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Guillain-Barré syndrome following falciparum malaria infection: a case report

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Abstract

Background Malaria is an infectious disease caused by Plasmodium parasites, transmitted to humans by infected female Anopheles mosquitoes. Five Plasmodium species infect humans: P. vivax, P. falciparum, P. ovale, P. malariae, and P. knowlesi. Guillain-Barré Syndrome (GBS) is an inflammatory condition that can lead to paralysis, autonomic dysfunction, respiratory failure, and sensory symptoms. GBS typically follows an infection with Campylobacter bacteria, commonly found in undercooked poultry, but is rarely associated with malaria.

Clinical presentation A 16-year-old female patient presented to our emergency department with a 1-day history of altered mentation. She had experienced a severe global headache and fever for 3 days prior to presentation. The patient tested positive for falciparum malaria and was admitted to the ward, where she received IV artesunate and other supportive management. After 3 days of admission, she noticed weakness and numbness in her lower extremities. Subsequently, the weakness progressed upward to involve her upper extremities. After extensive workup, the patient was managed with consideration of Guillain-Barré Syndrome (GBS), and she made a complete recovery after 12 weeks.

Discussion Guillain-Barré Syndrome (GBS) is an acute paralytic illness often triggered by infections, particularly viral ones. It is the leading cause of sudden muscle weakness, typically following respiratory or gastrointestinal infections, with Campylobacter jejuni being the most common cause. This patient's neurological symptoms pointed to paralysis of the lower motor neurons. Guillain-Barré Syndrome is also suggested by elevated protein levels and a lack of cells in the cerebrospinal fluid. This clinical picture emerged following a Plasmodium falciparum infection. Although the specific subtype (demyelinating or axonal) was not determined in this case due to the absence of a nerve conduction study, demyelinating subtypes have been found in GBS following Plasmodium infection.

Conclusion In conclusion, while malaria is an exceptionally rare cause of Guillain-Barré Syndrome (GBS), it should be considered in patients with recent malaria infection who present with symptoms of lower motor neuron lesions.

Highlights

- GBS is often triggered by infections, and cases have been reported following Plasmodium falciparum malaria, though this association is relatively rare.

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- It is believed that the immune response to the malaria infection may mistakenly target peripheral nerves, leading to the characteristic symptoms of GBS.
- Patients may present with progressive muscle weakness, tingling, and numbness that typically starts in the legs and can ascend. This can lead to respiratory difficulties in severe cases.
- Diagnosis is primarily clinical, supported by nerve conduction studies and lumbar puncture to analyze cerebrospinal fluid (CSF), which often shows elevated protein levels with normal cell counts (albuminocytologic dissociation).
- Treatment for GBS may include immunotherapy options such as intravenous immunoglobulin (IVIG) or plasmapheresis. Supportive care, including monitoring respiratory function and rehabilitation, is also crucial.
- The prognosis for GBS varies; many patients experience significant recovery over weeks to months, but some may have residual weakness or other neurological deficits.
- In regions where falciparum malaria is endemic, healthcare providers should be aware of the potential for GBS as a post-infectious complication, enabling timely diagnosis and management.

Keywords Guillain-barré syndrome, Plasmodium falciparum, Paresis

Background

Malaria is an infectious disease caused by parasites of the Plasmodium genus. It is transmitted to humans through the bite of an infected female Anopheles mosquito. There are five species of Plasmodium that can infect humans: P. vivax, P. falciparum, P. ovale, P. malariae, and P. knowlesi [1, 2]. Globally in 2022, there were an estimated 249 million malaria cases in 85 malaria endemic countries and areas (including the territory of French Guiana), an increase of 5 million cases compared with 2021. The main countries contributing to the increase were Pakistan (+2.1 million), Ethiopia (+1.3 million), Nigeria (+1.3 million), Uganda (+597 000) and Papua New Guinea (+423 000). In 2015, the baseline year of the Global technical strategy for malaria 2016–2030 (GTS), there were an estimated 231 million malaria case [5]. The overall global mortality rate from malaria ranges from 0.3 to 2.2%. However, in tropical countries, the mortality rate for severe forms of the disease rises significantly, ranging from 11 to 30% [3, 4].

