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# Cerebral Malaria complicated with multiorgan failure: A Case Report with Review of literature

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**Abstract** Libya is free from local malaria transmission and has been reported as one of malaria free countries. The last local reported case in Libya, according to literature, was 1973. In this paper, we present a case of a 25-year-old Libyan male Patient who came to Sebha Medical Center on 14-09-2017. He complained from high-grade fever, rigors, sweating and fatigue for one week, he had showed a history of travel to an endemic area for malaria (Niger). The laboratory investigations were positive for Plasmodium falciparum Malaria. The course of the disease was complicated with multiorgan Failure.The following is a review of literature for malaria associated with complications.

## Introduction

**Malaria** is a serious and sometimes fatal disease caused by a parasite that commonly infects a certain type of mosquito, which feeds on human blood. 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. People who get malaria are typically very sick with high fever, chills, and flu-like illness. In general, malaria is a curable disease if diagnosed and treated promptly and correctly. Treatment depends on many factors including disease severity, the species of malaria parasite causing the infection and the part of the world in which the infection took place.[1]

Malaria infection is common in Sub-Saharan Africa. In Libya Malaria is rare but some cases of malaria outbreak have been reported, but the worst fear among the authority is the invasion of the mosquitoes that carry the deadly disease.

Malaria was endemic in Libya until 1973, when it was declared by WHO to be a Malaria-free country.[1] The situation continued like this until 1976 when there was an epidemic febrile illness among petroleum company workers. The blood samples of all cases were positive for falciparum malaria, as reconfirmed in a referral lab.[2]

In 2004 cases of malaria were again discovered in Libya. All cases were confirmed microscopically, except for one case loss from an imported case.[3]

The annual loss that was thought to have been introduced per year of healthy life per 100.000 people from malaria in Libya has increased by 19.3%. Since 1990, an average of 0.8/ a year though this has been the trend overall, adjust the filters at the top of visualization to see how the rate of annual loss of healthy life due to malaria has changed over time for men and women of specific age groups in Libya.[4]

**Malaria in Libya by sex over a lifetime:-**

The health burden of malaria in Libya, as measured in years of healthy life loss per 100.000 for men, peaks at age 15 -19. It affects men at the lowest rate at age 80. Women are affecting at highest rate from malaria in Libya at age 40-44. The least harmful rate was identical for men and women at 0.1.

Malaria impact is relative to other location in North Africa and the Middle East.

**Mortality –years of healthy life lost**

| Location | mortality rate (per 100.000) | change (1990-2013) |
|---|---|---|
| Yemen | 21.2 | -45% |
| Sudan | 14.0 | -67% |
| Syria | 0.1 | -70% |
| Saudia Arabia | 0.0 | -76% |
| Marocco | 0.0 | -39% |
| UAE | 0.0 | -47% |
| Iran | 0.0 | -69% |
| Egypt | 0.0 | -68% |
| Algeria | 0.0 | -71% |
| Oman | 0.0 | -68% |

**Case presentation**:-

A 25-year-old Libyan male attended Sabha Medical Center with a history sudden onset of high grade fever, rigor, sweating and fatigue (flu like illness) for one week before admission, and also abdominal pain mostly at right hypochondrium and epigastric area for three days and also decreased level of consciousness for one day. The past medical history showed, no H/o drug intake, drug abuse or blood transfusion and no H/o of any surgical intervention. He gave a history of recent travel to an endemic area (Niger). The patient stayed abroad for about 33 days and the symptoms started 10 days after returning to Libya. He did not receive any prophylactic drugs before departure. He had no history of previous malaria illness. He did not undertake any preventive measures against Mosquito bites abroad such as bed nets, clotting or apply insect repellent.

**On examination**: Blood pressure was 150/90, Temp was 40.5, Heart rate was 100, RR was 36, Urine output was 1500/24 h. The patient was not feeling well. He was ferbile, dehydrated, palle, deep yellow jaundice, tachyapnic, fine tremor at upper limbs at rest. He had no skin rash, no lymphadenopathy.

CNS: no neck stiffness, pupils RRR, generalized hypotonia and hyporeflexia, power right 4/5 and left 2/5, sensation normal no cranial lesion,

CVS: normal S1 and S2, tachycardia, no legs oedema,

Chest: clear

Abdomen: soft and lax and tender hepatomegaly, tenderness at epigastric area, no mass no ascites.

