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Case Reports

A Strange Manifestation of Malaria in a Native Nigerian Boy

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Abstract. The protective role of Sickle Cell Trait (SCT) in malaria endemic areas has been proved, and prevalence of HbS gene in malaria endemic areas is high. Splenic infarction is a well-known complication of SCT, while the association with malaria is considered rare. A Nigerian boy was admitted to our ward after returning from his country of origin, for *P. falciparum* malaria. He underwent abdominal ultrasound for upper right abdominal pain, showing cholecystitis and multiple splenic lesions suggestive of abscesses. Empiric antibiotic therapy was undertaken. *Bartonella, Echinococcus, Entamoeba* serologies, blood cultures, Quantiferon test, copro-parasitologic exam were negative; endocarditis was excluded. He underwent further blood exams and abdomen MRI, confirming the presence of signal alterations areas, with radiographic appearance of recent post-infarction outcomes. Hemoglobin electrophoresis showed a percentage of HbS of 40.6% and a diagnosis of SCT was then made. Splenic infarction should be taken into account in patients with malaria and localized abdominal pain. Moreover, diagnosis of SCT should be considered.

Keywords: Malaria, Sickle Cell Trait, Splenic Infarction.

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Case Report. In 1948 Haldane firstly hypothesized the existence of a protective relationship between an otherwise harmful genetic mutation and a population with a high frequency of parasite infection. Since then, the protective role of Sickle Cell Trait (SCT) in malaria endemic areas has been proved in several studies.[1,2] In fact, if red cells are abnormal, the chance of success of the parasite is affected, reducing death rate due to *Plasmodium spp.*

Splenic infarction is a well-known complication of SCT, in particular during exercise at high altitude, but it has also been described at rest in aircrafts or with exercise at sea level. Splenic vaso-occlusion is related to hemoglobin S polymerization and red cell deformation. Clinical presentation consists of severe upper quadrants abdominal pain, vomiting, and nausea. Fever, leukocytosis and elevation of LDH usually occur in the first 3 days.[3]

In contrast, malaria-associated splenic infarctions are considered rare. Anyway, reports of single or small series of cases have appeared almost annually.[4] Is therefore really unusual to find these three conditions co-existing?

We report the case of an 11-year-old Nigerian boy, living in Italy since 2010. On August, 26th he flew back from a one-month stay in Nigeria, and two days later he started presenting fever. On August, 31st he complained vomiting and abdominal pain and was then conducted to the Emergency Room of our Hospital. Here, after an initial suspect of appendicitis, a diagnosis of *Plasmodium falciparum* malaria was made, and the patient was admitted to the Infectious Diseases ward. Body temperature was 38°C, while other vital signs were normal. His complete blood count showed leukopenia (WBC 4060, nv 4500-10800) and thrombocytopenia (PLT 59,000, nv 100,000-400,000), while hemoglobin was 13 g/dL (nv 13-16.5 g/dL). His chemistry profile showed hyperbilirubinemia (2.93 mg/dL, nv 0.2-0.5 mg/dL), AST 136 UI/L and ALT 122 UI/L (nv 13-51 UI/L and 15-47 UI/L, respectively), creatinine was 1.06 mg/dL (nv 0.3-0.9 mg/dL) and an increase of LDH values (657 U/L) was present (nv 120-330 U/L); C-reactive protein was 85.6 mg/L (nv <5 mg/L). He started therapy with piperachin/diidroartemisin 320/40 mg, 3 tablets qd, and as long as he kept presenting well-localized right upper quadrant abdominal pain, an ultrasound (US) was performed on September, 1st. The exam showed a starred sky appearance of the liver associated with a slightly enlarged gallbladder, with transonic content and thickened walls, suggestive of cholecystitis. A slight increase of the spleen's dimensions (pole-to-pole diameter 11 cm) was present, and in its context a hypo-anechoic, inhomogeneous ovalar lesion (diameter 1.5 cm) was found, raising a diagnostic doubt (Abscess? Hematoma? Cyst?). The pediatric surgeon confirmed a non-surgical approach for cholecystitis and antibiotic therapy with piperacilline/tazobactam 4.5 g tid (body weight of 42 Kg) was undertaken. As long as he kept presenting fever (**Figure 1**) although therapy for malaria was considered over (piperachin/diidroartemisin 320/40 mg, 3 tablets qd, from August, 31st to September, 2nd) and hemoscopy resulted negative, as suggested by the radiologist, the next day the US was repeated, showing multiple splenic abscesses. Therefore, serologies for *Bartonella*, *Echinococcus* and *Entamoeba* and blood cultures were sent.

