Case Report

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Sickle cells are not necessarily protective against falciparum- A case report

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Abstract:

The relation between sickle cell disease (SCD) and malaria is captivating where sickling of the infected red blood cells (RBCs) causes premature hemolysis and parasite death. Although patients with sickle cell trait are relatively protected, malaria can often lead to marked anemia in them due to hemolysis. We report an unusual case of a child with homozygous SCD presenting with falciparum malaria and had hyper parasitemia and severe anemia which completely resolved following treatment. Clinical suspicion in our case arose considering the endemic nature of malaria in our country. The two overlapping injuries to spleen reduced the clearance of parasites by the spleen as evidenced by high parasite load. Our case report reinforces malaria as a cause of clinical worsening of SCD and highlights the importance of a multifactorial approach in the management of worsening anemia in SCD.

Keywords:

Hemolysis, malaria, sickle cell diseases

Introduction

The relation between sickle cell disease (SCD) and malaria is captivating where sickling of the infected red blood cells (RBCs) causes premature hemolysis and parasite death. Homozygotes for HbS are reproductively disadvantaged because of their severe hematologic disease. In malarial endemic regions, SCD heterozygotes offer better survival fitness and protection against malaria than normal HbA through plasmodium-induced sickling, impairing parasite growth. Although patients with sickle cell trait are relatively protected, malaria can often lead to marked anemia in them due to hemolysis.

We report a case of a child with homozygous SCD, diagnosed at 3 years of age planned for an allogeneic hematopoietic stem cell transplant with her brother, who presented with a history of high-grade fever and cola-colored urine.

Case Report

A 8-year-old female child diagnosed to have homozygous SCD at the age of 3 years presented with complaints of high-grade fever, cola-colored urine, left-sided intermittent abdominal pain which would subside on analgesic medications only to recur.

For the initial 2 years after diagnosis, she was on regular blood transfusion, once every 2 months. She was started on hydroxyurea following which she was transfusion independent for 8 months, again to become transfusion dependent requiring blood transfusion once every 15 days. Therefore, she was planned for allogeneic stem cell transplantation with brother as the HLA identical stem cell donor.

In the present admission, she was evaluated for the above-mentioned complaints. On physical examination, she was febrile with severe pallor and gross hepatosplenomegaly. Initial evaluation showed hemoglobin of 4.9 g/dL, platelet count of 67000/cumm,

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normal white blood cell (WBC) counts, and mildly elevated reticulocyte count 5.73% [Table 1]. There was mild indirect hyperbilirubinemia (total bilirubin of 2.74 mg/dl with direct of 1 mg/dl) and raised lactate dehydrogenase 889U/l. Her hemoglobin showed increment up to 8.1 gm/dL after three units of packed RBC transfusions, which dropped again to 6.1 g/dL within 24 h, suggesting an ongoing hemolytic process. Evaluating the cause for hemolysis, an indirect antiglobulin test and antibody screen to rule out antired alloantibodies was done which was negative. Her renal and other liver functions were all within normal limits. Ultrasonography showed massive splenomegaly of 20 cm.

Considering that the patient traveled from a highly endemic zone for malaria with a high burden of malaria in those regions, the peripheral smear was closely reviewed and a QBC malaria (quantitative buffy coat) test was done. Peripheral smear revealed numerous *Plasmodium falciparum* rings with delicate cytoplasm and one or two chromatin dots [Figure 1a-c]. Crescentic gametocytes and ring forms were seen [Figure 1d]. The percentage of parasitized RBCs with ring forms was estimated to assess the parasite load. This was done using a thin smear and counting the total number of ring forms in 1000 RBCs. This percentage of parasitemia was 6% in our case. Sickle cells with ring forms were also seen [Figure 1e]. She was started on antimalarial therapy with injection artesunate, tablet primaquine, artemether, and lumefantrine. She was discharged by day 14 of admission, afebrile with hemoglobin of 10.6 g/dL. All the donor units transfused to the patient were rechecked and malaria was ruled out in them. Subsequently, this child underwent an allogeneic stem cell transplant and is now asymptomatic.

Discussion

The greatest burden of malarial anemia is carried by young children. This report describes a case of falciparum malaria in a SCD child, with WHO-defined criteria for severe disease, including hyper parasitemia and severe anemia which completely resolved following treatment. The patient had hemolysis developing within 48 h after the onset of fever probably due to rupture of parasitized RBCs. In India, the average frequency of HbS trait in the Central and West Indian states is approximately 20%, but in north and eastern states, the frequency

Table 1: Complete blood count of patient

Parameters	Patient results
RBC count	2.33 ×10^6 cells/µl
Hemoglobin	6.5 g/dL
Platelet count	48,000/cumm
Mean corpuscular volume	83.2 fL
Mean corpuscular hemoglobin	27.8 pg
Mean corpuscular hemoglobin concentration	33.4 g/dL
Red cell distribution width	16.1%
Peripheral blood examination	Numerous plasmodium falciparum ring forms with delicate cytoplasm and one or two small chromatin dots seen. Rings seen at the periphery of RBCs. Crescentic gametocytes present

