

CASE REPORT

Rift Valley fever and malaria co-infection: A case report

Yousif Ali¹ | Emmanuel Edwar Siddig^{2,3}  | Nouh Mohamed⁴ | Ayman Ahmed^{5,6,7} 

¹Sudan Field Epidemiology Training, Health Emergencies and Epidemics Control General Directorate, Sudan Federal Ministry of Health, Khartoum, Sudan

²Faculty of Medical Laboratory Sciences, University of Khartoum, Khartoum, Sudan

³Department of Medical Microbiology and Infectious Diseases, Erasmus University Medical Center Rotterdam, Rotterdam, The Netherlands

⁴Molecular Biology Unit, Sirius Training and Research Centre, Khartoum, Sudan

⁵Swiss Tropical and Public Health Institute (Swiss TPH), Allschwil, Switzerland

⁶Faculty of Science, University of Basel, Basel, Switzerland

⁷Institute of Endemic Diseases, University of Khartoum, Khartoum, Sudan

Correspondence

Ayman Ahmed, Institute of Endemic Diseases, University of Khartoum, Khartoum, Sudan.

Email: ayman.ame.ahmed@gmail.com

Key Clinical Message

We report a case of febrile illness that was presented with mild symptoms. However, laboratory investigation confirmed a malaria and Rift Valley fever co-infection. Healthcare providers in settings endemic with several infectious diseases should seek rolling out possibilities of other infections prior to starting treatment for achieving effective case management with less resources and better safety of patients.

Abstract

Here we report a case of febrile illness that confirmed to be a co-infection of malaria and Rift Valley fever. The patient was initially diagnosed with malaria and started on treatment immediately. However, due to the lack of response to the treatment further laboratory investigations were pursued.

KEYWORDS

chronic diseases, critical care medicine, environmental health, infectious diseases, virology

1 | BACKGROUND

Rift Valley fever (RVF) is a mosquito-borne zoonotic viral disease that is associated with high morbidity and mortality rates among both human and animals populations in endemic countries.¹ The disease is caused by the Rift Valley fever virus (RVFV) that belongs to genus *Phlebovirus* and family *Phenuiviridae*.² The disease was described for the first time in 1931 in the Rift Valley area in Kenya; this how the disease obtained its name

(Ref). The RVFV is transmitted mainly through several species of *Aedes* and *Culex* mosquitoes; however, other modes of transmission including vertical transmission from mother to child, sexual transmission, and through the consumption of raw milk and uncooked meat were documented.³

In addition to malaria,^{4,5} Sudan is endemic with several arboviruses including RVF, Chikungunya, Crimean–Congo hemorrhagic fever (CCHF), dengue, and West Nile virus.^{1,6–11} Infections with the RVFV

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were detected in Sudan in early 1930s.^{3,12} Since then, outbreaks of RVF occur frequently in the country.^{1,13} The disease is associated with high abortion among human and domestic animals, therefore, in addition to its negative health affects it has devastating socioeconomic impacts on animals-dependent communities in endemic countries.^{1,13,14} Recently, several outbreaks of emerging infectious diseases including RVF occurred in Sudan.^{1,6–11,13–17} Additionally, there is rapidly growing evidence about the emergence and spread of invasive diseases vectors in the region including Sudan.^{10,18–21} Studies have suggested that the major risk factors that drive this upsurge in the burden and outbreaks of infectious diseases and rapid spread of invasive diseases vectors include climate change, armed-conflicts and the growing size of population living in humanitarian crisis, globalization, and unplanned urbanization.^{1,13,22–27} These risk factors increase the dynamic and the interactions of different populations of human and animals substantially, this in turn magnifies the occurrence of spill over and pathogens sharing events across the different species of diseases-susceptible hosts.²⁸

Despite the frequent outbreaks of arboviral diseases in Sudan, still there is a huge gap in the local knowledge about the epidemiology, pathology, and the clinical presentation and outcome of patients, particularly in cases of co-infection.^{3,6} This gap mainly because of the limited sharing of information about these diseases of local public health and global health concerns.²⁹ In this communication, we report a case of a differential diagnosis challenge in areas endemic with several causes of febrile illness. Our case, a young (19-year-old) female from central Sudan was confirmed to be co-infected with RVFV malaria.

2 | CASE PRESENTATION

A 19-year-old student female from Kampo five, Kenana, White Nile state (Figure 1), has arrived at the emergency unit of Kenana. She was presented on 23th October 2019; with fever, headache, joint pain, fatigue, and loss of consciousness. The patient is a student resident in kenana district and she reported staying at home for the week before the onset of the symptoms; she reported no contact with sick or apparently ill people or animals. However, she reported being recently exposed to heavy mosquitoes' bites during that time. She complained from fever, severe diffuse throbbing headache, and joint pain specifically in the knee and elbow. These symptoms were also accompanied by progressively fatigue and muscle pain.