**The management done as the following:**

| Investig. | 14.09 | 17.09 | 22.09 | 25.09 | 01.10 |
|---|---|---|---|---|---|
| WBC | 7.6 | 18.5 | 7.3 | 17.4 | 6.1 |
| HB | 9.5 | 3.5 | 6.3 | 11.2 | 8.6 |
| Platelets | 82 | 21 | 108 | 172 | 269 |
| T.BILI | 10.7 | 17.7 | - | 3.1 | - |
| D.Bili | 8.6 | 7.8 | - | - | - |
| LDH | - | 1980 | - | - | - |
| SGOPT | 56 | - | - | - | - |
| SGPT | 59 | - | - | - | - |
| AL.phos | 2 | - | - | - | - |
| FBS | 109 | - | - | 139 | 105 |
| Urea | 31 | 417 | 199 | 157 | 54 |
| Crea. | 1 | 10.5 | 16.9 | 4 | 2.2 |
| Pottassium | 3.2 | 5 | 4.9 | 4.7 | 3.9 |
| ESR | 39 | | | | |
| Bl.group | O+ | | | | |
| Urianalysis | RBCs 8-19 | | | | |
| Blood Film | Positive for P. Falciparum | | | | |
| Abd.US | Mild hepatomegally | | | | |
| CT Brain | Not done | | | | |

The patient is treated in ICU with close observation of vital sigs, UOP, level of consciousness. He was treated by IVF 2000cc, Qunine inj 600 mg in 200 cc d/w5/ at rate 50cc/1h every 8 hours, Panadol 1gm inj every 6 hours, NGT feeding, doxycycline tab100mg 1x2, vit k inj, dexamethasone 4mg every 4hours, Mannitol 20/100cc every 8 hours, folic acid 5mg tab and vit B complex inj once a day, omeprazole 40mg inj twice a day and plasil 10 mg every 8 hrs. The patient suffered severe anemia and thrombocytopenia, so fresh blood transfusion and platelet were given. Then Patient complained epigastric pain with vomiting o\E. He was still confused and febrile with normal UOP. Blood sample was urgently taken and analysed. The analysis indicated abnormal renal function, so a nephrologist was called and haemodylsis was done. After three sessions of HD, the pt became well alert afebrile after 15 days from admission. RFT was near normal and he was treated by conservative IVF. He received qunine for 15 days. Before the patient was discharged, doxycycline 100mg was prescribed to be taken once a day for ten days. Folic acid, vit B were also prescribed. After 10 days, RFT and abdominal sonar were normal.

**Discussion**

Malaria is a life threating mosquito-brone blood disease caused by plasimodium parasite. It is transmitted to human through bites of anopheles mosquito.

There are many species of plasmodium, but only five infect humans, and cause malaria:

1-Pasmodium falciparum: This kind is found in tropical and subtropical areas, and is a major contributor to death from severe malaria.

2- Pasmodium vivax: This kind is found in Asia and Latin America and has a dormant that can cause relapse.

3- Pasmodium ovale: This kind is found in Africa and the Pacific islands has adormant that can cause relapse.

4- Pasmodium knowlesi: This kind is found throughout south east Asia. It can rapidly progress from a complicated case to a severe malaria infection.[5-8]

Malaria does not spread from person to person, except in pregnancy, but occurs in rare certain circumstances and usually found in transmission from mother to fetus (congenital malaria). It spreads through blood transfusion or with intravenous drug abusers who share needles. Except from the above conditions, malaria is not considered to be contagious.

More than 210 million cases of malaria occurred worldwide in 2015. The world health organization estimated that 438.000 people died of malaria in 2015. The vast majority were young children in sub-Saharan Africa. There has been a significant decrease in deaths since 2000 due to increased prevention and control measures.

The risk factors for high mortality of malaria include late referral, short acute illness, high parasitemia, and presentation with oliguria, hypotension, severe anaemia or significant jundance.

Patients with severe diarrhea, multisystem involvement, hepatitis and acute respiratory distress have a grave prognosis. In children, age, and absence of splenomegaly are associated with higher mortality. Opportunistic pulmonary viral or bacterial infections may be encountered in patients with malaria ARF (MARF), increasing the risk of mortality.

**Other manifestations of malaria**

Neurologic defects may be occasionally persisting following cerebral malaria, especially in children. Such defects include trouble with movement (ataxia), palsies, speech difficulties, deafness, and blindness.

Recurrent infection with p–falciparum may result in severe anemia. This occurs especially in young children in tropical Africa with frequent infections that are inadequately treated.

Malaria during pregnancy (especial p–falciparum) may cause severe disease in mother, and leads to premature delivery or delivery of low birth weight babies.

On rare occasion, p–vivax malaria can cause rupture of the spleen.

Nephrotic syndrome (a chronic sever kidney disease) can result from chronic or repeated infection with p- malaria.
Hyper reactive malarial splenomegaly, also called (tropical splenomegaly syndrome), occurs infrequently and is attributed to an abnormal immune response to repeated malaria infection. The disease is marked by a very enlarged spleen and liver, abnormal immunological findings, anemia, and a susceptibility to other infections (such as skin, respiratory infections).[4-8]

**The life threating complications of malaria**
Cerebral malaria swells the blood vessel of the brain. It manifested with abnormal behavior, impairment of consciousness, seizures, coma, or other neurologic abnormality.
Pulmonary oedema is an accumulation of fluid in the lungs that causes breathing problem or acute respiratory distress syndrome (ARDS). It is an inflammatory reaction in the lung that inhibits oxygen exchange, which may occur even after the parasite counts have decreased in response to treatment.
Severe anemia due to hemolysis (destruction of RBC), and hemoglobinuria can also occur.
Hypoglycemia (low blood sugar), hypoglycemia may occur in pregnant women with uncomplicated malaria, or after treatment with qunine.
Abnormalities in blood coagulation, and low blood pressure caused by cardiovascular collapse also occur.
Acute kidney injury, and organ failure of liver or spleen can happen.
Metabolic acidosis (excessive acidity in the blood and tissues fluids) occur often in association with hypoglycemia.
Malaria can be a fatal disease when seriousness, prevalence are neglected, the monetary cost would be high.

