Case Study

Misdiagnosis of an imported case of malaria caused by *Plasmodium falciparum*

Waleed Mohammad Hussain[1], *Syed Zahid Bukhari[2], Mohammad Ibrahim Fatani[3], Talal Mohammad Karima[1], Tariq Ahmed Madani[4], and Samar Badreddine[5]

[1]*Department of Internal Medicine, Hera General Hospital, Makkah, Saudi Arabia*
[2]*Department of Microbiology, Hera General Hospital, Makkah, Saudi Arabia*
[3]*Department of Dermatology, Hera General Hospital, Makkah, Saudi Arabia*
[4]*Department of Internal Medicine, King Abdulaziz University Hospital Jeddah, Saudi Arabia.*
[5]*Department of Infectious Diseases, King Faisal Specialist Hospital & Research Center, Jeddah Saudi Arabia*

Abstract

An unusual case of malaria presented with gastroenteritis and bloody diarrhoea in a 46-year-old male. The patient was a non-Saudi resident of Makkah, Saudi Arabia. Fever was not the presenting complaint, and the patient had not experienced any chills or sweating. He gave history of recent travel to Pakistan. Initial laboratory investigations showed anemia, thrombocytopenia, normal liver function, and negative blood film for malaria. His widal, *Brucella*, and dengue serology was negative. Endoscopic examination showed gastroenteritis. On the fifth day of admission, a sexual form of *Plasmodium falciparum* on peripheral smear was reported by chance. Malaria was misdiagnosed because of initial negative blood film which may have been due to false microscopy or a long period between exposures and positive blood film. We concluded that a repeat blood film for malaria at 12- to 24-hour intervals for 48 to 72 hours is cost effective when a patient has recently travelled to an endemic area.

Keywords: *Plasmodium falciparum*, malaria, diagnosis

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Introduction:

Malaria is a potentially life-threatening disease for travellers to the tropics. Imported malaria is a major clinical problem in nonendemic areas of the world because of the increasing number of travellers, overseas workers, and immigrants from endemic areas.[1] Among travellers, mortality remains a serious issue due to failure to obtain and use preventive measures, delay in seeking medical attention, and misdiagnosis.[2] This report describes an imported case of *P. falciparum* malaria misdiagnosed initially by many physicians before admission to our hospital.

Case report

A 46-year-old male patient was admitted to the Hera General Hospital, Makkah, Kingdom of Saudi Arabia (KSA), in September 2007. A non-Saudi, Pakistani national, he had been residing in the western region of Saudi Arabia for the past 10 years. Previous to admission, he vacationed in Pakistan for 45 days, where he travelled to Peshawar, Northwest Frontier Province (NWFP) and Quetta, Balochistan. He returned to KSA two weeks before admission. He presented with 10 days' history of gastrointestinal symptoms including abdominal pain, vomiting, and loose stools. The most recent complaint was bloody diarrhoea, which appeared a day before admission. There was no history of any particular pattern of fever and no feeling of cold and flushing of face. His past medical history was unremarkable.

Upon admission, the patient had a report of negative blood film for malarial parasites from a local private laboratory. His endoscopic examination revealed diffuse congested mucosa of the stomach mainly on the cardia and fundus as shown in Figure 1. The duodenum showed thick irregular mucosa with multiple erosions. His abdominal ultrasound and echocardiogram was normal. Microbiological blood, urine and stool culture reports were negative. Major haematological findings were as follows: anaemia with haemoglobin 7.17 G/dl (4.4mmol/l) due to obligatory destruction of red cells by merogony, accelerated destruction of non-parasitized red cells.

Massive gastrointestinal haemorrhage can also contribute to the anaemia. The patient also had thrombocytopenia (PLT 81.0/ml). On admission the renal function was slightly impaired while liver

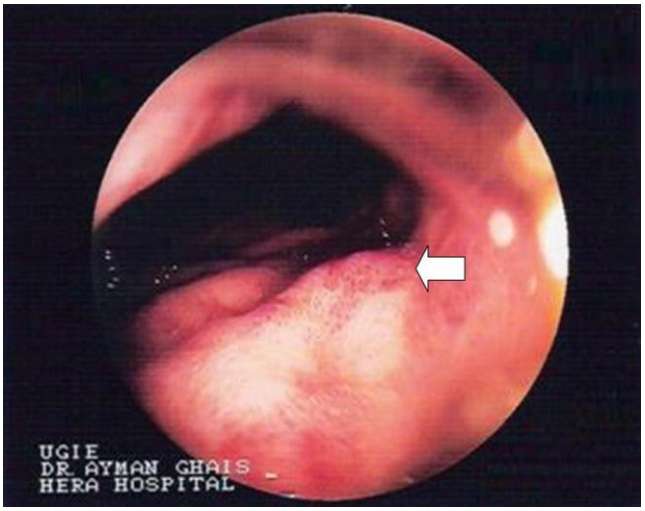
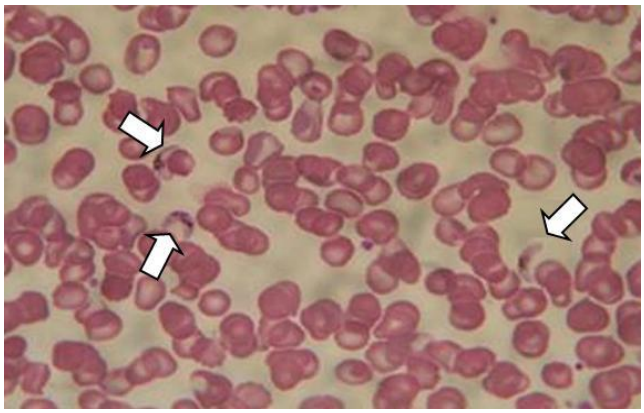


