



CASE REPORT

Odyssean malaria in the Western Cape Province of South Africa

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Abstract

Due to the unexpected diagnosis of Odyssean malaria, cases are often missed, and the presentation is usually delayed resulting in severe complications. What makes these infections so intriguing is the lack of travel history from patients who acquire the infection while living in a non-endemic malaria area. We report the first case of Odyssean malaria in a young girl from Cape Town who presented multiple times to the health care services with a non-resolving fever amongst many other non-specific symptoms.

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Background

Laboratory confirmation of malaria is quintessential for the diagnosis of Odyssean malaria. The name Odyssean malaria is derived from Greek mythology where the Greek king Odysseus survived the Trojan War and then spent a decade wandering in the Mediterranean Sea trying to return home. Malaria transmitted through the bite of a mosquito that has passively travelled thousands of kilometres (by plane, road or train) from a malaria endemic area to survive until its next meal in a non-malaria area has been called Odyssean malaria, likened to this mythical king's journey.¹ We report a case of this rare kind of malaria in a child from Lotus River, a suburb of Cape Town, in the Western Cape Province of South Africa.

Case presentation

On the 25th of December 2021, we saw the index presentation of what was later discovered to be Odyssean malaria on a well-grown 7-year-old girl who is HIV negative and fully immunized. She initially presented with fever of 38.4°C, lethargy, diarrhoea and three seizures, one focal in nature. A series of investigations were performed including analysis of urine, stool, blood and cerebrospinal fluid following a normal computed tomography of the brain. Despite a normal full blood count (FBC), her inflammatory markers were significantly raised with a C-reactive protein (CRP) of 247mg/L. Her remaining blood work was unremarkable. The patient was commenced on ceftriaxone, a broad-spectrum intravenous antibiotic, and her 48hr CRP level improved to 53mg/L. Even though a source of infection was not identified, she recovered well and was discharged after five days of intravenous antibiotic cover. Despite conflicting evidence regarding performing electroencephalograms (EEGs) on patients presenting with febrile seizures, an elective EEG was booked for the 18th of January 2022.²

Approximately two weeks later, on the 14th of January 2022, the patient presented to hospital again with a two-day history of fever (39.8°C), vomiting and diarrhoea, backpain, poor appetite and lethargy. She was diagnosed with acute gastroenteritis and discharged on zinc and paracetamol after receiving rehydration therapy. She re-presented to the emergency unit on Sunday the 16th of January with ongoing fever, vomiting and lethargy and was diagnosed with acute otitis media and discharged on oral amoxicillin. The following day, marking the 4th presentation to health services in a period of a month, she was referred to the medical emergency unit with persistent lethargy after her elective EEG showed abnormal moderate encephalopathy.

Upon arrival at the medical emergency unit, she had a Glasgow Coma Scale of 14, she was pyrexial (38.5°C) and strikingly pale. She was haemodynamically stable with a 1/6 ejection systolic murmur and a 2cm hepatomegaly. Once again, her CRP was elevated (254mg/L), but the FBC on this admission showed a significant bicytopenia with a haemoglobin of 5.4g/dL and a thrombocytopenia of 59 x 10⁹/L. She also tested positive for COVID-19. On recognition of the abnormal FBC, the laboratory astutely performed a thick and thin film which was positive for *Plasmodium falciparum* with a high parasitaemia of 9.3%—an indicator of severe malaria. Other markers of severity were renal impairment (urea of 11.6 mmol/L), impaired level of consciousness and history of seizures on first presentation. A subsequent diagnosis of cerebral malaria was made. The patient fully recovered after treatment with intravenous artesunate. However, we were curious about how this young girl who was without a travel history and living in a non-malaria-endemic area acquired this infection. An environmental investigation by The National Institute for Communicable Diseases of South Africa could not find a source of infection but suspected a vector source mosquito that potentially hitch-hiked in the luggage of a neighbour who travelled from Mozambique in the last week of December 2021.³

Discussion

Billions of dollars are invested annually into malaria research and global malaria elimination strategies. As a result, malaria deaths have significantly reduced in the past two decades. The COVID-19 pandemic however hindered some of the progress when 2020 saw a 12% global increase in malaria deaths compared to 2019.⁴ In many developing countries malaria remains a leading cause of morbidity and mortality.⁵ In South Africa, only certain areas are seasonally endemic to malaria (Limpopo, Mpumalanga and Northern KwaZulu-Natal); the risk of transmission being higher between September and May.⁶ Technological advances in tourism and transportation however puts traveling and non-travelling South Africans at perennial risk of acquiring imported malaria and the more unusual Odyssean malaria.

