

Occupationally Acquired *P. Falciparum* Malaria

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Abstract

Although low, the risk of occupational malaria does exist. This report describes a rare case of occupational malaria in a non-endemic area with a favorable outcome despite the delayed diagnosis and calls for further research in the field of malaria post-exposure prophylaxis following accidental exposure to biological fluids.

Keywords: Occupational malaria; Needlestick injury; *Plasmodium falciparum*; Post-exposure prophylaxis

Introduction

Malaria is a vector-borne disease caused by the protozoan parasite *Plasmodium* [1]. Non-vectorial transmission of malaria includes mother-to-child transmission [2] and may occur through blood transfusion [3], organ transplantation [4], intravenous drug use [5] or, occasionally, after accidental occupational exposure [6]. Out of five different *Plasmodium* species pathogenic for humans, *P. falciparum* is responsible for the majority of malaria-related deaths [7].

The trend of increasing imported malaria cases in Lithuania has become very apparent in recent years: in 2012-2016, 30 malaria cases (1 death) were registered, comparing to 16 cases (1 death) in 2006-2011. The vast majority (72%) of cases was *P. falciparum* malaria [8].

The risk of health care workers (HCW) being exposed to rare pathogens increases with increasing intercontinental travel and migration. We present an exceptionally rare case of occupationally acquired malaria in Lithuania.

Case Report

On April 23, 2016, a previously healthy 25-year-old female nurse sustained an accidental blood-letting needlestick injury of her finger while taking blood from a patient with *P. falciparum* malaria from Cameroon. At the time of the injury, the patient's parasitemia was 5.5% and he was on the intravenous quinine treatment. The nurse immunization against hepatitis B was confirmed. For two days-that is, until the patient's human immunodeficiency virus (HIV) test result came as negative-she was given Lamivudine/Zidovudine and Lopinavir/Ritonavir. The risk and symptoms of malaria were discussed with the injured nurse.

On May 2, 2016, the nurse started suffering from a fever of up to 39°C, right-side abdominal pain, headache, malaise, and muscle pains; she was presented to the Emergency Department the next morning. Her temperature at presentation was 39.1°C, heart rate 120 beats/min, blood pressure 110/60 mmHg, and she felt upper-right abdominal tenderness on palpation. Her full blood count and urine sample indicated normal values, and CRP was 61.8 mg/L. Thick and thin blood smears for Plasmodium parasites were done twice on May 3, but were negative (Table 1). The nurse had no significant medical or travel history.

| | May 3 | May 4 | May 5 | May 6 | May 7 | May 8 | May 9 | May 10 | May 13 | May 16 |
|-----------------------------|-------|-------|-------|-------|-------|-------|-------|--------|--------|--------|
| WBC (× 10 ⁹ /L) | 5.6 | | | 2.7 | 4.1 | 4.8 | 4.9 | 5.8 | 9.4 | 10.6 |
| RBC (× 10 ¹² /L) | 4.37 | | | 3.77 | 3.48 | 3.33 | 3.14 | 3.63 | 3.29 | 3.62 |
| Hgb (g/L) | 131 | | | 111 | 103 | 99 | 91 | 105 | 97 | 108 |
| PLT (× 10 ⁹ /L) | 192 | | | 42 | 42 | 37 | 50 | 76 | 143 | 362 |
| ALT (U/L) | 37 | | | 172 | 212 | 193 | | 111 | | 173 |
| AST (U/L) | 45 | | | 258 | 329 | 193 | | 56 | | 107 |
| Creatinine (µmol/L) | 56 | | | 47.6 | 43.4 | 49.7 | | 63.3 | | 58.1 |
| Bilirubin (µmol/L): | | | | | | | | | | |
| Direct | 2 | | | 11.5 | 7.2 | 5.7 | | 6 | | |
| Indirect | 7.5 | | | 11.6 | 7.7 | 8.7 | | 12.7 | | |