Quantiferon test and coproparasitologic exam were executed, resulting both negative. An echocardiogram showed no endocarditic vegetations. On September, 5th the boy was transferred to the Pediatrics ward for cholecystitis and splenic abscesses. Antimicrobial spectrum was broadened with Claritromicine 250 mg bid per os. Blood tests were performed, including peripheral blood smear, quantitative Ig, total IgE, lymphocyte typing, hemoglobin electrophoresis and dihydrorhodamine 123 test, in order to evaluate any underlying hematologic diseases. On September, 8th, magnetic resonance imaging (MRI) of the abdomen was performed, confirming the presence of seven focal areas of signal alteration, with prevalent peripheral subcapsular distribution (maximum size 1.7 mm).

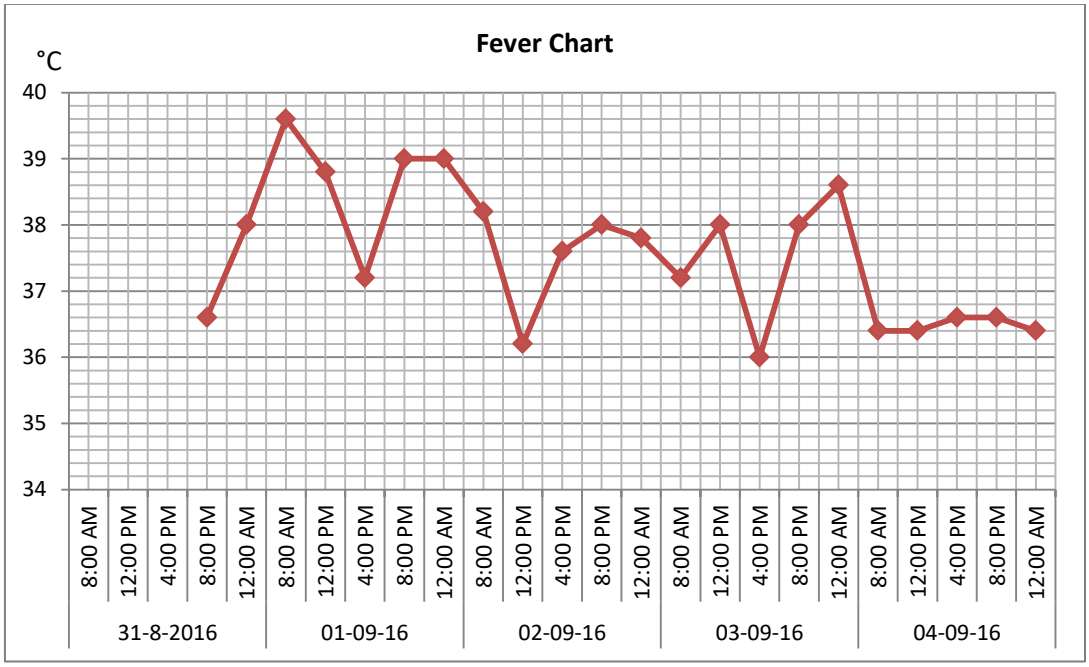

Figure 1. Fever chart during the admittance in the Infectious Diseases ward.

