



MALARIA WITH HEMOGLOBINURIA –A PEDIATRIC CASE REPORT

Paediatrics

**Dr Ramya
Ramanathan**

Assistant professor, Department Of Paediatrics, Sree Balaji Medical College And Hospital, Chennai

ABSTRACT

Malaria is a major public health problem of developing countries. Approximately, 2.48 million malaria cases are reported annually from South Asia of which 75% cases are contributed by India alone¹. The clinical manifestations of malaria vary with geography, epidemiology, immunity, and age. In areas where malaria is highly endemic, young children (6 to 36 months) are at greatest risk. In areas where malaria is transmitted throughout the year, older children and adults develop partial immunity after repeated infections and are at relatively low risk for severe disease. Travelers to malarious areas generally who had no previous exposure to malaria parasites or have lost their immunity if they left the endemic area; they are at very high risk for severe disease if infected with *Plasmodium falciparum*^{2,3}. For this reason, it is important to consider malaria in all febrile patients with history of travel to malarious areas. hereby we are reporting a 2 year old child who had severe malaria with hemoglobinuria after travelling to assam in north eastern part of india. Malaria is endemic in most North Eastern States of India with Plasmodium falciparum being the predominant parasite.^{4,5,6}

KEYWORDS

Malaria, Hemoglobinuria, North East India.

INTRODUCTION:

Malaria, a disease caused by protozoan parasites of the genus Plasmodium, is still considered a serious global public health problem⁷. There were approximately 198 million cases and 584,000 deaths in 2013, according to the World Health Organization (WHO)⁸. Vector-borne diseases, including malaria, Japanese encephalitis (JE), lymphatic filariasis and dengue/chikungunya, continue to plague tropical countries globally.⁹ Malaria should be suspected in patients with any febrile illness if they have had exposure to a region where malaria is endemic. The initial symptoms of malaria are nonspecific and may also include tachycardia, tachypnea, chills, malaise, fatigue, diaphoresis, headache, cough, anorexia, nausea, vomiting, abdominal pain, diarrhea, arthralgias, and myalgias.^{10,11,12} Children who are partially immune (e.g., newly arrived immigrants or refugees from areas where malaria is highly endemic) frequently present with signs such as hepatosplenomegaly, anemia, and jaundice. It is not unusual for these patients to have very minimal symptoms, such as anorexia or decreased activity, or even to be asymptomatic.

CASE REPORT:

A 2 year old, first order male child born out of non consanguineous marriage presented to our department with fever for one week and passing dark colour urine for two days and lethargy for one day. History of travel to assam one week back. On examination child was febrile, dull looking, irritable, severe pallor and icterus was present. Oxygen saturation was 88 percent in room air. Per abdomen examination showed hepatosplenomegaly. Blood investigations were sent and child was started on oxygen through face mask, intravenous fluids, cephalosporins (ceftriaxone), paracetamol was given. Child also received PRBC at 10 ml per kg following which oxygen saturation, pallor and general condition improved, but fever spikes persisted with hemoglobinuria. In view of persisting fever spikes, hemoglobinuria and history of travel to malarious area severe malaria was suspected and peripheral smear was sent which was suggestive of hemolytic anemia with no hemoparasites. Because of strong clinical suspicion inj artesunate was started following which child became afebrile and passed normal urine. Though the smear was negative for malarial parasite, rapid diagnostic kit which was done on the next day of admission was positive. Blood investigations are given in the table 1.

TABLE 1

INVESTIGATIONS	BEFORE TRANSFUSION	AFTER TRANSFUSION
Hemoglobin	5.7gm/dl	8gm/dl
Total wbc count	41370	10540
Total bilirubin	2.3	0.4
Direct	0.6	0.2
Indirect	1.7	0.2

Reticulocyte count – 3.2%(corrected retic count-1.4),G6PD -

7.3(NEGATIVE),Renal function test-normal, Widal test-negative, Hepatitis B surface antigen –negative, Urine analysis-normal.

Child was discharged with oral anti malaria.

DISCUSSION:

Malaria is a global health problem, causing disease on a vast scale. According to the World Malaria Report 2017, in the year 2016, more than half of the population (698 million) was at risk of malaria. According to the Report, India accounted for 6% of all malaria cases in the world, 6% of the deaths, and 51% of the global *P. vivax* cases. The Report estimates the total cases in India at 1.31 million (0.94-1.83 million) and deaths at 23990 (1600-46500)¹³. With increasing global warming, it is projected that in 2050s, malaria is likely to persist in Orissa, West Bengal and southern parts of Assam, bordering north of West Bengal, but may shift from the central Indian region to the south western coastal states of Maharashtra, Karnataka and Kerala. Also the northern states, including Himachal Pradesh and Arunachal Pradesh, Nagaland, Manipur and Mizoram in the northeast may become malaria prone.¹⁴

The clinical manifestations of malaria, the severity and course of a clinical attack depends on the species and strain of the infecting plasmodium parasite, as well as the age, genetic constitution (ethnicity), immune status, malaria specific immunity, and nutritional status of the child, the mode of transmission of infection, whether the individual was on prophylaxis or had previous exposure to antimalarial drugs, as the latter may present with only minimal symptoms or signs.¹⁵