On initial examination, she had a normal pulse rate (74/min), respiratory rate (19/min), blood pressure (95/55),

and temperature (39°C). Blood samples were drawn from the patient and sent to the local laboratory.

A blood film was made and was positive for the presence of malaria parasite; blood film showed asexual stage trophozoites of *Plasmodium falciparum* and ICT was also positive. She was started on malaria treatment. However, considering that she did not show clinical response after 3 days on the treatment, and that the country is endemic with several arboviral diseases, which are commonly presented with overlapping or similar symptoms and clinical manifestations.³ Therefore, another sample of blood was taken on the third day and sent to the reference National Public Health Laboratory (NPHL) in Khartoum to be tested for the major viral infections endemic in the country including dengue, RVF, CCHF, and chikungunya.³ Nonetheless, considering the recent reports about RVF outbreaks in different states of the country, namely River Nile and Gedaref (Figure 1), and a sudden increase in abortion rate among cattle and sheep was reported in the area, the sample was prioritized for testing RVFV infection. The result of the real time-polymerase chain reaction (RT-PCR) confirmed infection with RVFV.

For the treatment, the patient received paracetamol infusion for the pain. For the malaria infection, the patient received artemether/lumefantrine four tablets (20 mg artemether; 120 mg lumefantrine per tablet) orally (PO) as an initial dose, followed by four tablets PO after 8 h, then four tablets PO twice daily (morning and evening) for 2 days for a total course of 24 tablets. She was advised to stay all day under mosquito net to avoid infecting mosquitoes with RVFV and maintain the virus transmission in the area and she was followed up closely to monitor her case, she responded well and recovered after 3 days. After 2 week follow-up, she showed no signs of sequela or any damage.

3 | DISCUSSION

Here we report a case of malaria and RVF co-infection that was presented with mild symptoms without the main clinical characteristics of hemorrhagic fevers including RVF, namely the hemorrhage.³⁰ This none severe presentation of RVF infection has been observed during a recent outbreak in the northern side of the country (Figure 1).¹ However, during another outbreak of RVF in the south-eastern side of the country during the same year, cases were presented with severe manifestation (Figure 1).¹³ This difference in the overall manifestation of several patients could be attributed to the sensitivity of the surveillance system and its capacity to identify and detect none severe cases during the outbreak.^{3,29} Therefore, healthcare

