Case Report

An Imported Case of Multi-variant Complicated Severe Malaria — A Rare Case Report

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Abstract

Background : Malaria is caused by the Parasite Plasmodium and is transmitted by mosquitoes called Anopheles. A case of malaria has been reported in a 37 year old male patient who has been in a Malaria-endemic country and returned to India. India is a country where Indian nationals often travel to foreign countries for business and other purposes. An elderly male, 34, reported a fever for 15 days, vomiting four episodes, headache for 14 days and intermittent loss of consciousness for two episodes. When the patient came to casualty and hospital course, the patient developed other manifestations of Severe Malaria. Our case report describes a case of Multi-variate Severe Malaria successfully treated with intravenous antimalarial drugs and oral primaquine in our hospital.

Key words : Severe Multi-variant Malaria, Hypoglycaemia, Acute Respiratory Distress Syndrome, Severe Multi Complicated Malaria, Plasmodium Vivax, Plasmodium Falciparum

Malaria is a highly prevalent parasitic infection, and a serious public health issue. It is known to Prevalent in 84 countries Worldwide and 247 million cases in the world and there are 4,09,000 deaths due to Malaria each year as per data till 2021 By WHO[1]. The genus plasmodium has six important species named P falciparum, P vivax, P ovale, P malariae, P simium, P cynomolgi. The human is an intermediate host and the anopheles mosquito is the definitive host for Plasmodium falciparum. Plasmodium falciparum is an essential determinant of the patient's admission to the Intensive Care Unit. As published earlier, Plasmodium falciparum causes increased immortality in patients and Plasmodium vivax causes morbidity, so aggressive treatment is essential[10]. In this case report, the patient is affected with Multi-variant Malaria caused by Plasmodium falciparum and Plasmodium vivax which has been treated successfully in our hospital.

Case Report

An elderly male of 34 years reported a fever for 15 days, vomiting four episodes, headache for 14 days and intermittent loss of consciousness of two episodes. The patient does not have any other health problems. Patient has a travel history to South Africa for eight months and returned to India 20 days before and then the patient started developing symptoms. Personal history Patient is having long-term alcoholism and smoking. The patient was having icterus but there were no signs of edema, clubbing, cyanosis, pallor and lymphadenopathy on general examination. The spleen is palpated in the left midclavicular line between the left subcostal margin and umbilicus corresponding to grade-2 of hackett's grading system. The patient was drowsy but acutely aware of the time, place and person. The differential diagnosis at this point is alcoholic Hepatitis and all required investigations have been sent. Then suddenly the patient had chills and rigor, breathlessness and bilious large volume vomiting and patient became unconscious. In the view of aspiration and impending respiratory failure, the patient was intubated and kept on mechanical ventilation. The patient's urine gradually became black in color as shown in the picture (Fig 1). On investigations, the peripheral smear was positive for Plasmodium vivax (Fig 2). Patient indirect bilirubin was increased to 9.7 and other investigations as follows Hb 5.7, WBC count 17000, Platelets 26000, Urea 26, creatinine 0.8, Direct bilirubin 5.2 SGOT 91, SGPT 70, Random Blood Sugar 58, HIV- non-reactive and HbsAg-negative. Malaria RDT also came positive for Plasmodium vivax malaria. By confirming it as P vivax Malaria, we have started the patient with injection artisunate 2.4 mg/kg stat and tablet primaquine 0.25 mg/kg and tablet pyrimethamine 1.25 mg/kg and sulphadoxine 25 mg/kg. On day 3 of hospital admission Patient's X-ray

Editor's Comment :

- Early detection and aggressive management, particularly in imported cases, are crucial when it comes to severe multi-variant malaria.
- This patient's successful treatment for cerebral malaria, ARDS and hemolytic complications emphasizes the importance of vigilant monitoring and supportive intensive care when treating cerebral malaria and ARDS, respectively.

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Fig 1 — Complicated Severe Malaria Patient

AP view discloses the bilateral infiltrates in the Lungs. In the probability of Acute Respiratory Distress Syndrome[6], secondary to sepsis due to Plasmodium falciparum infection, we have repeated the peripheral smear and it came positive for Plasmodium falciparum as shown in picture (Fig 2). The patient started on 3rd generation cephalosporins in the view of ARDS. In this stage, the patient is on mechanical ventilation, not responding to painful stimulation and has multiple fever spikes and impaired consciousness (coma) as shown in the picture (Fig 1). On day 5 of hospital admission the patient's urine started to change in color and the icterus was reduced. Patient was continued with artemisinin combination therapy. On consecutive days the patient's condition became better and the patient's urine started changing in color to normal, infiltrates are reduced in Chest X-ray. The patient was partially conscious and able to respond to oral commands followed by the mode of ventilation changed to spontaneous mode. On day 7 of hospital admission the patient's Oxygen requirement was reduced and the patient kept on on T-piece for 4 hours and then extubated. On day 10 Patient was conscious oriented and able to do minimal movements. On day 14 the patient was discharged and sent home.

