Short Communication

Thrombocytopenia due to *Plasmodium Falciparum* malaria in children in paediatrics department, Alamal National Hospital, Sudan

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Abstract

Malaria is a major public health problem in Sudan. Thrombocytopenia has been reported to be associated with malaria with incidence between 24-94% in some studies. Usually it runs a benign course and causes no bleeding. It responds usually to anti-malarial treatment. Case reports: 28 patients were treated in paediatric department diagnosed as having malaria due to plasmodium falciparum infection and one patient had mixed infection (falciparum and vivax) from September 2012 to March 2013 (7 months). Their age ranged from 10 months to 15 years. 15 patients (53.5%) had malaria associated with thrombocytopenia (one of them was treated as out-patient). Only 2 patients (13.33%) had severe thrombocytopenia (7,000 and 19,000/ cumm). The rest (13 = 86.66%) had mild and moderate thrombocytopenia i.e. > 20,000/ cumm. 10 patients (66.66%) treated with quinine (I.V. and oral) and 5 patients (33.33%) treated with IM Artemether. All patients (15 = 100%) recovered from malaria and thrombocytopenia and discharged home. No one of them had bleeding from any site. Conclusion: In general, mild and moderate thrombocytopenia is very common in falciparum malaria and has got a benign course and improves with treatment. Severe thrombocytopenia is uncommon and rarely associate with bleeding. Malaria should be considered in febrile patients with low platelets.

Keywords: falciparum malaria, children, thrombocytopenia, Sudan.

INTRODUCTION

Malaria is a major public health problem in Sudan. It leads to 7.5 million cases and 35,000 deaths every year in Sudan (2000 estimates). There are 4 species of malaria: plasmodium falciparum (responsible for 90% of cases in Sudan), P. vivax, P. ovale and P. malariae. Anopheles arabiensis is the main vector together with A. gambiae and A. funestus. (The National Protocol for Treatment of Malaria, 2004) Worldwide, there are more than 250 million cases of malaria every year, killing between 1-3 million people. (Gursharan and Neha, 2011; Colonel et al., 2010), 88% of them occurred in sub-Saharan African children < 5 years. Most deaths are due to plasmodium falciparum infection which causes life-threatening cerebral, respiratory, renal, hepatic, hemodynamic, and hematologic dysfunction in 1% of cases. (Gursharan and Neha, 2011).

Malaria affects almost all blood components. Thrombocytopenia has been reported to be associated with malaria (Gursharan and Neha, 2011; Colonel et al., 2010; The National Protocol for Treatment of Malaria, 2004; Shamez et al., 2005), as well as anaemia. and the most frequent hematological malaria associated
complications. The incidence ranging from 60-80% (Colonel et al., 2010; John and Jay, 1983), with some studies reporting a lower incidence with vivax malaria as compared with Falciaparum. The normal platelets count is 150,000 – 450,000/ml. Thrombocytopenia is defined as platelet count less than 150,000/ml (Shamez et al., 2005). Thrombocytopenia is classified according to protocol used by Memon et al i.e. mild (< 150,000/ml to > 50,000/ml), moderate (< 50,000/ml > 20,000/ml) and severe (< 20,000/ml). (Colonel et al., 2010). In endemic areas, malaria has been reported as the major cause of low platelet counts. This is so characteristic of malaria, that in some places, it is used as an indicator of malaria in patients presenting with fever. Platelet counts of less than 150,000/L increase the likelihood of malaria by 12-15 times.

The exact mechanism of thrombocytopenia associated with malaria is poorly understood (Colonel et al., 2010; John and Jay, 1983). But both non-immunological destruction as well as immune mechanisms involving specific platelet-associated IgG antibodies that bind directly to the malarial antigen in the platelets have been recently reported to play a role in the lysis of platelets and the development of thrombocytopenia (Gursharan and Neha, 2011; Yamaguchi et al., 1997; The National Protocol for Treatment of Malaria, 2004). Other mechanisms include oxidative stress, sequestration in non-splenic areas and pseudo-thrombocytopenia due to clumping of platelets. Decreased thrombopoiesis, as a cause of low platelets, has been ruled out, because platelet-forming megakaryocytes in the marrow are usually normal or increased. In rare instances, platelets can be invaded by malarial parasites themselves (Shamez et al., 2005). Tumor Necrosis Factor and IL-10 have been implicated in the development of Plasmodium falciaparum malaria induced anaemia, but the role of these cytokines has not been studied in the development of thrombocytopenia in patients with acute malaria.

Case reports

28 patients were treated in paediatric department diagnosed as having malaria due to plasmodium falciaparum infection and one patient had mixed infection (falciaparum and vivax) from September 2012 to March 2013 (7 months). Their age ranged from 10 months to 15 years. 15 patients (53.5%) had malaria associated with thrombocytopenia (one of them was treated as outpatient). 9 patients (60%) with thrombocytopenia were boys and 6 (40%) were girls (M: F ratio = 1.5: 1) (figure 1). All patients (100%) had fever as the main complaint of short duration (1 – 5) days. 3 (20%) patients had generalized convulsions i.e. cerebral malaria and one patient had severe respiratory distress and pulmonary oedema. 2 patients (13.33%) had hepatosplenomegally and only one patient had hepatomegaly alone and splenomegally alone. 7 patients (46.66%) had anaemia. Only 2 patients (13.33%) had severe thrombocytopenia (7,000 and 19,000/ cumm). The rest (13 = 86.66%) had mild and moderate thrombocytopenia i.e. > 20,000/ cumm. 5 patients (33.33%) had hyperparasitaemia. Only one patient (6.66%) with very low platelet count (7,000/ cumm) received platelet transfusion but he had no evidence of bleeding from any site. One patient (6.66%) with low haemoglobin (6.5 g/dl) received packed RBCs. 10 patients (66.66%) treated with quinine (I.V. and oral) and 5 patients (33.33%) treated with IM Artemether (figure 2). Most of the patients stayed 2-5 days at hospital. The mean for hospital stay was 4.5 days. All patients (15 = 100%) recovered from malaria and thrombocytopenia and discharged home. No one of them had bleeding from any site.