The Plasmodium falciparum parasite is primarily responsible for the majority of neurological complications associated with malaria. However, Plasmodium vivax can also cause seizures in children and lead to neurological complications such as Guillain-Barré Syndrome (GBS) [3, 5]. Other neurological manifestations of malaria include psychiatric symptoms, seizures, myelopathies, peripheral neuropathies, myopathies, extrapyramidal syndromes, intracranial hemorrhage, and, less commonly, reversible cerebral vasoconstriction syndrome (RCVS) and posterior reversible encephalopathy syndrome (PRES). Neurological issues can also arise as side effects of antimalarial treatments [6, 7].

Guillain-Barré Syndrome (GBS) is an inflammatory condition characterized by generalized paralysis, bulbar muscle weakness, autonomic dysfunction, respiratory failure, and the presence or absence of sensory symptoms. It most commonly occurs following an infection with Campylobacter, a type of bacteria often found in undercooked poultry. However, its occurrence following malaria is very rare [8, 9].

The occurrence of Guillain-Barré Syndrome (GBS) associated with malarial infection is very rare, with only a few cases documented in the literature [11, 14, 17]. Here, we present a case of acute flaccid quadriparesis of the lower extremities in a patient with a positive Plasmodium malaria infection.

Clinical presentations

A 16-year-old female patient presented to our Emergency department with a 1 day history of altered mentation and the patient had severe global type of headache and fever for 3 days before presentation. The patient was stabilized in the ED and tested positive for falciparum malaria. She was then admitted to the ward and received IV artesunate along with other supportive care. After 3 days of admission the mentation started to improve but the patient noticed weakness and numbness on her lower extremities and she couldn't lift her leg upward without support. Subsequently the weakness progressed upward to involve the upper extremity.

On her initial evaluation in the ED, pertinent findings were that she appeared acutely sick but was not in respiratory distress, with a respiratory rate of 22 bpm, BP of 120/80, and a pulse rate of 110 bpm. Other pertinent findings were noted in the CNS examination: GCS was 14/15, pupils were midsized and reactive bilaterally, power was 5/5 in all extremities, and deep tendon reflexes were normal.

On retrospective history, the patient denied any history of back pain or trauma to the back. There were no preceding gastrointestinal or respiratory symptoms.

On reevaluation on the third day of her hospital stay, physical examination revealed that the patient appeared anxious but showed no signs of cardiorespiratory distress. Her blood pressure ranged from 100/70 to 120/80

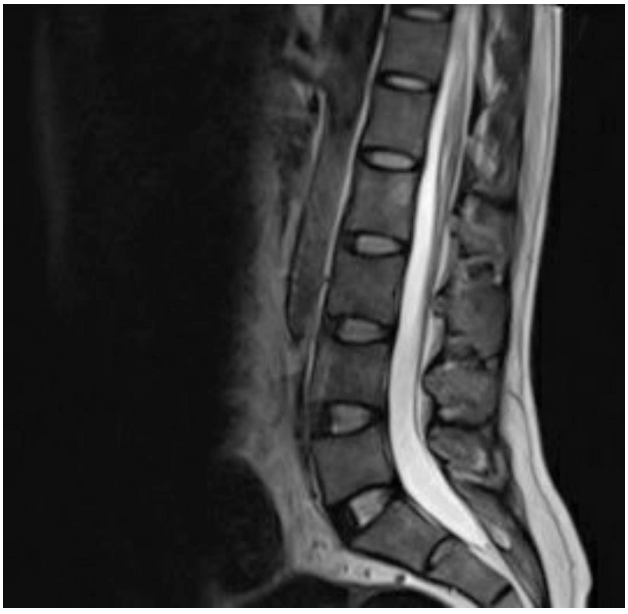

Fig. 1 Mid saggital T2 weighted image of lumbosacral spine MRI showing normal vertebral height, inter-vertebral disc, cord, nerve roots as well as normal intra and extra dural spaces

mmHg, and her pulse rate ranged from 90 to 100 beats per minute. Her respiratory rate was 24 breaths per minute, temperature was 37.7 °C, BMI was 18.4, and oxygen saturation was 95% on room air. She was alert and oriented to time, place, and person, with a Glasgow Coma Scale (GCS) score of 15/15. Pupils were reactive bilaterally and midsized. Motor examination revealed a motor score of 3/5 in both lower extremities and 4/5 in the upper extremities, decreased muscle tone, absent deep tendon reflexes (DTR) of 0/4, and a negative Babinski sign, consistent with lower motor neuron injury. There were no cranial nerve abnormalities, but there was hyperesthesia in both lower extremities. Meningeal signs were negative. Conjunctivae were pink, and sclerae were non-icteric. Heart sounds S1 and S2 were well heard with no murmurs or gallops. The chest was clear and resonant. Abdominal examination revealed no masses or organomegaly, and there was no edema in the extremities.