Between the period of 1996 and 2004, 46 cases of Odyssean malaria were reported in the non-endemic Gauteng Province. This was followed by an 8-cluster outbreak of 21 cases between 2007 and 2013, and a 2-cluster outbreak of 5 cases in January 2021.¹ It is not surprising that all the cases were detected in the province of Gauteng as it is the hub for travellers from Sub-Saharan endemic Africa. Gauteng also lies within proximity to endemic provinces which makes windborne malaria transmission not impossible — Anopheles mosquitoes may cover up to 300km of distance on high-altitude flights.⁷ The

case of Odyssean malaria in the Western Cape is intriguing and to the best of our knowledge has not previously been reported.

True thrombocytopenia, one of the signs of severe malaria, should be confirmed by examining a blood smear to exclude ethylenediamine tetra-acetic acid induced platelet clumping.⁸ On a smear, the malaria trophozoite can be seen which is how the laboratory identified the infection in our case. The symptoms and clinical presentation of malaria are non-specific which made this laboratory process critical in this diagnosis of Odyssean malaria and lifesaving for this patient. Malaria should be suspected in any patient presenting with a fever in a malaria-endemic area. In a non-endemic area, investigating all patients with a fever would be costly, therefore clinicians should be trained to conduct a parasitological test where there is a fever with no obvious cause, especially in association with thrombocytopenia, even in the absence of travel.⁹

The clinical symptoms of both malaria and bacteraemia overlap, and concomitant bacteraemia has been frequently reported in association with severe malaria in endemic areas with a notable increased risk of mortality in children.¹⁰ Third-generation cephalosporins such as ceftriaxone are recommended as an add-on therapy with appropriate antimalarials in cases of severe malaria to cover concomitant sepsis.⁹ Our patient showed a good clinical response and remained symptom free for two weeks after receiving five days of ceftriaxone. This is an appropriate response when third generation cephalosporins are used to treat gram negative/ gram positive sepsis but an unlikely response for a severe malaria infection. It is therefore possible that the malaria infection occurred after the presentation and treatment of the initial sepsis.

The vector source in our case was thought to be linked to Mozambique, one of South Africa's neighbouring countries where there is malaria risk throughout the year. The time period of the identified traveller, which is noted to be the last week of December, corresponds with the incubation period of malaria (which is a minimum of seven days) and the patient's second clinical presentation on the 14th of January. This may suggest the possibility of the malaria infection occurring after treatment of the initial sepsis. Another possibility which should be considered is a mosquito bite during one of many play dates at a nearby diverse community that is occupied by individuals and families from South Africa and Sub-Saharan African countries with endemic malaria, who could have unwittingly transported an infected Anopheles mosquito from an endemic area along an 'Odyssean journey' of more than thousands of kilometres.

For the past two years COVID-19 has impacted all spheres of life (social, economic, psychological) including putting a major strain on the South African Health Department. Its dominating presence has resulted in delayed treatment-seeking behaviour due to movement restrictions and reduced healthcare-worker malaria awareness.¹¹ It is important to note that COVID-19 infection in children is often an 'incidental finding' and may not be the cause of severe illness in critically unwell children but rather a red herring that can further delay the true identification of unusual presentations of fever.

COVID-19 has also disrupted and complicated malaria control programmes at all levels.¹¹ The World Health Organization encourages the world to refocus on global control and elimination strategies even during the COVID-19 pandemic. Specifically for South Africa, the aim is to eliminate malaria (eradication of local transmission) by 2023.¹²

Conclusion

Modern transportation has made travel easily accessible. In the same breath, it's that accessibility that facilitates spread of infectious diseases to unlikely places and to global proportions. This case of Odyssean malaria is a stark reminder that malaria has no borders. Clinicians should consider and test for malaria in all patients presenting with an unknown cause of a fever, even during the COVID-19 pandemic where co-infection is possible in order to avoid delays in diagnosis and progression to severe

presentations of the disease as in our patient. This should be promptly followed by notification, which is equally important, to ensure timely investigation by the malaria control programme.

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