Annals of Clinical and Medical Case Reports

Case Report ISSN 2639-8109 Volume 7

A Case Report of Fever in Returned Traveller

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Received: 01 Aug 2021
Accepted: 14 Aug 2021
Published: 19 Aug 2021

Keywords:

Falciparum malaria; Anopheles mosquitoes; Prognosis and management

Citation:

Lwin ZT, A Case Report of Fever in Returned Traveller. Ann Clin Med Case Rep. 2021; V7(4): 1-3

1. Abstract

We report a rare case of severe falciparum malaria in a healthy 28-year-old gentleman in the UK. Malaria is one of the common fatal diseases in tropical countries where doctors are remarkably familiar with handling different types of malaria. In contrast, in the UK, malaria cases are not commonly seen, and all are imported cases so far. As such, clinicians in the UK may not be confident enough to tackle such kind of cases when they encounter them. In this case report, clinical presentation, how to make diagnosis and management of severe falciparum malaria based on our local hospital protocol are emphasized.

2. Introduction

Plasmodium falciparum is the deadliest species of plasmodium that begets malaria in human. The parasite is transmitted through the bite of a female anopheles mosquito and it causes the most dangerous form of the disease, falciparum malaria. Thus, patients with falciparum malaria should be admitted for a minimum of 24-hour observation. Since falciparum malaria is a curable disease, early diagnosis and prompt treatment is of paramount importance. Something to bear in mind is that patients with severe falciparum malaria can deteriorate rapidly so early involvement of intensivists is critical. Patients generally present symptoms within a month of returning from the tropics but 10% of cases present symptoms up to 3 months after travel. All patients should be referred to ID team. Despite falciparum malaria being severe and fatal, if patients receive early diagnosis and prompt treatment, their lives could be saved.

3. Case Report

This is a 28-year-old gentleman who was initially admitted to COVID assessment Unit, Ninewells hospital complaining of feeling generally unwell, high fever with sweating and headache for 4 days. He described headaches as shooting pain and that came on when waking up in the night and in the morning radiating to the occipital region but there was neither photophobia nor pain on neck flexion. The fever accompanied by shivering came every day.

Furthermore, He had an episode of loose stool 3 days prior to his fever. On exploring his travel history, he spent nearly a month in Zambia, Africa where he slept without a net and was bitten by mosquitoes. Those symptoms started 10 days after returning from Zambia. He did not take any malaria prophylaxis when he travelled there.

On clinical examination, he looked very tired, lethargic and quite sleepy most of the time. On admission, his temperature was 39.1 C with BP being 104/66 mmHg and Heart rate being 128/min. His oxygen saturation was 97% on room air and respiratory rate was 20/min. As to systemic examination findings, moderately enlarged spleen was palpable. Apart from that, other examination findings were unremarkable.

When it comes to initial investigations, rapid covid test was performed and that came back as negative. In light of travel history and clinical presentation pattern, 3 sets of malaria blood films were carried out urgently within an hour of admission. A couple of hours later, haematology lab directly informed the doctor in charge over the phone that plasmodium falciparum malaria accounted for 6% was detected on blood film. His blood tests on admission were as follows:

Hb 125 g/L, WBC 4.3 x 109 L, Platelet 45x 109 L, PT ratio 1.2, APTT ratio 1.2, Na 132 mmol/L, K 3.3 mmol/L, Urea 10.6 mmol/L, Creatinine 125 μmol/L, CRP 259 mg/L, Lactate 2.3 mmol/L, ALT 62 μ/L, Bilirubins 32 μmol/L, corrected Calcium 2.20 mmol/L and glucose 7.4 mmol/L.

As soon as falciparum malaria was confirmed, we discussed with ID consultant on call overnight and commenced IV artesunate 2.4 mg/kg bolus at 0 hours, 12 hours and 24 hours within 3 hours of admission then brought him to medical High Dependency unit for close monitoring in view of severe falciparum malaria.

The following day, he became much better clinically and his parasites count decreased, he was stepped down to Infectious disease ward. He got 2 days of IV artesunate in total and then changed to oral Riamet (artemeter with lumefantrine) on day 3 of his admission. On day 3, his blood tests showed significant improvement as below:

3.1. Malaria Blood Film: Negative

Hb 119, WBC 3.4, Platelet 76, Na 140, K 3.2, Urea 5.8 and creatinine 71, ALT 62, Biliriubin 13, lactate 1.3, blood cultures negative.

On day 3, he managed to eat and drink well, and no longer required IV fluids and IV injection then he was discharged on 3rd day of admission with oral regime (artemeter with lumefantrine) at 0 hour, 8 hours, 24 hours,36 hours,48 hours and 60 hours respectively. On discharge, he was advised to avoid contact sports for 6 weeks in light of his splenomegaly and the team asked his GP to recheck full blood count in two weeks' time.

4. Discussion

Malaria is a life-threatening disease caused by the plasmodium parasites that are transmitted to people through the bites of infected female Anopheles mosquitoes. It is curable if patient receives (early) diagnosis and treatment promptly and correctly.

According to the latest World Malaria report on 30 November 2020, there were 229 million cases of malaria in 2019 compared to 228 million cases in 2018. The estimated number of malaria deaths stood at 409,000 in 2019 compared to 411,000 deaths in 2018. The WHO African Region continues to carry a disproportionately high share of the global malaria burden. In 2019, the region was home to 94% of all malaria cases and deaths. In 2019, 6 countries counted for approximately half of all malaria deaths worldwide: Nigeria (23%), the Democratic Republic of the Congo (11%), United Republic of Tanzania (5%), Burkina Faso (4%), Mozambique (4%), and Niger (4%) each [1].