Laboratory investigations in the ward included a complete blood count (CBC) showing a white blood cell (WBC) count of 10,600/mm^3, hematocrit (HCT) of 32.2%, mean corpuscular volume (MCV) of 90, and platelets of 160,000/mm^3. Urinalysis and stool occult blood test results were normal, with no parasites or pus cells identified. Random blood sugar (RBS) was 183 mg/dL, and tests for Anti-Nuclear Antibody (ANA), Antineutrophilic Cytoplasmic Antibody (ANCA), and Antiphospholipid Antibodies (APLA) were normal. Renal function tests (RFT), serum electrolytes, coagulation profile, and erythrocyte sedimentation rate (ESR) were all normal. Serology for syphilis was negative. Chest radiograph, echocardiogram, EKG, and carotid doppler were normal. Lumbosacral spinal MRI was unremarkable (Fig. 1).

Nerve conduction test was not readily available but Cerebrospinal fluid (CSF) analysis via lumbar puncture done on her 10th day of hospital stay (after 7 days of weakness) showed a normal WBC count (2 WBC/HPF) but elevated albumin level (90 mg/dL) and negative gram staining.

The diagnosis of a lower motor neuron lesion secondary to Guillain-Barré Syndrome (GBS) was considered. The patient was monitored in the ward, and the patient's family was advised on the possibility of administering IV immunoglobulin (IVIG); however, they were unable to afford it. With no further management, the patient showed improvement after 4 weeks, with the motor examination returning to 4/5 in the lower extremities and 5/5 in the upper extremities. She continued home physiotherapy and was advised to adhere to follow-up visits. She has been seen in the neurology clinic on several occasions, and the patient made a complete recovery in 12 weeks.

Discussion

This patient's neurological symptoms pointed to paralysis of the lower motor neurons. Guillain-Barre syndrome is also suggested by elevated proteins and a lack of cells in the cerebrospinal fluid. This clinical picture emerged following a Plasmodium falciparum infection.

Guillain-Barré Syndrome (GBS) is a well-known acute paralytic illness that often arises after infections, especially viral ones. It's the leading cause of sudden muscle weakness, usually following respiratory or gastrointestinal infections, with Campylobacter jejuni being the most common culprit [6, 10]. Besides viruses, GBS can also be triggered by bacterial infections like Mycoplasma, Haemophilus influenzae, and Rickettsia rickettsii, as well as protozoal infections such as Leishmania donovani and Plasmodium species, including both Plasmodium falciparum and Plasmodium vivax. In rare instances, GBS has been associated with inflammatory conditions like sarcoidosis and the use of certain medications. [11.12.13.14]

Guillain-Barré Syndrome (GBS) is an immune-mediated, acute inflammatory disorder affecting nerves globally and at any age, where the immune system mistakenly targets nerve antigens due to molecular mimicry [10, 11]. In cases associated with malaria, the immune response during the parasite's asexual stage, involving cytokine release, is believed to cause nerve damage, though the exact mechanism is not fully understood.[7,] Immune-mediated damage is thought to drive the development of GBS, with the inflammation triggered by cytokines affecting the axons and leading to demyelination. This could explain the link between malaria infection and GBS. Another possible explanation is that GBS might

result from occlusion of the vasa nervorum by malaria parasites or immune complexes [6, 12, 13].

Although demyelinating or axonal subtype was not known in this case because nerve conduction study was not done, the previous literature suggests demyelinating subtypes were found in GBS post plasmodium infection [11, 13, 17].

An analysis of 11 cases revealed that three patients were infected with P. vivax, while eight had a history of falciparum malaria. All but two of the patients exhibited distal symmetric sensory impairments. Among the cases, seven (three with P. vivax and four with P. falciparum) experienced mild paralysis, which completely resolved within two to six weeks without requiring special treatment. However, severe paralysis and respiratory failure were observed in four cases of falciparum malaria, leading to the deaths of three patients. One recipient of intravenous immunoglobulin made a full recovery [17].

