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LETTER TO THE EDITOR

Severe thrombocytopenia with bleeding manifestations in two children secondary to Plasmodium vivax

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To the Editor

The occurrence of thrombocytopenia in vivax malaria is well documented [1]. However, severe thrombocytopenia is relatively uncommon. We report our experience on the occurrence of severe thrombocytopenia leading to bleeding manifestations in two children.

The first case was an 8-year-old girl from the north Indian state of Uttar Pradesh. She was admitted with history of low to moderate grade fever without any chills or rigors for 4 days. There was history of epistaxis 1 day prior to admission. She also had one episode of hematemesis. Parents noticed increasing pallor. There was a mild cough but no history of any other systemic complaints. The child was on Cefixime and Nimesulide twice daily. There was no history of any pre-existing illness or past history of bleeding from any other site.

The patient was sick looking at admission. She had tachycardia with hyperdynamic pulses, though there were no signs of heart failure. She was febrile and blood pressure was maintained. Pallor was present. A generalized petechial rash, with ecchymotic spots was present. There was no significant lymphadenopathy. Abdominal examination showed a firm hepatomegaly 3 cm below the costal margin and a firm spleen tip.

Initial blood counts revealed hemoglobin of 4.7g%, total leukocyte count of 3400/mm^3, differential of P34 L58 E5 M3, ESR 110 mm and platelet count of 21 000/mm^3. In view of the pancytopenia and organomegaly, possibility of hematological malignancy was kept, though infective etiology could not be ruled out and a bone marrow aspiration was performed. The child was started on a broad spectrum of antibiotics and given urgent platelet and packed cell transfusions. The peripheral smear showed a normocytic hypochromic picture. Ring forms of Plasmodium vivax were seen with a parasite density of 1–1.5%. There were no premature or atypical cells. Urine examination, liver function tests and kidney function tests were normal. Malaria antigen was positive for Plasmodium vivax and negative for Plasmodium falciparum. The bone marrow showed normal cellularity. Plasmodium vivax was present.

The patient was started on oral chloroquine. She remained afebrile throughout the stay. Spleen initially increased, but then regressed. Blood count after 48 hours had improved to the total count of 5600/mm^3 and platelet count of 51 000/mm^3. She was discharged and platelet count after discharge was 165 000/mm^3.

Second case

The second case was a 4.5-year-old girl admitted with a history of high grade fever of 4 days, two episodes of epistaxis and one episode of melena. Examination revealed a temperature of 38.4°C, tachycardia, tachypnea, raised jugular venous pressure and pallor. Abdominal examination revealed a hepatomegaly of 3 cm below costal margin and a firm splenomegaly of 5 cm below costal margin. Initial investigations revealed hemoglobin of 8.7g%, totally leukocyte count of 4700/mm^3, differential of P30L64M6 and ESR of 98. Platelet count was 35 000/mm^3. The peripheral smear and malarial antigen test was positive for Plasmodium vivax. The patient was given packed cells and platelet transfusions and started on oral chloroquine. She was hemodynamically stabilized and became afebrile within 24 hours. Her platelet count ranged between 35 000/mm^3 to 45 000/mm^3 for 48 hours and then

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Table I. Summary of reported cases of severe thrombocytopenia with Plasmodium vivax.

Serial number	Location	Adult/child	Platelet counts (10^9/L)	Bleeding site(s)	Treatment	Complications	Ref.
1.	India	Two children	48	Upper GI	Intravenous quinine, anti convulsants	Intracranial bleeding, Hydrocephalus	[6]
2.	India	Child	6	Gum bleeds, Petechiae	Oral/iv quinine, corticosteroids	None	[2]
3.	India	Child	24	Petechiae	Intravenous quinine	Acute renal failure and uremic encephalopathy	[4]
4.	Turkey	Newborn	17	None	Chloroquine	None	[3]
5.	India	Children	5–42	Petechial rashes		Three out of six children had alteration in sensorium	[5]
6.	Japan	Two adults	22–53	None	Fansidar, Chloroquine	None	[7]
7.	Venezuela	Adult	57	None	Chloroquine	Bilateral hydronephrosis	[11]
8.	India	Adult	8	Gum bleeds	Quinine	None	[12]
9.	Georgia, USA	Adult	19	Epistaxis	Quinine, Doxycycline	None	[13]
10.	India	Adult	5	None	Chloroquine	None	[14]

started rising slowly. They were 54 000/mm^3 at discharge and 1 week post discharge it was 240 000/mm^3. Both the patients were discharged on primaquine.

Thrombocytopenia can occur with all the four types of human malarias. However, severe thrombocytopenia leading to massive bleeding episodes in children is rare especially with vivax malaria. Few such cases have been described mainly from malaria endemic areas [2–5].

The patient usually presents with an episode of high grade fever, chills and rigors. Occasionally, they may sometimes have mucosal bleeds. On investigation, the patient is found to have thrombocytopenia. The platelet counts in various case reports have ranged from 6–53 000/mm^3 (Table I). The patient is anemic, but the leukocytic count is near normal. In a few case reports, in which bone marrow has been studied, it may show the presence of Plasmodium vivax [2]. A summary of reported cases of severe thrombocytopenia with vivax malaria is given in Table I.

These patients need to be treated just like any other patient with malaria. However, occasional cases may require corticosteroids [2]. Platelet transfusions need to be restricted to patients with obvious bleeding manifestations since in most of them the platelet count starts rising after starting on antimalarials. The patients usually respond within 3 to 4 days of starting antimalarial treatment. There are no long term studies in these children but immediate complications include a presentation like cerebral malaria [5], renal failure [4] and hydrocephalus secondary to intracranial bleeding [6].

The mechanism of thrombocytopenia in vivax malaria is not apparent. The proposed mechanisms are platelet antibody production [7], pro-inflammatory and anti-inflammatory cytokine production [8], oxidative stress [9], splenic pooling and shortened platelet life span [10].

To conclude, severe thrombocytopenia with bleeding manifestations is a rare complication of vivax malaria, but needs to be kept in mind, especially in cases with high grade fever and bleeding manifestations in a malaria endemic area.

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