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# Think outside the Box for Diagnosing Malaria as a Cause of Sickle Cell Crisis in an Urban Hospital - Case Report

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**Abstract** *Plasmodium falciparum* (PF) causes the most deadly form of malaria. This is a case of a 43 year old male with sickle cell disease who presented to a community hospital in Philadelphia and was admitted for sickle cell crisis secondary to *Plasmodium falciparum* malaria. His last visit to malaria endemic area (Nigeria) was 13 months prior, when he contracted malaria and was treated successfully by the local health center. Sickle cell disease is known to have a protective effect against malaria. This case illustrates the importance of high index of suspicion that clinician must have when encountering patients with prior histories of malaria or traveling to remote, endemic areas, even in patients with sickle cell disease and those who are outside of the one year window period of exposure.

***Keywords:*** *Plasmodium falciparum, sickle cell disease, sickle cell trait*

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## 1. Case Report

A 43-year-old male with a past medical history of sickle cell anemia and appendectomy, originally from Nigeria, who recently moved to Philadelphia from Georgia 2 months ago, presented to the emergency room in a community hospital in Philadelphia with complaints of dizziness, shortness of breath, jaundice, severe chest pain and back pain for 1-2 days duration, and was admitted for sickle cell crisis. His only home medication was folic acid. Initial physical examination showed RR 16 per min, HR 76/min, Temp 98.1°F, oxygen saturation of 100% on room air. The physical examination showed significant scleral icterus, enlarged liver, and blisters below the right nostril. The patient's labs were significant for anemia with a hemoglobin of 5.2 g/dl, hematocrit of 15%, MCV of 92 fL, reticulocytosis with absolute reticulocyte 0.21 thou */µL* (50-100X$10^9$L), percent reticulocyte count of 8.6%, and increased bilirubin (total bilirubin 5.2 mg/dL and direct bilirubin of 1.4 mg/dL). Hemoglobin electrophoresis and peripheral smears were sent on admission. He was started on IV fluids and IV pain medication. He developed fevers up to 103.8°F within 24 hours of admission. Chest x-ray showed no active pulmonary disease, blood and urine cultures were negative. CT abdomen without contrast showed evidence of remote left renal infarct, enlarged liver, atrophic calcified spleen, and biconcave lumbar vertebral endplates all consistent with the patient's history of sickle cell anemia. On the second hospital day, his sickle cell crisis was resolving however he still remained febrile. He was then started on oral Valtrex for oral herpes and oral doxycycline empirically. Persistent fevers raised concern for underlying undiagnosed infection. Further history revealed that 13 months ago, during his last trip to Nigeria, the patient had developed malaria and was treated with an antimalarial regimen. The specific regimen is unknown with which he had made full recovery.

His malaria rapid antigen test was found to be positive, peripheral blood smear showed ring-form trophozites of *p. falciparum* (A) along sickled erythrocytes (B). The parasitemia level was 1.73% (0.0001-0.0004% higher is required for a positive level). He was treated with atovaquone/proguanil 4 tablets daily for 3 days. With treatment, he showed prompt clinical improvement, and his fevers resolved.

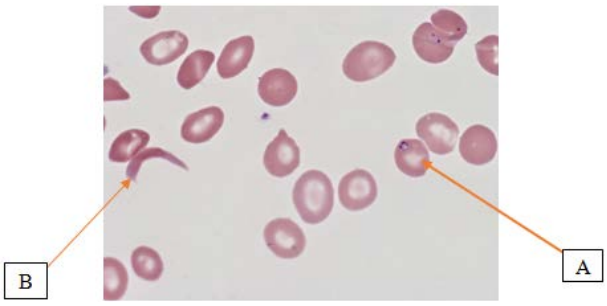


**Figure 1.** Thin peripheral blood smear showed ring-form trophozites of *p. falciparum* (A) along sickled erythrocytes (B)

## 2. Discussion

*Plasmodium falciparum* (PF) causes the deadliest form of malaria and is accountable for more 50% of all malaria cases worldwide. [1,2] The incubation period is 7-15 days but recrudescence is possible within a year after an untreated or incompletely treated infection. [2] A

recrudescence is thought to originate from circulating Plasmodium blood stages which do not cause fever before a certain level of a microscopically detectable parasitemia is reached. [3] It is not possible to estimate how common recrudescence infection with *P. falciparium* might be, but with more than 50% malaria caused by *P. falciparium* worldwide even if only a small proportion of untreated or partially treated infection becomes indolent, this represents a large potential reservoir of sustained transmission.

Although the exact mechanism for recrudescence is unclear in our patient, possibilities include incomplete treatment of his first episode of malaria, drug resistance, inappropriate regimen or re-infection prior to leaving the endemic regimen 13 months prior. It is notable that exposure risks have increased with the expansion of air travel [4] and even rare cases where malaria was acquired from contact with packages sent from an endemic region have been reported [5].

Another important aspect of this case resides in the fact that the patient has sickle cell disease (Hb SS) which is known to have protective effects against infection with *P. falciparum* compared to sickle cell trait (Hb AS), but is associated with higher mortality and morbidity [6]. In a study investigating patients with sickle cell disease in West Kenya, blood slides of 728 cases of malarial parasites were studied, and parasite was found in only 0.5% in sickle cell disease (HbSS), compared to 35.5% in HbAA, and 5.8% in sickle cell trait (HbAS). Malaria prevalence per genotypic group were 44.1% in HbAAs, 36.2% in HbASs, and 20% in HbSSs [7].

Innate and acquired mechanisms have been postulated as protective in patients with sickle cell trait and sickle cell disease, however they are not fully understood. [8,9] One of them is increased cell sickling, which has been proven in studies using cultured parasitized sickle trait red cells, revealing that increased sickling promotes a faster removal of these cells. [10] Another mechanism is the impaired growth of the parasite caused by various factors such as deoxygenation, disregulated microRNA insertion, loss of potassium, increase activity of the calcium-potassium dependent channel and enhanced phagocytosis [11,12,13,14].

This case illustrates the importance of a high index of suspicion that a clinician must have, to consider *P. falciparum* malaria as a cause of sickle cell crisis in a patient in the urban setting with a history of treated malaria more than a year prior in a malaria endemic region.

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