The clinical symptoms of malaria vary depending on the parasite type and infection severity. Common symptoms include cyclical fever with chills and sweating, severe headache, intense muscle and joint pain, fatigue, nausea, vomiting, abdominal pain, and sometimes diarrhea. Anemia and jaundice due to liver involvement are also common. Severe malaria, which demands urgent care, may present with impaired consciousness, respiratory distress, acute renal failure, severe anemia, hypoglycemia, and shock. Symptoms typically appear 7 to 30 days after a mosquito bite, though they can manifest later [3, 6].

Although electrophysiological studies are useful for confirming nerve involvement, Accurate diagnostic criteria are essential for patient care and research, including clinical trials and vaccine safety studies [18]. Key indicators of GBS include progressive muscle weakness in multiple limbs, areflexia (absent reflexes), and possibly sensory changes, pain, autonomic dysfunction (such as heart rate variability and blood pressure fluctuations), or cranial nerve involvement. CSF analysis showing elevated protein levels with a normal white blood cell count (cyto-albuminogenic dissociation) supports the diagnosis, especially when there is a recent history of infection [10, 14–16]. In this case, the neurological signs suggested progressive lower motor neuron paralysis with areflexia, autonomic dysfunction, and paraesthesia, while CSF analysis confirmed cyto-albuminogenic dissociation. The patient also had confirmed Plasmodium falciparum malaria. Typically, the interval between fever and weakness ranges from 1 to 6 weeks, but this case showed a seven-day delay. This report illustrates that GBS may follow Plasmodium falciparum malaria.

Treatment of Guillain-Barré Syndrome (GBS) primarily involves supportive care, managing symptoms, and addressing the autoimmune response. Intravenous Immunoglobulin (IVIG) and Plasma Exchange (plasmapheresis) are commonly used first-line therapies to reduce the immune attack on the nerves. Although GBS can resolve without these treatments like this case, recovery may be slower and more variable. Supportive care is crucial, especially for respiratory management, with mechanical ventilation required in severe cases. Pain management strategies help alleviate severe muscle pain, while physical therapy is essential for improving strength, mobility, and function, and preventing complications from immobility. [11.14.17] In this case, the patient was managed with gabapentin for pain, physiotherapy, and labetalol for autonomic dysfunction; she did not require mechanical ventilation.

Conclusion

In conclusion, while malaria is an exceptionally rare cause of Guillain-Barré Syndrome (GBS), it should be considered in patients with recent malaria infection who present with GBS symptoms. Further research is essential to elucidate the molecular mechanisms linking severe malaria with neurological complications such as GBS. This case report underscores the importance of recognizing the potential association between GBS and malaria, aiming to increase awareness among physicians in endemic regions.

Limitation of the study

- Due to a lack of resources, the report does not provide electrophysiological testing results that could support the diagnosis of GBS, even though it notes clinical presentations, increased proteins, and a lack of cells in cerebrospinal fluid (CSF) as signs.
- Longer follow-up would give more information about the long-term results and possible recurrence of symptoms or consequences related to GBS post-malarial infection, even though the patient recovered well after 12 weeks.
- As with any case report, the presentation of the case may contain inherent biases, such as selectively emphasizing some data while downplaying others that would contradict the conclusion.

Abbreviations

CSF	Cerebrospinal fluid
CBC	Complete blood count
GBS	Guillain-Barré syndrome
LP	Lumbar puncture
AFI	Acute febrile illness

Supplementary Information

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Supplementary Material 1

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Author contributions
MAK: Involved in the conception and design of the study, drafting and revising of the article and final approval of the version to be submitted and also involved in direct management of the patient. MAE: Involved in the conception and design of the study, drafting and revising of the article and final approval of the version to be submitted and also involved in direct management of the patient. ABT: Involved in the conception and design of the study, drafting and revising of the article, final approval of the version to be submitted.EPS: Involved in the study's design, drafting, and revising of the article and final approval of the version to be submitted.MTB: Involved in the design of the study, drafting and revising of the article, and final approval of the version to be submittedETA: Involved in the design of the study, drafting and revising of the article and final approval of the version to be submittedHMN: Involved in the design of the study, drafting and revising of the article and final approval of the version to be submitted.

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Data availability
On a valid request, the corresponding author will provide access to the datasets that were gathered and used to conduct this article.

Declarations

Ethical approval
The Ethical approval for this report was obtained from College of Medicine and Health Science, Mizan-Tepi University [R.N. HSE/00429/2012].

Informed consent
Before preparing the case report, the patient's family provided written informed consent to write the case and be published.

Competing interests
The authors declare no competing interests.

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