Discussion

Most of the Imported Malaria is caused by Plasmodium falciparum (P falciparum), and there have been few reports of mixed infections with P falciparum or P vivax. This report describes a case of mixed malarial infection involving P falciparum and P vivax. The people traveling to endemic areas and having fever episodes should be evaluated as earliest possible though the elimination programs , control measures, prophylactic measures are followed[3]. These methods are strictly followed in India still patients are affected with Malaria. In previous studies it is found that

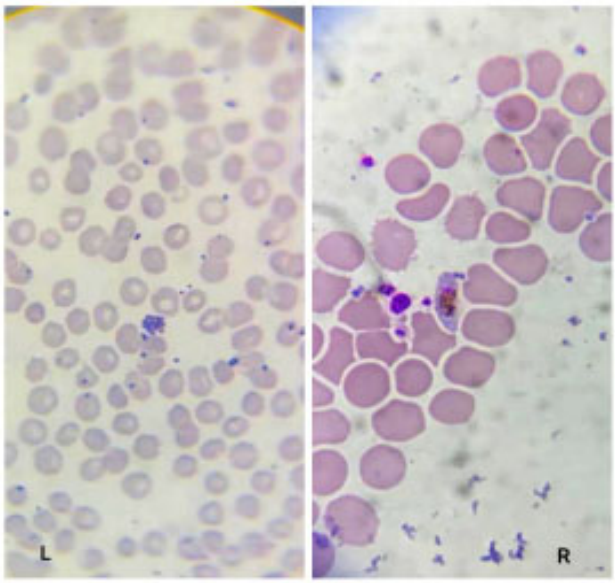

Fig 2 — Image Showing Slide with P vivax and P falciparum

most of the mixed infections caused by P vivax and P falciparum do not occur as a result of simultaneous inoculation with both parasites[5]. When this female anopheles mosquito bites and inoculates sparrows into human skin. These motile parasites will travel to the blood and then the liver. The asexual phase of the life cycle will take place in hepatocytes and release more than 30,000 merozoites through amplification[8]. These merozoites will enter blood circulation again and invade Red Blood Cells and make them infected. After entering into red blood cells these joints will be converted to trophozoites and multiply every 48 hours. These infected Red Blood Cells will burst and release trophozoites and these released trophozoites will again enter other non-infected Red Blood Cells and make them infected. When a mosquito bites the human in this stage, these trophozoites will enter into the mosquito for sexual phase of life cycle and convert into male and female gametocytes. By fusing this gametocytes against sporozoites will be formed and move to salivary glands. When this mosquito bites a human being these sporozoites will enter into the human being and the cycle continues[8]. Patients will be symptomatic and trophozoites are being multiplied in the RBC. The typical fever of Malaria, which is evening rising temperatures are because of when these RBC lies cytokines, inflammatory barker will be released so that patient will have evening rise of temperatures typically, malaria is having fever paroxysms namely, which are cold stage, hot stage and wet stage in uncomplicated malaria. Complex Malaria accompanied by Cerebral Malaria, Severe Hemolytic Anemia, Jaundice, Acute Kidney Injury, Acute Respiratory Distress Syndrome, Hypoglycaemia, Convulsions, Loss of Consciousness, Pulmonary Edema and Metabolic Acidosis. In our subject we have observed Severe Hemolytic Anemia, Jaundice, Acute Respiratory Distress Syndrome, Hypoglycemia,

