

Atypical presentation of *Plasmodium ovale* malaria with severe hepatic and renal damage

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Introduction

Non-falciparum malaria refers to malaria infection due to *Plasmodium* species other than *P. falciparum*: *P. vivax*, *P. ovale*, *P. malariae*, and *P. knowlesi*.^{1,2} The non-falciparum species usually cause febrile illness but are rarely fatal, although deaths and severe presentations have been reported in the setting of *P. vivax* and *P. knowlesi* infections.^{2,3,4}

We report a case of atypical *Plasmodium ovale* malaria with severe hepatic and renal damage and with successful outcome.

Case presentation

A 60 year old Italian female presented high fever (T 39.6°C), shivering and severe renal colic pain in February 2008. She was on levothyroxine substitutive therapy for a previous thyroidectomy and she had a previous admission for renal colic pain. Her medical history contained nothing else of note.

She had travelled in West Africa (Togo) in August 2007 for one month as a volunteer in a humanitarian mission 2007. Before travel she had been regularly vaccinated for yellow fever, meningococcal infection, typhoid fever, hepatitis A and B (boosted in January 2008). She had taken prophylaxis for malaria with mefloquine (250mg/week starting one week before reaching the endemic area and for 4 weeks after returning)⁵ without any side effect.

She was treated as an outpatient with amoxicilline/clavulanate for 4 days followed by a 4 days course of fluoroquinolone without any improvement. Urine culture was positive for multi-resistant *E. coli* and consequently she commenced treatment with ceftriaxone 1gr i.m. 3/day. Temperature normalised but it rose again after 24 hours.

The patient was then admitted to the nephrology department. Blood examination showed severe hepatic and renal damage (Hb 10,2 gr/dl, Plt 75.000 mg/dl, PT 57%, BUN 178 mg/dl, creatinine 6.85 mg/dl, ALT 50 U/l, AST 38 U/l).

A blood smear was sent to ISS (Istituto Superiore di Sanita) the leading technical and scientific public body of the Italian Health Service and it resulted negative for plasmodia. Antigenemia for malaria was tested by Bimax Now (FDA approved) with a sensitivity of 89% and a specificity of 100%⁶ and was also negative. PCR was not available in our setting. After three days the patient was transferred to the Infectious Diseases department suspecting a sepsis originating in the urinary tract. She was in poor general condition and dehydrated (BP 95/60, CF 96/m). Her temperature reached 40°C in evening. Examination was otherwise unremarkable.

Echocardiography showed a pericardial effusion (2mm). Abdominal ultrasound showed a mild enlargement of the spleen, a picture of interstitial nephropathy, and a peritoneal sub hepatic effusion. Chest X-Ray was normal and all blood cultures were negative.

Treatment was started with Imipenem, hydration with 0,9% NaCl and 5% dextrose infusion, and support therapy with KCl, Calcium and Vitamin K1. Serial Blood test performed during the admission in infectious diseases are summarized in table 1.

In the following days the fever persisted (T max 40°C), with shivering and deterioration of the general condition. Renal and hepatic function were progressively worsening (table 1). Blood smear and antigenemia for malaria were repeated on day 4 and both were negative. On day 5 a blood smear revealed a schizont and a trophozoite, but initially the species was not identified.

Antimalarial treatment was started with oral quinine (8 mg base/kg three times/day) and doxycycline (100 mg twice/day) for 5 days⁵. Intravenous treatment was not started since there wasn't any cerebral involvement, the patient was able to swallow and there wasn't conclusive evidence of *plasmodium falciparum* infection. One day later, plasmodium was identified as ovale spp and the same therapy was continued.

Her clinical condition improved, the fever disappeared and the alterations of hepatic and renal function progressively improved without dialysis. The severe anaemia required transfusion of 2 blood units. After 6 days of treatment the patient clinically recovered and the laboratory parameters were almost normal (WBC 5.040, Hb 1,2, Plt 253.000, PT 85 %, BUN 52, creat 1,13).

Treatment with Primaquine (15 mg/day for 14 day) was given to eradicate the intra-hepatic forms after G6PD testing.⁵

Conclusion

P. ovale usually causes mild illness characterized by erratic or continuous fever without organ involvement. Physical findings usually include enlarged spleen by the second week of infection and a palpable liver. Fatalities are rare but deaths have been reported occasionally following splenic rupture.⁷

Cases of atypical severe forms with organ involvement have never been reported in immuno-competent people. In our case the only data suggesting a possible infection by *P.ovale* was the epidemiologic one of a travel in West Africa but the clinical presentation was extremely uncommon for this infection. In fact, in our report *P. ovale* has been responsible of a very severe presentation with multi-organ damage, even with a very low schizont parasitaemia. The initial negativity of blood smear and malaria antigenaemia and the severe involvement of liver and kidney has been cause of delay in diagnosis, suggesting other diagnoses such as sepsis or pyelonephritis.

Another possible confounding factor could have been the correct use of prophylaxis with mefloquine, which is active against the haematic schizonts and can make the initial crisis milder, although mefloquine cannot block the cycle eso-erythrocytic and the relapses due to the hypnozoites.

This case is a reminder to never exclude the possibility of malaria in a patient with a risk factor. It is also a reminder to never exclude possibility of severe illness even in infections from non-falciparum plasmodia, even with low parasitaemia, taking in account that the sensitivity of antigenic tests is not always high (89% for the test used in our case) and the

negativity is not sufficient to exclude the infection. A useful tool to accelerate the diagnosis could have been PCR which was unfortunately unavailable in our centre.

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