ABSTRACT

Two Nigerian siblings, ages 10 and 4 years, respectively, were infected with Plasmodium falciparum and were admitted to the hospital on the same day. The younger child died on the day of admission, but the older child survived. The peripheral blood smears of the younger patient showed the ring forms, schizonts, free merozoites, and phagocytosis of malarial parasites by both monocytes and polymorphonuclear leukocytes, whereas the smear from the older patient revealed only ring forms. The prognostic significance of this unusual observation and the host factors that affect the survival of the patients are discussed. This is the first documented case in which phagocytosis of malarial parasites by polymorphonuclear leukocytes is observed.

Introduction

Malaria is not a common disease in this country. However, because of a worldwide resurgence and an influx of refugees into this country, a further increase in the incidence of malaria should be expected. Two cases are reported of malaria, owing to Plasmodium falciparum, in two siblings who contracted the infection at the same time. The boy died, and the girl survived. The peripheral blood smears of the boy showed phagocytosis of the parasites and the presence of schizonts and free merozoites. These phenomena are uncommon and are of prognostic significance.

Case History

Patient 1. A 4-year-old black Nigerian boy was admitted to Jamaica Hospital. His chief complaint was high fever, chills, nausea, and vomiting on the day of admission. Two days prior to admission, he had a low fever and headache.
The patient had been in the United States for one year but had travelled back to Nigeria four to five times during that period. His last visit to Nigeria was two weeks prior to admission.

Physical examination on admission showed a temperature of 105°F and respiration rate of 38 per minute. The patient was in acute stress, lethargic, weak and dehydrated but not emaciated (weight 36.5 lbs.). His liver was 3 cm below the right costal margin, and the spleen tip was palpable.

Laboratory tests for electrolytes showed potassium, 3.8 mEq per L; sodium, 129 mEq per L; CO₂ 11 mEq per L; BUN, 29 mg per dl; and glucose, 93 mg per dl. Hematologic examination revealed hemoglobin, 9.8 g per dl and WBC, 3,500 per mm³; including lymphocytes, 54 percent; atypical lymphocytes 7 percent; neutrophils, 20 percent; band form, 17 percent; monocytes, one percent; and myelocytes, one percent. Platelets were moderately decreased.

The peripheral blood smears were examined by the senior author. Microscopic examination of the smear showed approximately seven percent infected erythrocytes. Most of the parasites were early trophozoites (ring forms). The rings were small and delicate, showing frequent double chromatin dots. Some erythrocytes contained two to three ring forms. Infected erythrocytes were normal-sized with no Schüffner’s dots. Although no gametocytes were detected, the blood picture was consistent with Plasmodium falciparum infection. Unusual features were noted. Some phagocytized parasites still maintained a rosette pattern (figure 5), while others were partly digested (figure 6).

Initially the patient was given intravenous fluids to correct his dehydration. After the detection of P. falciparum in the peripheral blood smears, the patient received 80 mg of chloroquine dihydrochloride i.m. four and a half hours after admission and 70 mg one hour later. Within 10 minutes, the patient convulsed and was given 5 mg of Valium, but cardiac arrest ensued. Vigorous resuscitation was unsuccessful and he was pronounced dead 30 minutes later. An autopsy request was refused.

**Patient 2.** A 10-year-old black Nigerian girl, who presented with headache, high fever and vomiting for four days, was admitted to the Jamaica Hospital on the same day. The patient had been seen in another hospital the previous day and was given amoxicillin with no obvious effect.

The patient had “malaria” one year previously and was hospitalized in Nigeria. The date of her last visit to Nigeria was also two weeks previously, at the same time as her brother’s (Case 1).

On admission, her temperature was 104°F. Physical examination revealed nuchal rigidity and meningeal signs. Her liver was 3 cm below the right costal margin with right upper quadrant tenderness. The spleen was not palpable. No scleral icterus was noted.