| | | | | | | | | | | |
|---|----------------|-------|------|-----------------------------|-------|--------|----------------------|------|------|------|
| CRP (mg/L) | 61.8 | 163.5 | | 165.5 | 165.1 | | | 39.2 | | 0.2 |
| PTT (s) | | | | 47.4 | | 37.5 | | 37.4 | | |
| INR | 1.11 | | | 1.18 | 1.21 | 1.22 | | 1.18 | | |
| Fever (°C) | | | | | | | | | | |
| AM: | 39.1 | 38.2 | 38 | 39 | 37.2 | 37.8 | 37.2 | 37.5 | 36.2 | |
| PM: | 39.2 | 39.1 | 36.8 | 40 | 38.8 | 38.5 | 39 | 38.5 | 36.4 | 36.5 |
| Blood culture | | Neg | | Neg | | | | | | |
| Urine culture | | Neg | | | | | | | | |
| Throat culture | | Neg | | | | | | | | |
| Parasitemia level (%) | | | | | | | | | | |
| AM: | Neg | | | 0.35 | 10 | 0.03 | Several Parasites | Neg | Neg | Neg |
| PM: | Neg | Neg | | 17 | 0.4 | | | | | |
| Parasite count in visual field | | | | | | | | | | |
| AM: | Neg | | | | 25-30 | Upto 4 | 0.1-0 | Neg | Neg | Neg |
| PM: | Neg | Neg | | 40-50 | 15-20 | | | | | |
| Treatment | Cefuroxime i/v | | | Quinine dihydrochloride i/v | | | Quinine sulphate p/o | | | |
| Normal range: ALT: 10-28 U/L; AST: 9-36 U/L; Total bilirubin: 3.4-20.5 µmol/L; Direct bilirubin: <5.1 µmol/L; CRP: <5 mg/L; PTT: 30-45 s; INR: 0.88-2.0; Neg-negative | | | | | | | | | | |

Table 1: The laboratory test results, the fever pattern, and the treatment of the occupational malaria case.

At the Infectious Disease Department on May 4, she was still febrile and her CRP increased up to 163.5 mg/L. The repeated thick and thin blood smears were negative (Table 1). Her chest X-ray was normal, though abdominal ultrasound showed a dilated collecting system of the right kidney. Blood, urine, and throat cultures were taken and an intravenous cefuroxime was started (Table 1).

On the following day, the patient was less feverish (Table 1). Nevertheless, in the early morning of May 6, the blood smears were repeated. Additionally, a blood sample was sent to the National Reference Laboratory for immunochromatographic malaria antigen-detection test. Before the test results (positive *P. falciparum* antigen test and blood smear, showing parasitemia 0.35%) came back, the patient relapsed into a fever up to 39-40°C and became somnolent. In the afternoon of May 6, the *P. falciparum* parasitemia level increased up to 17% (Table 1).

Intravenous quinine plus oral doxycycline in standard doses were started immediately after *P. falciparum* parasitemia was detected. Her general condition started to improve, the parasitaemia level gradually decreased, and on May 9 she was switched to the oral quinine (Table 1). However, the patient started complaining of impaired hearing and an acute bilateral cochlear neuritis was diagnosed on May 10; it disappeared rapidly upon discontinuing quinine. On May 16, she was discharged as completely recovered. On the follow-up visit on June 20, 2016 she did not have any complaints. The laboratory test results were normal and thick and thin blood smears were negative. Her hearing recovered completely.

Discussion

This exceptionally rare occupational malaria case raised two challenging problems. First, whether to give post-exposure prophylaxis (PEP), and second, whether to start empirical therapy if suspicion of malaria is strong.