In children symptoms are more varied and often mimic other common childhood illness, particularly gastroenteritis, meningitis/encephalitis, or pneumonia. Fever is the key symptom, but the characteristic regular tertian and quartan patterns are rarely observed. There are no pathognomonic features for severe malaria in this age group. The well known clinical (fever, impaired consciousness, seizures, vomiting, respiratory distress) and laboratory (severe anaemia, thrombocytopenia, hypoglycaemia, metabolic acidosis, and hyperlactataemia) features of severe falciparum malaria in children, are equally typical for severe sepsis.¹⁶ It has been reported that >60% of malaria is misdiagnosed at initial presentation in areas where malaria is not endemic.¹⁷

Malaria infections may cause vital organ dysfunction and death. Severe malaria is defined by clinical or laboratory evidence of vital organ dysfunction. Nearly all deaths from severe malaria result from infections with *P. falciparum*.¹⁸ Malarial illnesses may take a variety of clinical forms, differing in pattern and severity, from uncomplicated to severe and complicated malaria. Severe falciparum malaria may manifest with wide variety of features as described by WHO haemoglobinuria being one of them. Haemoglobinuria occurs when the capacity of haptoglobin to bind free haemoglobin is exceeded.

Despite their sometimes similar visual appearances, the absence of red blood cells on microscopic examination distinguishes haemoglobinuria from haematuria. The most consistent findings in malaria haemoglobinuria are fever, pallor, jaundice and passage of dark urine.¹⁹

White blood cell (WBC) counts during malaria are generally characterized as being low to normal, a phenomenon that is widely thought to reflect localization of leukocytes away from the peripheral circulation and to the spleen and other marginal pools, rather than actual depletion or stasis. Leukocytosis is typically reported in a fraction of cases and may be associated with concurrent infections and/or poor prognosis.²⁰

Clinicians should routinely obtain a relevant travel history from the caretakers of any ill child like in our case which gave the clue for diagnosis. Malaria is a major public health illness in Assam. North-eastern states of India, representing ~4% of the country's population, are home to all these infectious diseases with indigenous transmission.²¹

A toxic-appearing child with a history of malaria exposure should be admitted to an intensive care unit, and aggressive diagnosis and treatment should be pursued. Appropriate laboratory work must be performed, including blood smears for malaria parasites, and empirical parenteral antimalarial therapy must be initiated. If no parasites are seen on initial smears, follow-up smears should be obtained every 8 h if there is continued concern about malaria. A child who emigrates from a holoendemic malarious area has a significant chance of having a positive blood smear, and the presence of malaria parasitemia does not preclude the possibility of other, coexisting illnesses.²²

The main aim of antimalarial treatment in children, which is also the basis of National Antimalarial Program, is to prevent morbidity and death by early diagnosis and prompt treatment (EDPT). Unfortunately, in our country prompt treatment is mostly presumptive based on clinical diagnosis. It is interesting to note that in the year 2000 out of 86.46 million blood smear examination throughout the country on presumptive diagnosis of malaria slide positivity rate (SPR) was found to be only 2.32%.²³ Extrapolating from these data it is evident that the use of presumptive treatment of malaria has the potential for facilitating resistance by greatly increasing the number of patients who are treated unnecessarily.

Hence, all efforts should be given to treat malaria after diagnosis by microscopic examination, rapid diagnostic tests or both as facilities and circumstances dictate.²⁴ Further, a complete and successful antimalarial therapy is possible only when the parasite species are known. In case of clinically suspected malaria at times the first smear examination may be negative but it is prudent to avoid the diagnosis of "blood smear negative malaria". In these cases repeated blood smear at 12 to 24 hours interval and RDTs are suggested and all other causes of fever are to be excluded.

One of the major problem in the successful treatment of malaria is the development of resistance of *P. falciparum* to first line drug chloroquine (CQ) in certain areas of our country. Malaria is prevalent in all parts below 5000 feet mean sea level. Before initiating treatment it is desirable to have some idea about the pattern of resistance in our country. To combat drug resistant malaria, the NVBDCP recommends the use of combination therapy *i.e.*, artesunate plus sulfadoxine/pyrimethamine (SP) for *P. falciparum* cases in chloroquine resistant areas.²⁵

High degree of suspicion of severe malaria is of utmost importance and any delay in initiation of treatment can be fatal. It should be treated as a medical emergency at highest level of medical facility available preferably in a intensive care setting. Confirmation of the diagnosis is preferable but one should not delay the treatment if it needs more than one hour.²⁶ Effective therapy in children with severe malaria includes antimalarial chemotherapy, supportive management and management of complications. All these three interventions are equally important and to be taken care of simultaneously.