Fig 1: Endoscope view showing diffuse congested mucosa on cardia.

function tests were normal. His lactate dehydrogenase (LDH) level was 395 U/L (range 180-360 U/L). Dengue IgM and antibodies for *Entamoeba histolytica* were negative. Widal and *Brucella* titers were within normal limits. The patient was negative for hepatitis B and C viral infection. On the day fifth of admission, a sexual form of *P. falciparum* was reported by chance from the laboratory on routine peripheral smear. Figure 2 shows the gametocyte which appeared as an elongated crescent or sausage-shaped structure. No clinical signs of organ damage caused by malaria were observed and the patient did not fulfil the World Health Organization (WHO) criteria for suspicion of severe malaria. This case of *P. falciparum* malaria was reported to the Preventive Medicine Department, Ministry of Health, according to the notification policy of infectious diseases for surveillance. There was no history of fever among other members of the patient's family. The patient was given quinine sulphate infusion for 48 hours, after which the same drug was given orally 600 mg TID. The following supportive drugs were given orally for one week: doxycycline 500 mg BD, pantoprazole 40 mg BD, and ferrous fumarate 200 mg TID for 7 days. During the course of management he was infused two pints of blood to correct anaemia. Anaemia in this patient was attributable both to malaria as well as to gastrointestinal bleeding. Stool examination revealed the following: reddish in colour, bloody in consistency, occult blood positive, and RBC 18-20/hpf which supports GI bleeding while elevation in LDH is suggestive of haemolysis, most likely due to malaria. The patient was seen in the outpatient department four weeks after discharge from the hospital. He was afebrile and his blood film for malaria was negative. Further follow-up was advised but the patient did not return to the clinic.

Fig 2: Peripheral smear showing sexual gametocytes of *P. falciparum.*



Discussion

Most of the malaria cases occur in travellers who recently visited areas where malaria is endemic as reported by the Center for Disease Control (CDC) [2]. In this case, the clinical pathway failed to match the diagnosis due to gastrointestinal symptoms and an initial negative blood film report for malaria from a local private laboratory. The additional relevant questions were asked during course of management. Our patient had recent history of travel to NWFP and Balochistan, Pakistan, in September 2007 without taking any chemoprophylaxis for malaria. Both *Plasmodium falciparum* and *Plasmodium vivax* are widely distributed in Pakistan. The major transmission period is post monsoon, *i.e.* from July to November, but a short spring transmission period during April and May is also possible. Geographically, the border area of two provinces of Pakistan NWFP and Balochistan are connected with the borders of Afghanistan and Iran respectively. These two neighbouring countries of Pakistan are already declared endemic for malaria by the WHO [3]. In the western region of KSA, the patient was residing in Azizah, which is a Porsche area of Makkah. According to the Preventive Medicine Department of the local health authority, no previous case of *P. falciparium* malaria has been reported from this area. Although there is no active

malaria transmission in KSA, imported infections still pose a significant health problem [4]. Al-Hassan *et al.* [5] report that the most frequently implicated organism is *P. falciparum*, accounting for 74.2% of cases. Similar to the circumstances of our patient, misdiagnosis due to gastrointestinal symptoms was previously reported by Yombi *et al.* [6] and by Weber *et al.* [1]. After positive blood film for malaria, the clinical presentation of diarrhoea was considered due to *P. falciparum* as reported by Robinson *et al.* [7]. Dengue serology was done because the Western region of KSA, especially Makkah and Jeddah, is the endemic area for dengue virus (Khan *et al.*) [8], and its concurrent infection has been proved recently by Kaushik *et al.* [9]. Therefore, the possibility of mixed infection with various *Plasmodium* species was excluded to ensure a better treatment outcome. Robinson *et al.* [7] reported a 32-week period between the return from an endemic area and diagnosis for *P. falciparum* infection. A long incubation period has also been reported by Ericsson and Gunther[10]. The incubation period in our patient appears to have been 1 week.

The patient in our case produced a negative blood film for malaria from a test by a private laboratory previous to admission. Therefore, the patient was initially treated as a case of gastroenteritis and the detailed travel history was not taken. The second blood film for malaria was not ordered by the treating physician; however, gametocytes were reported on routine blood film examination according to the laboratory protocol. The initial negative blood film for malaria can be explained by the long duration between exposure and blood film examination. Therefore, physicians should improve their ability to diagnose falciparum malaria by obtaining a thorough travel history of all patients with clinical features suggesting an infectious origin and considering this diagnosis in any patient with a history of travel to or migration from malaria-endemic areas. It is also recommended that travellers take adequate chemoprophylaxis when visiting the malaria endemic areas.

Conclusion

Malaria remains a health threat for those travelling to endemic areas and is associated with missed or delayed diagnosis due to nonspecific clinical features and the long period between exposure and positive blood film. Malaria should be suspected in a febrile traveller regardless of the symptoms. A proper history of the patient plays a key role in preventing misdiagnosis of such cases. If the initial film is negative and the patient is suspected of having malaria, blood films should be repeated at 12- to 24-hour intervals for 48 to 72 hours. Such testing is cost effective when a patient has history of recent travel to an endemic area.

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Corresponding author:
Dr. Syed Zahid Bukhari
Department of Laboratory & Blood Bank
Hera General Hospital
P.O. Box: 20865, Makkah, Saudi Arabia
Phone: +966-2-5203535, Ext. 4302
Cell Phone: +966-0501531042
Fax: +966-2-5200333
Email: zahidbukhari100@msn.com

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