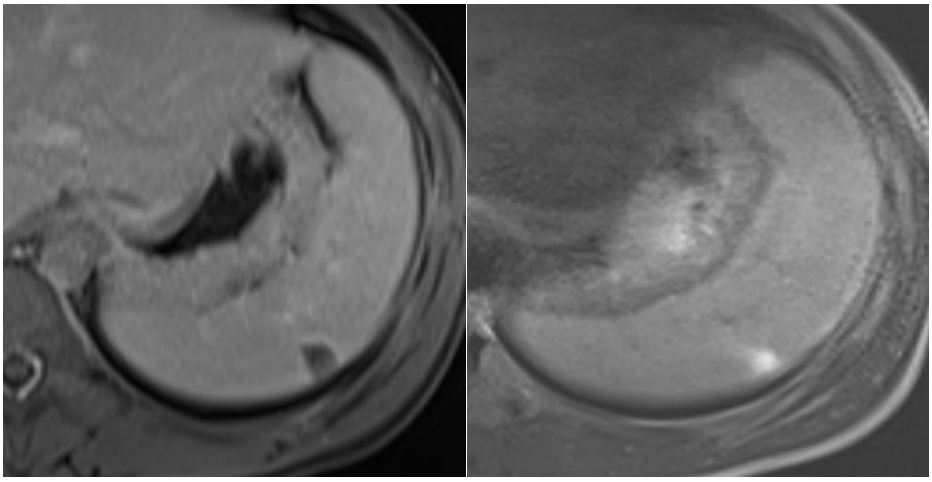

Figure 2 and 3. Abdomen magnetic resonance imaging (T1 and T2 weighted, respectively): Splenic focal areas of signal alteration, with prevalent peripheral subcapsular distribution.

The morphology of the formations, especially of the most voluminous, was a pyramidal wedge with the apex pointing towards the hilum, and the base of the splenic capsule, while profiles looked finely irregular (**Figure 2** and **3**).The radiographic appearance then made it less likely the possibility of splenic abscesses, in favour of a diagnosis of recent post-infarction outcomes or hematomas in a subacute phase. While all other requested exams resulted negative, on September, 13th, hemoglobin electrophoresis showed a percentage of HbS of 40.6%, HbA was 55.2% while HbA2 and HbF were respectively 3.5 and 0.7%. A diagnosis of SCT was then made.

On September, 15th the boy was discharged, with recommendations to radiologic follow-up and preconception counseling for him and his parents and without further antibiotic therapy.

On October, 13th the boy repeated the US, which showed a normal spleen. The timing of regression is compatible with the diagnosis of splenic infarction.

Discussion and Conclusions. SCT has a protective role in the pathogenesis of severe malaria, whereas HbS is not an absolute impediment to the infection by *Plasmodium spp*. Probably an early phagocytose of the parasited sickled cells by the reticulo-endothelial system is the mechanism for the increased fitness of patients with SCT.[1] Prevalence of HbS gene in malaria endemic areas can reach a percentage >20%; therefore this diagnosis must be taken into account in a patient hailing from one of these countries,[2] especially when anemia is present. Splenic infarction is a complication of SCT,[3] and it has been reported at rest in aircrafts, moreover it has been described as a rare complication of malaria, it is primarily caused by *P. falciparum*, occurring mostly during the acute phase of the infection,[4] even if the exact frequency of malaria-associated splenic infarction remains unclear because of under-diagnosis and under-reporting.[5]

In our case, as long as fever kept on after the conclusion of an adequate cycle of antimalarial therapy, in association with abdominal pain in the right upper quadrant and evidence of splenic lesions, further analysis have been undertaken in the suspect of a concomitant condition. Trauma was excluded. Therefore we considered as differential diagnosis splenic abscesses, both primary or secundary (e.g. endocarditis, patent foramen ovale), splenic infarction, primary hematologic diseases and granulomatous diseases (e.g. tuberculosis and chronic granulomatous disorder). Contrary to our case, abdominal pain is generally reported as localized to the left upper quadrant, when splenic infarction is present.[4] In the reported case, atypical clinical presentation, concomitant cholecystitis and radiological diagnosis of splenic abscesses were misleading.

Splenic infarction should be taken into account in a patient with malaria and abdominal pain, particularly when localized to upper quadrants, and US and CT scan should be performed to confirm the diagnosis. Computed tomography scan with contrast is the gold standard for diagnosis of splenic infarction. In our case, however, US has been primarly performed in the suspect of cholecystitis. MRI was then performed, taking into account the young age of the patient and the good sensitivity of this technique for spleen lesions.[5]

Conservative therapy must be attempted, and the prognosis is good.[6] Splenectomy should be reserved for those patients with severe damage to the spleen, also taking into account possible future complications,[7] including severe malaria.

Finally, as long as the number of international migrants worldwide kept on growing over the past decades, all of us clinicians should be aware of pathologies we haven't been familiar with in our daily activity.

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