PULSE PARA VOLVER AL ÍNDICE

# Complicated Malaria caused by Plasmodium ovale, Salamanca, Spain

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### **ABSTRACT**

Background: Monomicrobial imported infection by Plasmodium ovale is very rare. Case presentation: We report a case of complicated imported malaria by Plasmodium ovale in a man who suffered from subacute recurrent fever, thrombocytopenia and splenomegaly. Conclusion: Both the patient history and a search of epidemiological medical history were fundamental for confirming the suspicion.

**Keywords:** Imported malaria, Plasmodium ovale, paludism.

## **BACKGROUND**

*Plasmodium ovale* is distributed mainly in tropical Africa, South America, and Asia, but cases of *P. ovale* malaria have been reported outside endemic areas<sup>1</sup>. Monomicrobial imported *P. ovale* infection is very rare, being found in about 5% of malaria cases worldwide<sup>2</sup> and 1–2% of malaria cases in Spain<sup>3, 4</sup>. It usually presents as a co-infection with *P. falciparum* or *P. vivax*<sup>4</sup>.

## **CASE PRESENTATION**

The patient, a 36-year-old man sought care in our emergency department for intermittent fever up to 40 °C, accompanied by chills, asthenia, diaphoresis, left pleuritic pain, and vomiting that had evolved over 3 weeks. Between febrile episodes, he maintained good general health. He denied having travelled recently and had no animals or risky sexual contacts. On physical examination, he presented with a blood pressure of 103/71 mm Hg, a heart rate of 99 beats per minute, an ambient air oxygen saturation of 99% by pulse oximetry, a respiration rate of 14 breaths per minute, an axillary temperature of 36.4 °C, and pain in the left hypochondrium. Laboratory tests showed anemia (hemoglobin 10.5 g/dL), a normal white blood cell count (6.34  $\times$  10<sup>3</sup>/mm<sup>3</sup>) and normal leukocyte formula, thrombocytopenia (80  $\times$  10 $^3$ /mm $^3$ ), acute renal failure (estimated glomerular filtration rate 58,2 ml/min/1,73 m<sup>2</sup>), hyperbilirubinemia (total bilirubin 2.6 mg/dL, indirect bilirubin 1.6 mg/ dL), elevated lactate dehydrogenase (553 U/L), elevated C-reactive protein (10.0 mg/dL), elevated procalcitonin (14.0 ng/mL), and a decrease of haptoglobin (7.7 mg/dL). Additionally, an abdominal ultrasound revealed splenomegaly.

Upon initial suspicion of bacterial sepsis, empirical antibiotic treatment was started with ceftriaxone (2 g/day IV) and a single-dose of gentamicin (5 mg/kg IV). A computerized axial tomography showed two lesions compatible with splenic infarctions and signs of minimal perisplenic hemoperitoneum secondary to splenic fissure (figures 1 and 2). The surgery unit suggested observation of the hemoperitoneum. Therefore, the patient was re-interrogated and reported that he had undergone dental implant placement 15 days before the onset of symptoms. Given the suspicion of an endovascular focus, the antibiotic treatment was changed to daptomycin (10 mg/kg/day IV), cloxacillin (2 g every four hours IV), and gentamicin (3 mg/

Figure 1. Splenic Fissure in axial computerized tomografy (arrow)



Figure 2. Perisplenic hemoperitoneum in axial computerized tomography (arrow)



kg/day IV). Infective endocarditis was ruled out by transthoracic and transesophageal echocardiography. Serial blood cultures were also negative.

On the fifth day of admission the patient persisted febrile. Then, he reported having worked in Ghana and Equatorial Guinea for 18 months without antimalarial prophylaxis, two years before the date of admission. He asserted that he had not considered this data due to the long time that had elapsed since his return to Spain. In Africa he had presented a self-limiting febrile syndrome of unknown cause for which he did not receive any specific treatment. Studies to rule out *Plasmodium spp.* infection (peripheral blood smears and immunochromatography Binax NOW® twice), were negative. Nevertheless, serum polymerase chain reaction (PCR) for *Plasmodium* was ordered (the sample was processed at a centralized reference center in Spain, with results to be received later). Treatment with systemic artesunate (2,4 mg/kg/dose initially, followed by 1,2 mg/ kg at 12 hours, 24 hours, then 1,2 mg/kg /day for five days) was followed by oral atovaquone proguanil (Malarone® 250/100 mg, four tablets per day for three days). After the change of antibiotic therapy and start of antimalarial treatment, the patient experienced clinical, biochemical, and radiological recovery and was discharged. A week later, a positive PCR result or *P. ovale* was received.

#### DISCUSSION AND CONCLUSIONS

*P. ovale* hypnozoites can persist in the hepatocytes of infected patients producing a malarial relapse, months or even years after the initial infection<sup>5</sup>. Latency periods of up to 60 weeks in length have been described<sup>6, 7</sup>. Therefore, we emphasize the importance of thorough patient history to rule out malaria in every traveler coming from an endemic area who presents with fever, despite a long delay since returning<sup>5</sup>. In the current case, the patient had returned more than 80 weeks prior.

The belief that *P. ovale* can cause benign malaria with a low level of parasitemia should be cautiously considered because it is also able to produce complicated infections like those caused by *P. falciparum*, although it occurs less often<sup>8,9</sup>. In fact, mortality associated with complicated malaria caused by *P. ovale* is about 30%, with 70% of patients developing respiratory distress syndrome, 30% developing splenic rupture or infarction, and 10% developing acute renal failure<sup>9.</sup> In this case, the patient presented signs of splenic infarction and fissure, and renal failure.

Due to the potential severity of *P. ovale* infection, a correct diagnosis is critical<sup>10</sup>. In such infections, frequent false negatives have been described in studies of peripheral blood smears, and a sensitivity of 25–30% in immunochromatography<sup>7, 11</sup>. PCR provides enhanced detection sensitivity and allows for the identification of the species, conforming the

World Health Organization recommendations for the early diagnosis of imported malaria in non-endemic areas<sup>11, 12</sup>.

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