The first occupational *P. falciparum* malaria case in HCW was reported in 1924, and thereafter cases of occupational *P. falciparum*, *P. vivax*, *P. ovale* infection have been documented [9]. An extensive review of the occupational *P. falciparum* malaria in HCWs identified 22 cases, 59.1% of which occurred in females [6]. 54.5% of the cases were nurses, 27.3% were physicians, and the rest were biologists, researchers, nurses' aides, and a medical student. The most commonly encountered accidental blood exposure, observed in 66.7% of the cases, was a needlestick injury. However, in 28.6% of the cases, occupational *P. falciparum* malaria developed after mucocutaneous exposure to infected blood, which is several times more frequent than for documented cases of occupational hepatitis C and HIV infection. The median incubation time was 12 days (range 4-17), and severe form of disease was diagnosed for 45% of HCWs, including one lethal case. PEP with chloroquine was used in one case; however, the attempt was unsuccessful as the particular strain of *P. falciparum* was chloroquine-resistant [6].

We found two more published cases of occupational *P. falciparum* malaria [10,11], and a unique case of successful PEP for *P. falciparum* malaria after an occupational needlestick injury [12]. In this case, PEP was initiated on the following day with the same drugs (artemether

and lumafantrine) as given for the source patient. The injured doctor did not experience any side effects and did not have any malaria symptoms thereafter [12]. The summary of all these cases, including ours, is presented in Table 2.

| Gender | Occupation | Country of occurrence | Origin of plasmodia | Type of accidental blood exposure | Source patient parasitemia at the time of injury | Incubation period (days) | PEP | Form of disease | Outcome | Reference |
|--------|---------------------------------------|-----------------------|---------------------|--|--|--------------------------|-----|-----------------|----------|--------------|
| F | Nurse | Netherlands | Gambia | NSI | 0.2% | 18 | No | ND | Recovery | [10] |
| F | Technician of the clinical laboratory | France | Congo | Injury with the broken malaria test tube | 4% | 7 | No | Severe | Recovery | [11] |
| F | Resident doctor | Turkey | Sudan | NSI | 25% | | Yes | | | [12] |
| F | Nurse | Lithuania | Cameroon | NSI | 5.5% | 10 | No | Severe | Recovery | Present case |

HCW: Health Care Workers; NSI: Needle Stick Injury; ND: No Data; PEP: Post-Exposure Prophylaxis

Table 2: Demographic, epidemiological, clinical, and laboratory data of occupational *P.falciparum* malaria cases/exposure in HCW.

Our decision to withhold PEP was in line with the conclusions made by Tarantola et al. [6], which propose an immediate PEP to HCWs if there is a risk of losing the follow-up or if the HCWs wish so. Otherwise, if the HCW is available for follow-up, PEP may be withheld, provided the HCW is fully informed of the potential risk and of early malaria signs [6].

We initiated malaria treatment after parasitemia was documented, in accordance with all acknowledged malaria management guidelines [1,13-15]. The light microscopy of Giemsa-stained thin and thick blood films—that is, the gold standard malaria diagnostic test [15] was performed by qualified personnel available on-call even on off-hours, and was repeated at the recommended intervals, assuming that non-immune individuals may be symptomatic even at very low parasite densities that initially may be undetectable. The delay of a laboratory confirmation in our case calls for a better availability of PCR for a timelier diagnosis in extraordinary cases.

Despite the existence of well-documented occupational malaria cases, the actual rate of exposure to infected blood leading to malaria remains unknown, as such cases are most likely not published. Our patient was a prototype occupational malaria case: a female nurse of child-bearing age (fortunately, not pregnant) from a non-endemic area, who developed severe malaria caused by the most dangerous *Plasmodium* species. Such a high-risk scenario calls for a systematic notification and a follow-up of occupational malaria exposure, as malaria seems to be more easily transmissible than HIV or hepatitis C virus, for which a surveillance and standardized post-exposure management guidelines exist. Exploring such questions as whether PEP should be initiated depending on the level of parasitemia of the source patient and what the optimal regimen and duration of PEP should be is essential to ensure evidence-based care of similar cases in the future—cases likely to occur more frequently in the era of increasing international travel and migration.

Conclusion

Although low, the risk of occupational malaria does exist and, as such, calls for developing a set of standardized post-exposure

management guidelines for cases of accidental exposure to blood or biological fluids.

Disclosure Statement

No competing financial interests exist

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