Ehrlichia ruminantium, an emerging human pathogen – a further report

M Louw, M T E P Allsopp, E C Meyer

To the Editor: Following up on our previous report,[1] we provide further details on clinical investigations in several cases of rapidly fatal encephalitis that have come to attention in Pretoria during the past 4 - 5 years. All but one of the patients were children who presented initially with features of viral encephalitis.

The first case, an adult woman, died 3 weeks after her dog died of biliary fever. Unfortunately no further clinical history is available.

The second case, a 6-year-old boy, died within a week of admission to hospital with a clinical picture of encephalitis. He presented initially with a history of headache and fever. He was admitted to a private clinic but was discharged after his clinical picture improved. His condition subsequently deteriorated. He had gait disturbances (ataxia) and progressive sleepiness. He was admitted again, but deteriorated rapidly and became comatose. He was intubated and transferred to an intensive care unit, where he died about 3 days later. A computed tomography (CT) scan of the brain performed at this stage revealed oedema and hypodense lesions in the cortex.

A lumbar puncture performed on admission revealed only occasional lymphocytes. Nothing was cultured from the cerebrospinal fluid or from blood cultures. The white cell count was raised (19.8 x 10^9/l), with a platelet count of 489 x 10^9/l. Serological examination revealed nothing except an *Rickettsia conori* immunoglobin M titre of 1:128, which is not regarded as positive. The child died before the test could be repeated. A postmortem examination was requested.

The postmortem was unremarkable. The only positive findings were pulmonary oedema and an oedematous, hyperaemic brain. Hyperaemia of the brain is consistent with encephalitis. Histological examination revealed extensive vasculitis in the brain, most prominent in the midbrain and pons. Foci of associated necrosis were seen. After extensive enquiries it emerged that no history of a skin rash or eschar had ever been obtained. Given the above history, numerous methods to demonstrate organisms/pathogens were explored.

Rickettsiae are fairly large organisms, which can be demonstrated with silver stains. Repeated silver stains of the brain sections were negative. Electron microscopic examination of the vasculitic lesions was also negative.

Department of Anatomical Pathology, National Health Laboratory Services, Tshwane Academic Division, Pretoria
M Louw, MMed (Path)

Onderstepoort Veterinary Institute, Onderstepoort
M T E P Allsopp, PhD

Department of Family Medicine, Faculty of Health Sciences, University of Pretoria
E C Meyer, MPharmMed, MMed (Fam Med)

Corresponding author: *M Louw (melanie.louw@up.ac.za)*

Given the possibility that a rickettsia could be the pathogen, the Rickettsia Unit in Marseilles (Professor D Raoult) was consulted. Immunohistochemical stains for rickettsiae were negative.[2]

Finally, the Molecular Department at the Onderstepoort Veterinary Institute was consulted. Tissue samples and serum were examined, revealing the presence of *Ehrlichia ruminantium* DNA sequences in all the samples.[1]

After the initial 2 cases, a possible third case came to our attention. Serum from this child was also evaluated at Onderstepoort. Unfortunately the child died before results were available. *E. ruminantium* DNA sequences were also present in this case.

Recently serum from a child who died in the Cape Town region was also sent to Onderstepoort. This child also presented with encephalitis, with hypodense lesions on CT scan. The child had a rapidly fatal clinical course. Again *E. ruminantium* DNA sequences were retrieved from the serum sample.

All the cases but the first have several similarities. Most of the patients were young children between the ages of 4 and 7 years. All the children presented with a clinical picture of encephalitis and had a rapidly fatal clinical course.

After the first cases extensive enquiries were made into the habits of the children. All had lived close to agricultural holdings or nature reserves and engaged in outdoor activities.

E. ruminantium is transported by ticks and causes heartwater fever in ruminants. Currently there are no records in the literature of *E. ruminantium* infection in humans, although there is one report of a possible canine *E. ruminantium* infection.[3] However, the DNA sequence evidence from all the cases and brain lesions typical of those seen in heartwater-infected animals strongly suggest *E. ruminantium* infection.

There is no molecular evidence of *E. chaffiensis* in South Africa, for which the main target cells are monocytes[4] rather than the vascular endothelial cells observed in the current infections.

Ruminants infected with *E. ruminantium* are treated with doxycycline. Currently the only suggested way of treating this in human patients is with oral doxycycline which, unfortunately, is not always well tolerated.

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3. Allsopp MTEP, Allsopp BA. A novel Ehrlichia genotype detected in dogs in South Africa. *J Clin Microbiol* 2001; **39:** 4204-4207.
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Elizabeth Wasserman, Associate Professor and Chairperson, Department of Medical Microbiology, National Health Laboratory Service, Coastal Branch, and Stellenbosch University, comments: Tick-borne diseases are common and serious, yet we know relatively little about their causative agents, epidemiology and pathogenesis in South Africa. We are familiar with the typical clinical presentation of tick-bite fever, but it is difficult to confirm the causative agent in the routine laboratory. Serology for rickettsial infection often remains negative, even late in the disease, and the polymerase chain reation (PCR), offered at many laboratories, lacks sensitivity. Our knowledge of the so-called 'African tick-bite fever' caused by *Rickettsia africae* and transmitted by *Amblyomma* ticks originates mostly from cases reported from Europe in which the disease was contracted while travelling in sub-Saharan Africa.

Human ehrlichiosis (caused by *Ehrlichia chafeensis* and *E. ewingii*) is well described and frequently reported in the USA.[1] Ehrlichiosis is often associated with mild to severe disease,[2] with a mortality ranging from 2% to 3%, including healthy children. *E. ruminantium* and its *Amblyomma* vectors have an indiscriminate host range[3] and human disease is therefore conceivable.

Many questions regarding the aetiology and epidemiology of tick-borne disease in South Africa remain unanswered and require further study.

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