CONCLUSION:

Treatment of malaria depends on the (presumptive) identification of the species of Plasmodium causing the infection, knowledge of the

presence of resistant organisms in the area in which the malaria was contracted, national guidelines, antimalarial availability, individual patient factors and whether the malarial illness is categorized as either uncomplicated or severe. Further, in cases of strong clinical suspicion prompt antimalarial therapy is needed even if parasite are not found in the initial blood examination. With appropriate attention to the possibility of malaria and as new diagnostic and therapeutic tools and techniques become increasingly available, there is ever-greater potential for avoiding the severe morbidity and mortality associated with malaria.

REFERENCES:

1. World Health Organization, Development of South-Asia surveillance network for malaria drug resistance. Report of an informal consultative meeting, New Delhi, JAN 2002. WHO Project No. ICPCPC 400.
2. Wilson ME, Weld LH, Boggild A, et al. Fever in returned travelers: results from the GeoSentinel Surveillance Network. *Clin Infect Dis* 2007; 44:1560.
3. Svenson JE, MacLean JD, Gyorkos TW, Keystone J. Imported malaria. Clinical presentation and examination of symptomatic travelers. *Arch Intern Med* 1995; 155:861.
4. Patra SS, Dev V. Malaria related morbidity in central reserve police force personnel located in the North Eastern States of India. *J Hum Ecol.* 2004;15:255-9. [Google Scholar]
5. Dev V, Hira CR, Rajkhowa MK. Malaria attributable morbidity in Assam, Northeastern India. *Ann Trop Med Parasitol.* 2001;95:789-96. [PubMed] [Google Scholar]
6. Mohapatra PK, Prakash A, Bhattacharya DR, Mahanta J. Malaria situation in Northeastern region of India. *ICMR Bull.* 1998;28:21-30. [Google Scholar]
7. World Health Organization, Global Malaria Action Plan for a Malaria-Free World. Geneva, Switzerland: Roll Back Malaria Partnership; 2008, World Health Organization, 2008.
8. WHO, World Malaria Report 2014, World Health Organization, 2014.
9. World Health Organization. Vector-borne diseases, Factsheet # 387, March 2014. <http://www.who.int/mediacentre/factsheets/fs387/en> - accessed 12 July 2014.
10. Wilson ME, Weld LH, Boggild A, et al. Fever in returned travelers: results from the GeoSentinel Surveillance Network. *Clin Infect Dis* 2007; 44:1560.
11. Svenson JE, MacLean JD, Gyorkos TW, Keystone J. Imported malaria. Clinical presentation and examination of symptomatic travelers. *Arch Intern Med* 1995; 155:861.
12. White NJ, Breman JG. *Harrisons Principles of Internal Medicine*, 19th ed, Kasper D, Fauci A, Hauser S, et al (Eds), McGraw Hill, New York 2015, in press
13. WHO. World Malaria Report, 2017. WHO. Available at <http://www.who.int/malaria/publications/world-malaria-report-2017/en/>
14. Bhattacharya S, Sharma C, Dhiman RC, Mitra AP. Climate change and malaria in India. *Current Science.* 10 Feb 2006;90(3):369-375. Full text at <http://www.ias.ac.in/currsci/feb102006/369.pdf>
15. Bostrom S, Giusti P, Arama C, Persson JO, Dara V, Traore B, Dolo A, Doumbo O, Troye-Blomberg M. Changes in the levels of cytokines, chemokines and malaria-specific antibodies in response to Plasmodium falciparum infection in children living in sympatry in Mali. *Malar J.* 2012 Apr 5;11(1):109. <http://dx.doi.org/10.1186/1475-2875-11-109> PMID:18316995 PMCid:2607243
16. *Mediterr J Hematol Infect Dis* 2012,4(1): e2012073, DOI: 10.4084/MJHID.2012.073. This article is available from: <http://www.mjhid.org/article/view/10892>
17. Kain KC, Harrington MA, Tennyson S, Keystone JS. Imported malaria: prospective analysis of problems in diagnosis and management. *Clin Infect Dis* 1998; 27:142-9.
18. Management of severe malaria: a practical handbook – 3rd ed.
19. Severe falciparum malaria. World Health Organization, Communicable Diseases Cluster. *Trans R Soc Trop Med Hyg* 2000, 94(Suppl 1):S1-S90.
20. McKenzie et al. *J Infect Dis.* 2005 July 15; 192(2): 323-330.
21. Dev V, Hira CR, Rajkhowa MK. Malaria - attributable morbidity in Assam, northeastern India. *Ann Trop. Med. & Parasitol.* 2001;95: 789- 796.
22. Diagnosis and Treatment of Malaria in Children Downloaded from <https://academic.oup.com/cid/article-abstract/37/10/1340/451166> by guest on 14 July 2019.
23. Govt. of India, Annual Report 2001-2002 New Delhi: Ministry of Health and Family Welfare, 2002.
24. White NJ. Protozoan infections, malaria. In: Cook GC, Zumla A, eds *Manson Tropical Diseases*, 21st ed. London: Saunders, 2003 : 1205-1295.
25. Directorate of National Vector Borne Disease Control Programme. Report of Meeting of an Expert Group, New Delhi: NVBDCP, 2004.
26. World Health Organisation. Management of Severe Malaria. A Practical Hand Book, 2nd ed. Geneva: WHO, 2000.