In the UK, there were reports of 1792 imported cases in 2018 and out of 1792 cases, plasmodium falciparum accounted for 1375 cases. In addition, 1276 cases were imported from different parts of Africa while 1 case was from south Asia country and 99 cases were not mentioned where it came from [2].

It is prevalent in sub-Saharan Africa, Central and South America, the Middle East, South Asia, and South East Asia. [3] Many people travelling to areas within these countries will be at risk of malaria and will need to take appropriate precautions to protect themselves.

When it comes to symptoms, infection with malaria parasites may result in a wide variety of symptoms, ranging from absent or very mild symptoms to severe disease and even death. Malaria disease can be categorized as uncomplicated or severe (complicated). The initial symptoms of malaria are flu-like and include a high fever, headache, sweats, chills and vomiting. These symptoms are often mild and can sometimes be difficult to identify as malaria. Other symptoms can be muscle pains, diarrhea and generally feeling unwell.

Following the infective bite by the Anopheles mosquito, the incubation period goes by before the first symptoms appear. The incubation period in most cases varies from 7 to 30 days. The shorter periods are observed most frequently with P. falciparum and the longer ones with P. malariae [4].

With some types of malaria, the fever occurs in 48-hour cycles. During these cycles, patients feel cold at first with shivering. They then develop a fever, accompanied by severe sweating and fatigue. These symptoms usually last for 6 to 12 hours.

The most serious type of malaria is caused by the Plasmodium falciparum parasite. Without prompt treatment, this type could lead to quickly developing severe and life-threatening complications, such as breathing problems and organ failure [5].

According to the 1990 initial world health organization [6], cerebral malaria, severe anaemia (hemoglobin < 50 g/l), acute renal failure, pulmonary oedema and acute respiratory distress syndrome [7], hypoglycemia (blood glucose concentration <2.2 mmol/l), circulatory collapse (algid malaria), disseminated intravascular coagulation and metabolic acidosis were classified as severe and poor prognosis factors.

World health organization 2000 criteria added other symptoms such as impaired consciousness, prostration or weakness, hyperparsitemia >5% parasitized erythrocytes or > 250 000 parasites/ul, hyperpyrexia Tmax >40 C, hyperbilirubinemia (total bilirubin > 43 μmol/l) as indicators for severe malaria and poor prognosis factors.

Thrombocytopenia is the most common laboratory abnormality (60% of cases), followed by hyperbilirubinemia (40%), anaemia (30%), and elevated hepatic aminotransferase levels (25%). [9] The leukocyte count is usually normal or low, but neu-turophilia with a marked increase in band forms (left shift) is present in most cases. The erythrocyte sedimentation rate, C-reactive protein, and procalcitonin are almost invariably elevated. The severity of malaria corresponds to the degree of the laboratory abnormalities. In one study of travellers who returned from the tropics, thrombocytopenia and hyperbilirubinemia had a positive predictive value of

95% for malaria [10].

The optimum diagnostic procedure is examination of thick and thin blood films by an expert to detect and speciate the malarial parasites. To exclude reliably, at least three separate sets of malaria blood films are needed. P. falciparum and P. vivax (depending upon the product) malaria can be diagnosed almost as accurately using rapid diagnostic tests (RDTs) which detect plasmodial antigens. RDTs for other Plasmodium species are not as reliable [11].

5. Management

Any patients who have high suspicion of falicparum malaria should be admitted owing to the risk of rapid deterioration even after starting treatment.

Artemisinin combination therapy is recommended for the treatment of uncomplicated P. falciparum malaria. Artemether with lumefantrine is the drug of choice; artenimol with piperaquine phosphate is a suitable alternative. Oral quinine or atovaquone with proguanil hydrochloride can be used if the artemisinin combination therapy is not available. Quinine is highly effective but poorly tolerated in prolonged treatment and should be used in combination with an additional drug, usually oral doxycycline.

Severe or complicated falciparum malaria should be managed in a high dependency unit or intensive care setting. Intravenous artesunate is indicated in all patients with severe or complicated falciparum malaria, or those at high-risk of developing severe disease (such as if more than 2% of red blood cells are parasitized), or if the patient is unable to take oral treatment. Following a minimum of 24 hours of intravenous artesunate treatment, and when the patient has improved and is able to take oral treatment, a full course of artemisinin combination therapy should be given. A full course of oral quinine with doxycycline (or clindamycin [unlicensed]), or atovaquone with proguanil hydrochloride are suitable alternatives.

Treatment of severe or complicated falciparum malaria should not be delayed whilst obtaining artesunate. Quinine by intravenous infusion [unlicensed] should be given if artesunate is not immediately available; it should be continued until the patient can take oral quinine to complete a full course. Oral doxycycline (or clindamycin [unlicensed]) should also be given when the patient can swallow.

In most parts of the world, P. falciparum is now resistant to chloroquine which should not therefore be used for treatment. Mefloquine is also no longer recommended for treatment because of concerns about adverse effects and non-completion of courses.

Specialist advice should be sought when considering the use of pyrimethamine with sulfadoxine as an alternative drug in combination with quinine [12].

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