ulcer (possibly another smaller eschar—as sometimes multiple bites are noted).**2** Both wounds were excised for histological purposes. No further injuries or abnormalities to the body could be identified.

The brain weighed 1414 g and showed diffuse leptomeningeal congestion. Clouding of the leptomeninges in the parasagittal region was present. Serial sections of the brain showed demyelination of the brainstem. Lodox scanning (Lodox Systems (Pty) Ltd, Johannesburg, South Africa) showed a whiteout of both lungs. Both lungs were heavy, and section showed a friable parenchyma, bilaterally. The apical aspects of both lungs showed emphysematous changes. Watery fluid lined the tracheal mucosa. The left lung weighed 1474 g and the right lung weighed 1602 g. The heart was relatively enlarged and weighed 468 g. Advanced atherosclerosis of the large arteries was present. The liver was relatively heavy and weighed 2086 g. No signs of pancreatitis were present and the pancreas weighed 100 g. The spleen was relatively heavy and weighed 420 g. Both renal capsules stripped with ease, and both renal cortices had a grain leather texture suggestive of benign nephrosclerosis. The left kidney weighed 164 g and the right kidney 154 g. The bladder contained approximately 100 mL of murky urine. No further abnormalities could be detected.

Examination of the skin/eschar indicated ulcerated skin surface with necrotic skin tissue and a limited inflammatory response. Relatively few polymorphonuclear cells were present in the vicinity of the bite mark, chiefly in the superficial layers of the skin. Vascular congestion was present.

In summary, multiple comorbid factors were confirmed, such as background emphysematous changes in the lungs, moderate-to-severe background ischemic heart disease, and benign nephrosclerosis of the kidneys. No obvious thrombi could be identified.The differential diagnosis for cause of death included tick bite fever, cutaneous anthrax, Crimean-Congo hemorrhagic fever (CCHF), or disseminated fungal or bacterial disease.[2,3] The CCHF reverse transcription polymerase chain reaction (PCR) tested negative on a postmortem-collected blood sample. A PCR targeting the rickettsia citrate synthase (or *glt*A) gene tested positive

FIGURE 1. Approximately 6 cm superior from cervical vertebra C7, is present an eschar which measures 1,5 cm × 1,2 cm in size. Approximately 4 cm to the right of the eschar, is present a 0,5 cm in diameter superficial ulcer. Both lesions show signs of healing.

(results not shown) on the same blood sample. The amplicon was sequenced using a standard Sanger sequencing protocol. The consensus sequence obtained was subjected to National Center for Biotechnology Information Basic Local Alignment Search Tool platform and revealed a highest level of homology with *Rickettsia conorii*.

DISCUSSION

Postmortem identification of the eschar prompted specific investigation of a possible infectious cause of death. Eschars are necrotic skin lesions that are typically reported in tick bite fever (Fig. 1), cutaneous anthrax, and insect bites.[4]Tick-borne rickettsioses are caused by obligate intracellular bacteria belonging to the spotted fever group of the genus Rickettsia.**2** These zoonoses are among the oldest known vector-borne diseases.**2**In South Africa, tick bite fever is associated with either *R. conorii* or *R. africae* infection.[5] The former is associated with higher mortality and poorer clinical outcomes. The classical clinical triad for tick bite fever diagnosis is eschar, fever, and rash, but all 3 features are found in only 50% to 75% of cases.[6] The case reported here had no evidence of rash or vasculitis, and no fever was reported. *Rickettsia conorri* is most commonly associated with dog and kennel ticks belonging to the genus *Haemaphysalis* or *Rhipicephalus.* These are often reported in periurban/domestic locations in South Africa, therefore making exposure plausible in this case.[5]It is not clear whether our patient felt a bite or discovered the eschar. It is unlikely that he would have been bitten only 7 days before death, as an incubation period after a bite is typically 5 to 7 days and one would expect some clinical progression before death.[5] Larvae or nymph stages of ticks may be missed because of small size.**5**Anthrax, disseminated fungal, and bacterial disease were excluded. *Bacillus anthracis* is a rare cause of disease in humans in South Africa but causes outbreaks in wildlife.[7] Multiple environmental bacterial organisms were isolated from postmortem blood cultures after standard microbiology laboratory procedures, and these were likely due to contamination.[8–10]The lack of antemortem hemorrhagic signs and symptoms reported did not support a diagnosis of CCHF (an endemic tick-borne disease in South Africa).[11] A rickettsia PCR tested positive on postmortem blood sample, and sequencing and homology analysis pointed toward *R. conorii.* The presence of *R. conorri* in the blood of the case at the time of death supported the diagnosis of tick bite fever.The histological findings of necrotic tissue with inflammation and vascular congestion were in keeping with eschar formation. The pathophysiology of death in this case remains elusive. The demyelination of the brainstem remains of uncertain significance. The background comorbid factors may have contributed to an earlier death. Autopsies may sometimes be helpful in confirming or excluding a diagnosis of sepsis.[12]Tick bite fever is a common cause of febrile illness in South Africa, and timely treatment with doxycycline can be life-saving.**5**

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