Laboratory tests showed normal electrolytes. Hematologic examination revealed hemoglobin 9.9 g per dl; WBC, 6,400 per mm³ with 7 percent lymphocytes; 4 percent atypical lymphocytes; 5 percent monocytes; 81 percent polymorphonuclear leukocytes, and 3 percent band form. Platelet count was 35,000 per mm³. Liver function tests showed slightly elevated liver enzymes. Bilirubin was 1.6 mg per dl. Prothrombin time and partial thromboplastin time were normal. Sickle cell preparation was negative. Glucose-6-phosphate dehydrogenase (G-6-PD) was normal. Cerebrospinal fluid examination and blood culture were also negative. Urinalysis showed 3+ albumin, but no hemoglobinuria was demonstrated.

The peripheral blood smears were examined by the senior author. About 12 percent of the erythrocytes contained single and double delicate ring forms with the frequent presence of double chromatin dots in rings. Infected erythrocytes were of normal size and contained no Schüffner’s dots. Gametocytes, schizonts, and merozoites were not found. No phagocytosis was demonstrated.

The patient was started initially on intravenous fluids and ampicillin. After malarial parasites were found in the blood smear, she was treated with chloroquine dihydrochloride (150 mg) by muscular injection eight hours later. Chloroquine was continued until the fifth hospital day. She was discharged eight days after admission.

**Discussion**

The simultaneous malarial infection of two siblings with such marked difference in prognosis provides an opportunity for analysing the host factors in resistance to this disease. As young children of the same family, their genetic composition,
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Figure 3. A peripheral blood smear showing a cluster of free merozoites (arrow head) and a few merozoites (arrow) being phagocytized by a monocyte. Wright-Giemsa (×2,000).

Figure 4. A cluster of malarial parasites residing within a parasitophorous vacuole of a monocyte. Wright-Giemsa (×2,000).

nutritional background, and the time of exposure to the infection are probably similar. The time of treatment of both cases was also identical.

The question is why did the boy die and the girl survive? A study of a group of young adults showed no associations between age and course of infection, but cerebral malaria occurs most frequently in children of pre-school age in Africa. A recent study in Thailand, however, showed that most cases of cerebral malaria occurred in adults rather than in children. It was found in that study that 65 percent of the cerebral malaria patients were immigrants from non-endemic areas. Obviously, it is the previous exposure rather than age alone that determines the immune status of the host. In this report, the sister had a history of previous infection, which probably accounted for the relatively benign course; whereas the non-immune brother rapidly developed cerebral malaria. It is also interesting to note that the survivor did not have sickle cell disease and G-6-PD deficiency which might have contributed to her resistance to malaria.

In most cases of falciparum malaria, the older trophozoites, schizonts, and segmenters are sequestered from the peripheral circulation and thus they are seldom seen in the peripheral blood smear. In the light of ultrastructural studies, it has been found that the formation of electron-dense excrescences (knobs) on the erythrocytic membrane is responsible for the attachment of infected red blood cells to the venous endothelium of the internal organs, resulting in their retention.
gametocytes in the peripheral blood of patients infected with *P. falciparum*, Beaver et al point out that the existence of schizonts and other developing forms does not automatically rule out *P. falciparum* infection. It is rather a sign of grave prognosis because these forms are usually seen in heavily infected or moribund patients. However, the presence of free merozoites as seen in this case is extremely rare since merozoites invade other erythrocytes almost immediately after their being released. *In vitro* hemolysis in an old blood specimen may lead to the existence of extraerythrocytic merozoites; however, in our cases, blood smears were made immediately after specimen collection and thus *in vitro* hemolysis was unlikely.

The prognostic significance of the presence of the schizonts and/or merozoites in peripheral blood smears is obvious when comparing these two cases, because the survivor had even higher parasite counts than her brother who died. Parasite count has been regarded as the most important indicator for the prognosis of patients with malaria. However, when the developing forms are seen in the peripheral blood of a falciparum malaria case, a poor prognosis is indicated even though the parasite count is not very high, as seen in our Patient 1.

Although phagocytosis of *P. falciparum* was first documented in human cases as recently as in 1980, it is probably not a very rare phenomenon in heavily infected cases.* The unique feature in this observation is that the para-

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* W. A. Krotoski, personal communication.
sites were not only demonstrated in monocytes but also in polymorphonuclear leukocytes.

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References