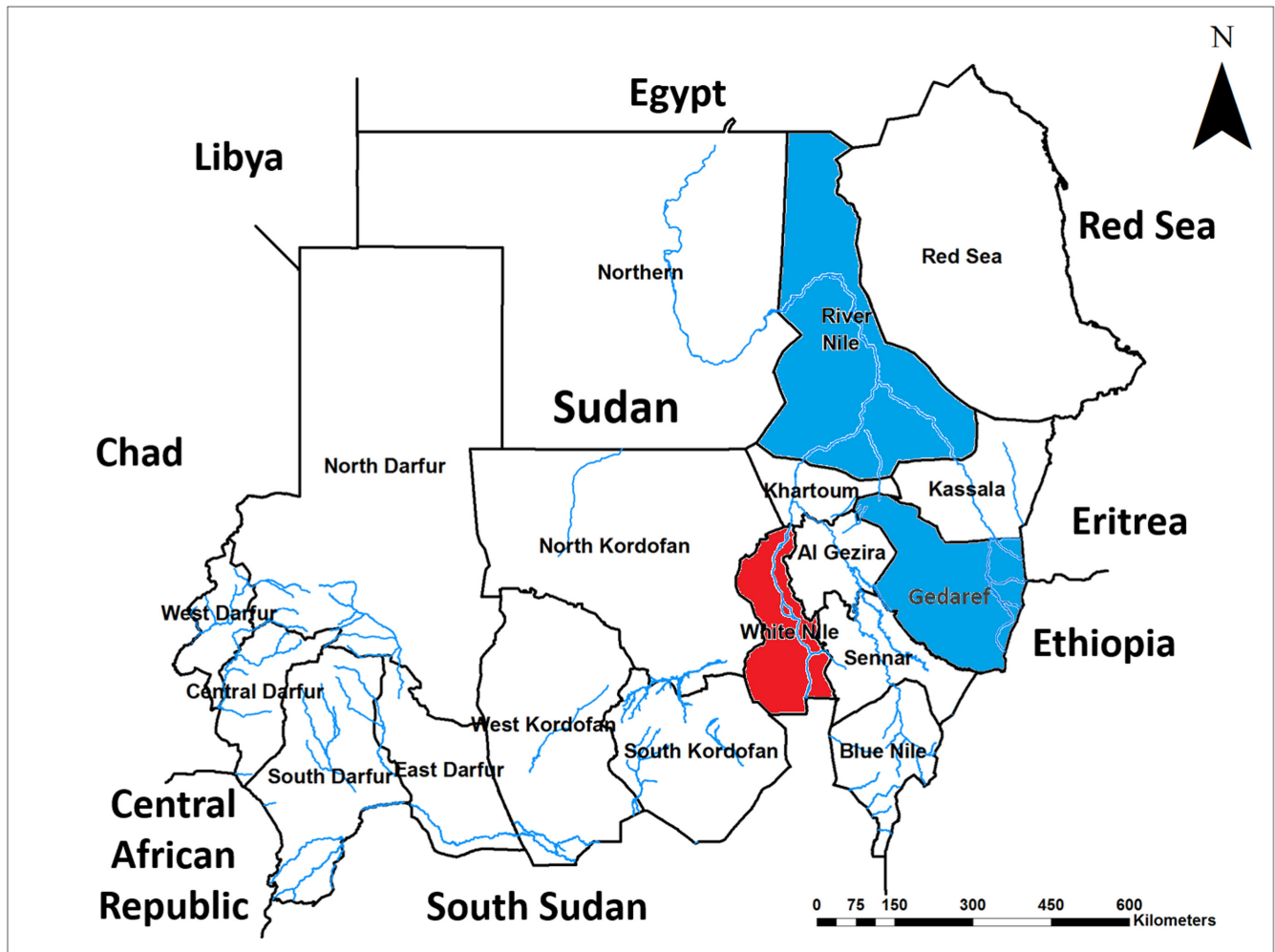


FIGURE 1 Map of Sudan shows the area of the current case study highlighted in red and the states (shaded in blue) where outbreaks of Rift Valley fever were reported during the case presentation.

providers in countries endemic with several causes of febrile illness should pay extra attention during the differential diagnosis and the possibility of co-infection should be high expected in such settings.^{3,6,7,31–33} Recently, there is growing evidence about disease emergence and unusual presentation of endemic diseases.^{24,33–35} Alternatively, this difference in the clinical manifestation of RVF infection could be attributed to variation in the virus strains of some clades of viruses are more associated with severe clinical presentations of the disease.^{36–38} A similar situation has been observed during the currently ongoing Mpox outbreak of global concern.³⁹ Clade IIb of the Mpox virus that diverged from the West African lineage is associated with globally expanded transmission outside the endemic areas with none severe clinical presentation. While on the contrary, the Democratic Republic of Congo/Central African lineage (clade I) is associated with local transmission in Africa and a higher Case Fatality Rate.³⁹

Interestingly, a substantial increase in outbreaks frequency of endemic and emerging infectious diseases has

been observed throughout the country. Several outbreaks of vector-borne diseases including malaria,¹⁷ CCHF,¹¹ chikungunya,¹⁰ dengue,³¹ RVF,¹ leishmaniasis,¹⁶ and other zoonotic emerging infectious diseases such as cholera,⁴⁰ COVID-19,⁴¹ and hepatitis E¹⁵ were reported in Sudan. These outbreaks were associated with climate change and sudden forcible displacement of human and animals populations as well as international travel and unplanned urbanization.²⁵

Considering the lack of effective treatment and zoonotic nature of arboviral diseases, their prevention and control rely on the implementation of a transdisciplinary One Health strategy^{13,42} including the integration of diseases control programs,⁴³ enhanced surveillance and control of diseases vectors,^{18,43,44} improving the water sanitation and hygiene,⁴⁵ and the use of vaccines.^{40,46} More importantly, stakeholders of health, humanitarian, and development sectors should invest more on long-term and comprehensive solutions including restoring peace and social construction, improving living

conditions, implementing adaptation and mitigation plan for climate change.²⁵ Such investment will be more rewarding and cost-effective in the long-term and will greatly contribute in achieving the Sustainable Development Goals.

In conclusion, in areas endemic with several infectious diseases like Sudan, co-infection should always be expected and investigated to improve the case management and the clinical outcome. Therefore, investment should be done on training clinical epidemiologists and improving the diagnostic capacity and surveillance system. Additionally, further studies are needed to investigate disease progress and clinical outcome in case of co-infection with two or more infectious diseases.

AUTHOR CONTRIBUTIONS

Yousif Ali: Data curation; investigation; visualization; writing – review and editing. **Emmanuel Edwar Siddig:** Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; supervision; validation; visualization; writing – original draft; writing – review and editing. **Nouh Mohamed:** Data curation; formal analysis; investigation; methodology; visualization; writing – original draft; writing – review and editing. **Ayman Ahmed:** Conceptualization; data curation; formal analysis; investigation; methodology; project administration; resources; supervision; validation; visualization; writing – original draft; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The author reports no conflicts of interest in this work.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

CONSENT STATEMENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

ORCID

Emmanuel Edwar Siddig  <https://orcid.org/0000-0001-6314-7374>

Ayman Ahmed  <https://orcid.org/0000-0002-9516-9508>

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