DISCUSSION

Malaria is a major health problem in Sudan. Plasmodium
Figure 2. Type of treatment received

Falciparum infection is responsible for 90% of cases. It is associated with severe life-threatening complications such as cerebral malaria, severe respiratory distress, black-water fever and other haematological complications such as DIC, thrombocytopenia and anaemia. Thrombocytopenia is the most common haematological complication of malaria. The maximum thrombocytopenia occurred on the fifth or sixth day of infection, and gradually returned to normal within 5-7 days after parasitaemia ceased. Thrombopoietin is the key growth factor for platelet production and is elevated in states of platelet depletion. Its serum levels have been shown to be significantly higher in subjects with severe malaria, normalizing within 14-21 days of therapy.

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The incidence of thrombocytopenia associated with malaria is 24 – 94% with some studies reporting a lower incidence in vivax compared to falciparum infection. This is consistent with the finding in our cases where thrombocytopenia is found in 53.5% of reported cases. Bashwari et al in Saudi Arabia reported the incidence of thrombocytopenia associated with malaria as 53%. Shuaib et al in India, colonel Khursheed Mohammad Uttra et al in Pakistan, (Colonel et al., 2010; Mahmood et al in Liberia reported the incidence as 69.18%, 72% and 75.18% respectively. F Moulin et al studied thrombocytopenia during acute Plasmodium falciparum malaria in 64 traveller children from Paris (France), 85 children from Dakar (Senegal) with an intermittent exposure and 81 children from Libreville (Gabon). Initial thrombocytopenia was present in 43–58% of children with P falciparum malaria (The National Protocol for Treatment of Malaria, 2004).

In our cases most of the patients (n=13 = 86.66%) had mild to moderate thrombocytopenia i.e. > 20,000/cumm. Only 2 patients (13.33%) had severe thrombocytopenia i.e. < 20,000/cumm. In one patient it was found to be 7,000/cumm and the other was 19,000/cumm without any evidence of bleeding from any site. The least reported thrombocytopenia was as low as 5,000/ microlitre reported in the Indian literature in a 43-year old female patient with vivax malaria (Colonel et al., 2010). The incidence of severe thrombocytopenia with malaria in our study was found to be 13.33%. Similar results were obtained by Jadhav et al. (2004); Shuaib et al. (2009); Jaganmani et al. (2012) where they found the incidence of severe thrombocytopenia associated with malaria in 8.5%, 10% and 12% respectively. In contrast Colonel et al. (2010) in Pakistan Colonel et al. (2010); Guraprasada et al. (2012) in India reported severe thrombocytopenia with malaria in 25% and 29% in their cases respectively.

A good tolerance of low platelet counts is well known in malaria. This could be explained by platelet activation and an enhanced aggregability. In most of the studies, including ours, thrombocytopenia has not been associated with death in malaria. It usually disappears with the treatment of the disease and requires no treatment. (Colonel et al., 2010). Bleeding due to malaria complicates about 5% of cases. It is due to a combination of DIC, low coagulation factors and thrombocytopenia. Fortunately, in our cases there was no any case.
associated with bleeding tendency even those with severe thrombocytopenia. Strikingly, Elawad et al. (1999) in Saudi Arabia had a 12 years Saudi boy with falciparum malaria and profound thrombocytopenia associated with significant bleeding. Immunoglobins was used to treat this case. However, immunoglobulin has not been mentioned or used before to treat such cases. It is the first report describing the potential benefit of immunoglobulin in profound thrombocytopenia complicating malaria. Moreover, Gursharan Singh Narang and Neha Singla had 1 patient with thrombocytopenia associated with malaria and mucosal bleeding that required platelet transfusion. (Gursharan and Neha, 2011).

In April 2011, and based on new scientific evidence, the World Health Organization (WHO) released new guidelines recommended injectable artesunate as the first line treatment for severe malaria in both children and adults. Injectable artesunate, when compared to parenteral quinine, has been shown to reduce mortality by 35% in adults and 22% in children (The National Protocol for Treatment of Malaria, 2004). Injectable artesunate is not yet available in Sudan. In our case reports, ten patients (66.66%) were treated with quinine (IV then oral) and five patients (33.33%) were treated with IM Artemether. All of them (15 patients) improved in regards to malaria and thrombocytopenia. They stayed 2-5 days at hospital with the mean of 4.5 days.

CONCLUSION

Malaria is usually associated with mild to moderate thrombocytopenia and to less extent with severe thrombocytopenia. Both plasmodium falciparum and vivax may cause thrombocytopenia but the incidence and severity seemed to be more with falciparum malaria. Severe thrombocytopenia doesn't necessarily indicate the severity of malaria. It is rare to have bleeding with thrombocytopenia caused by malaria. Usually thrombocytopenia responds very well to anti-malarial treatment and necessitates no platelets transfusion. Based on our findings, we recommend that malaria should be considered in the differential diagnosis for any febrile child with thrombocytopenia particularly those coming from endemic areas even if the initial malaria screen is negative. Furthermore, Emergency Department blood samples with thrombocytopenia should be routinely screened for malaria.

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