**Management of malaria**:-
Chloroqine used to be the gold standard treatment of malaria. Although it remains effective against Pasmodium vivax, Pasmodium malaria, most Pasmodium falciparum strains are chloroquine-resistant, with increasing frequency in endemic area. Alternative therapies includes: Fanidar (pyrimethamine +sulfadoxm), the qinghaosu alkaloids particularly Artemether, Artesunate and Atovaquone and other chemotherapeutics such as Mefloquine, Benfumetol and Proguanil administered as monotherapy or in combination. Primaquine is still used in Pasmodium vivax and Pasmodium oval to prevent relapse.[3-4]
Intravenous Qunine remains the most widely used in the treatment of cerebral and other serious complication of falciparum malaria.
However, it may induce hemolysis in G6PD deficient patient, leading to fatal (black water fever). In severe cases cardiac toxicity is another important complication of qunine treatment. It can be avoided by monitoring the blood level and ECG changes. A quinine therapy often lead to hyperinsulinemia which contributes to characteristic hypoglycemia of malignant malaria.
Qunine and chlorquine are scarcely removed by dialysis or hemofiltration, hence the necessity monitoring the blood level in patient prolonged oliguria. Both drugs induce hepatic cytochrome P450, hence the necessity to augment cyclosporine doses in kidney transplanted patients.
The treatment of ARF usually poses challenging problems owing to complexity of the syndrome.
Large doses of frusemide have been consistently ineffective in altering the course of malaria ARF. However when used in conjunction with renal dose dopamine in early cases, it may obviate the need for Hemodialysis. Other agents reported to be effective in reducing the need for Hemodialysis by malaria ARF include intravenous prostacyclin and direct intera renal infusion of the calcium channel blocker gallopamil.
50-80% of Patients in different series require Hemodialysis. Early Hemodialysis is often needed to deal with the hypercatabolic state. Although peritoneal dialysis is less effective because of the complicating circulatory disturbances, it is often the only available dialysis modality in area where malaria is endemic. In some cases, arteriovenous hemofilteration or continuous peritoneal dialysis may be indicated. Exchange transfusion is helpful with heavy Parasitemtemia >10/mL those with severe jaundice and those with SIR Syndrome with an over reduction of mortality by 20%. Apheresis has been reported to successfully support anuric patients with cerebral and pulmonary complication. There is no place for corticosteroid in the treatment of malaria. They have been reported as deleterious in cerebral malaria and at least ineffective in the management of other complications.
People with malaria who receive treatment typically have a good long-term outlook. If complication arise as a result of malaria, the outlook may not be as good.
Cerebral malaria can cause brain damage.
The long-term outlook for patient with drug resistant may also be poor. In these patients malaria recur, and may cause other complications.
Acute kidney injury (AKI) is one of the most dreaded complication of sever malaria organization criteria, acute renal failure serum creatinine level = or > 3mg/dl. It occurs as complication of falciparum plasmodium malaria in less than 1% of cases, but the mortality rate in these cases may be up to 45% is more common in adult than children.
The renal involvement varies from mild proteinuria to severe azotemia associated with metabolic acidosis. It may be oliguric or nonoliguric. A R F is commonly caused by p – falciparium but p–vivax and Plasmodium Knowlesi ARF may be present as a component of multiorgan dysfunation or as sole complication. The prognosis in later stages is better. Several pathogenic mechanisms interplay for the clinical manifestation. The predominant lesion are acute tubular necrosis and mild proliferative glomerulo-nepheropathy. These patients do not progress to chronic kidney disease.[5-8]

The management of malaria induced ARF includes appropriate antimalarial (parenteral Artesunate or Qunine, fluid, Electrolyte management, and renal replacement therapy at the earliest stages. The use of diuretics should be avoided.

**Conclusion**

**Malaria** is a serious and sometimes fatal disease caused by a parasite that commonly infects a certain type of mosquito, which feeds on human blood. The disease still kills thousands of people worldwide. The vast majority are young children in sub-Saharan Africa. Although Libya has been declared by WHO as Malaria-free-country since 1973, malaria cases has been diagnosed on different occasions. In the South of Libya, where there is no control over the borders with other neighbouring countries, the number of infected people crossing the border is likely of increase. It is important for doctors in practice to test those patients with fever and high H/o travel to an endemic area for malaria. Travelling to endemic areas should be restricted to control the spread of Malaria.

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