RBC=Red blood cell

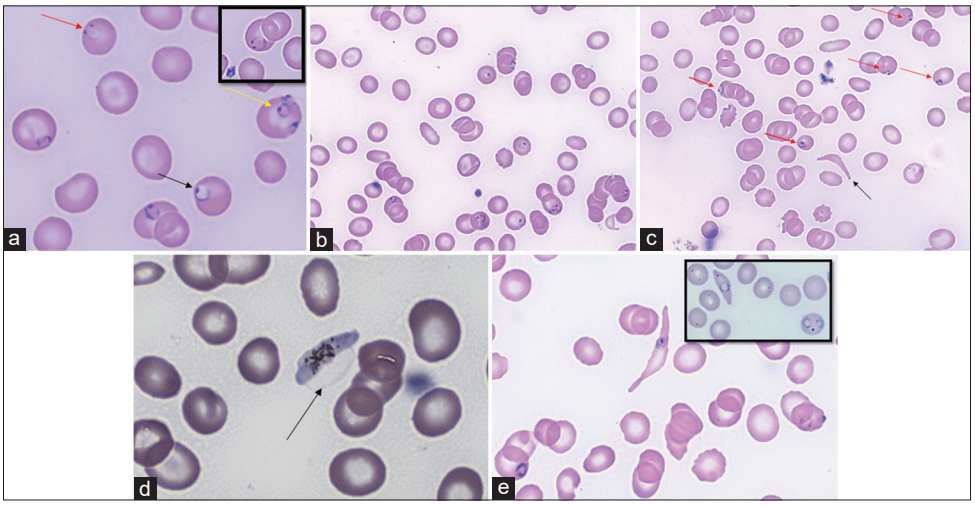

Figure 1: (a) *Plasmodium falciparum* rings with delicate cytoplasm and one or two small chromatin dots (black arrow). Multiply infected red blood cells shown by yellow arrow. Classic "head phone" form shown with red arrow and in the inlay picture. (b) High percentage of parasitemia seen with numerous affected red blood cells. (c) Thin smear with sickle cell (black arrow) and ring forms (red arrows). (d) Gametocyte in a thin smear showing the membrane of red blood cells. Laveran's bibs can be seen (black arrow). (e) Sickle cells with ring forms. Inlay picture showing infected sickle cell and multiply infected red blood cells

is ≤1%.[1] Clinical suspicion in our case arose considering the endemic nature of malaria in our country.

Our case had peculiar characteristics, as it describes a homozygous sickle disease showing the presence of a high percentage of parasitemia and severe anemia. In general, homozygous SCD develops clinical malaria at a lower frequency than carrier patients. Our patient had a high percentage of parasitemia, a finding very similar to Nigerian patients which showed a mean parasite density of 1070/μl in children with SCD versus matched healthy controls with a parasite density of 1759/μl.[2]

Second, the child in our reported case had gross splenomegaly at presentation. The spleen is the first organ injured in SCD with evidence of hyposplenism present before 1 year in the majority of children and repeated splenic vasoocclusion leads to fibrosis and progressive atrophy, which is generally complete by 5 years.[3] However, late persistent splenomegaly with high prevalence was also reported among SCD patients of eastern Saudi Arabia and showed changes of fibrocongestive splenomegaly comprising diffuse congestion of sinusoids and cords by sickled RBCs.[4] The two overlapping injuries to the spleen reduced the clearance of parasites by the spleen as evidenced by high parasite load.

Clinical suspicion of malaria in SCD is challenging because the signs and symptoms overlap with the sickle hemolytic crisis and malarial hemolysis. Special methods such as Giemsa-stained thick blood film, quantitative buffy coat, rapid diagnostic tests, and recombinase polymerase amplification are available for the diagnosis of malaria. In spite of their high sensitivity and specificity, they require special facilities to perform them. However, malaria and sickle can be screened using automated complete blood count results. Hemozoin produced by malarial parasites is phagocytosed by neutrophils and monocytes. These pigments can be analyzed to allow the identification of malaria infection by automated methods. The parasite-infected RBCs cannot be lysed by the stromatolyser solution and will enter the WBC counting block. In such case, the WBC histogram will not start from the baseline and can be used as a screening method in malaria-endemic areas [Figure 2].

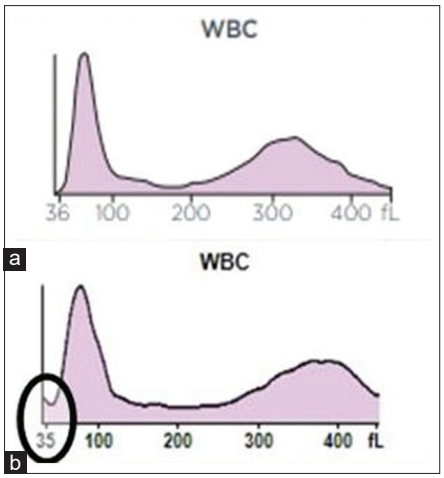

Figure 2: (a) Normal white blood cell histogram in automated cell counter. (b) White blood cell histogram does not begin at the baseline. A spurious increase in the baseline population (black circle) can be an indicator of the presence of malarial parasites in the red blood cells. This occurs because the parasite infected red blood cells cannot be lysed by the stromatolyser solution and will enter the white blood cell counting block

Conclusion

Transfusion management in SCD can be a challenge. Patients may become highly alloimmunized leading to problems in getting compatible units. There is evidence that anemia can be exaggerated in SCD patients suffering from malaria. Therefore, efforts must be taken to avoid unnecessary transfusions. Clinical management of patients with this association of diseases should be centered on fast parasitic clearance and supportive measures. Our case report reinforces malaria as a cause of clinical worsening of SCD and highlights the importance of a multifactorial approach in the management of worsening anemia in SCD. Treatment of malaria in our patient avoided the deleterious effect on red cells, thereby reducing the need for transfusion, its associated risks and reducing severe anemia in the patient.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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