Convulsions and Cerebral Malaria. It has been reported that adults with severe P falciparum malaria are susceptible to ARDS in 5 to 25% of instances, with mortality rates ranging from 20% to 95%[6]. It has been reported that parasitized Red Blood Cells sequester themselves in cerebral microcirculation, but others attribute consciousness impairment to metabolic factors and inflammation with coma appearing suddenly and with seizures soon after fever onset[7]. Both health care settings and the community can suffer from severe anemia when suffering from vivax malaria. Plasmodium vivax has stronger propensity to RBC than Plasmodium falciparum hence bursting mechanisms for releasing merozoites from RBC is more for P vivax. Reticulocytes that are infected with P vivax die prematurely, so results in extreme anemia over several months by cutting off the supply of mature Red Blood Cells[11]. It is likely that vivax malaria's hematological effects are complicated by Gastrointestinal helminth infection, Haemoglobin and Red Blood Cell abnormalities[11]. Observations have shown that malarial Hepatitis is one of the common causes of jaundice associated with P vivax malaria, following intravascular hemolysis, disseminated coagulation. Hepatic dysfunction and predominantly unconjugated Jaundice in our patient suggest that both hemolysis and hepatic dysfunction are contributing to the patient's Jaundice. A disruption in glucose supply and markers of disease severity were associated with hypoglycemia occurrence[13]. Hyperparasitemia was not observed with our patient and it gave strong support to studies described several patients admitted to the ICU had not been diagnosed with hyperparasitaemia and were originally from malaria-endemic regions[9]. According to previously published data it is thought to be inoculated by multiple bites and P vivax relapse may be triggered by symptomatic falciparum malaria infection, which seems more plausible[3]. People may be infected with multi-variate malaria but published studies show that the vivax malaria will come positive initially and falciparum will be detected next. A combination therapy of artemisinins is recommended by WHO as the preferred treatment against falciparum malaria and vivax malaria[1]. As of the moment, in India, there are five combination therapies registered to treat falciparum malaria: Artemether-Lumefantrine (AL), Artesunate-amodiaquine, Artesunate-mefloquine, Dihydroartemisinin-piperaquine, Artesunate + Sulfadoxine-pyrimethamine (AS + SP) and Arterolane Maleate + Piperaquine Phosphate[2]. As shown in Table 1 and Table 2, treatment options are available for corresponding variants and severity of malaria[8]. Mixed infections of P falciparum and P vivax should be treated with artemether and lumefantrine, combined with a radical treatment of primaquine (0.25 mg/kg for 14 days)[4]. As a contrast, artemether-lumefantrine and primaquine (0.25 mg/kg) should be used for P falciparum. However, chloroquine and a radical cure with primaquine can be used for P falciparum because they are less toxic[2]. In this case we treated this patient with

Table 1 — *Treatment options for uncomplicated Malaria in India*

Drugs with dose	Comments
P vivax malaria :	
Chloroquine 25 mg/kg over 3 days	Chloroquine 10 mg/kg on day1
or	10 mg/kg on day 2
Primaquine 0.25mg/kg/day for 14 days	5 mg/kg on day 3
P falciparum malaria :	
Artemisinin Combination Therapy (ACT) and Primaquine 0.75mg/kg on day 2 single dose	All of India except North eastern states (ACT-AS+SP) Artesunate 4 mg/kg qid for 3 days and sulfadoxine 25 mg/kg+ pyrimethamine 1.25mg/kg on day 1 North eastern states of india ACT-AL Artemether/lumefantrine 1.5/9 mg/kg twice a day for 3 days along with food
Mixed infections with P vivax and P falciparum : Artemisinin Combination Therapy (ACT) and Primaquine 0.25 mg/kg/day for 14 days	

Table 2 — *Treatment options of severe complicated Malaria in India*

Treatment options	Other comments
Initial parenteral treatment for at least 24 hours with one of the following drugs	Follow-up treatment when patient can take oral medication
Artesunate 2.4 mg/kg IV given on admission then at 12 hours then 24 hours then once a day continued till 5th day	Full oral course of area specific ACT
Or	All of India except North eastern states
Artemether 3.2 mg/kg IM given on admission then 1.6mg/kg twice/day for 3 days	(ACT-AS+SP) for 5 days + primaquine 0.25 mg/kg for 14 days
Or	North eastern states of india
Arteether 150 mg daily IM for 3 days in adults only	ACT-AL for 3 days + primaquine 0.25 mg/kg on 2nd day
Or	
Artemisinin 10 mg/kg at 0 and 4 hours followed by 24,36,48 and 60 hours	
Quinine 10 mg/kg 8 hourly in 5% dextrose saline is preferred	Patients should be switched to oral quinine 10 mg/kg 8th hourly for minimum 7 days And Doxycycline 3mg/kg once a day for 7 days Or Oral quinine 10 mg/kg 8th hourly for minimum 7 days And Clindamycin 10 mg/kg twice a day (for pregnant women and children under age of 8 years for 7 days)

ACT-AL- Artemisinin Combination Therapy (ACT) - Artemether/lumefantrine
ACT-AS+SP-Artemisinin Combination Therapy (ACT) - Artesunate + Sulfadoxine + Pyrimethamine

Injection Artesunate 2.4 mg per kg STAT followed by 2.4 mg /kg at 12 hours and 24 hours followed by 5 days of Artemisinin Combination Therapy that includes Artesunate + Sulfadoxine-Pyrimethamine (AS + SP) along with 0.25 mg/kg of TAB Primaquine for 2 weeks and 3rd generation cephalosporin in the view of co-infection with bacteremia.

Conclusion

A severe complex Multi-variant Malaria may be encountered in imported cases only 2% of the time and only 2% of patients have been evaluated for both variants and treated accordingly, Plasmodium falciparum is associated with high mortality rates and Plasmodium vivax is associated with severe illness (morbidity), indicating the importance of evaluating patients early and providing them with an effective anti-malarial treatment,which gives immense results in the treatment of patients in developing countries like India.

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