SHORT REPORT

MANAGEMENT OF PLASMODIUM KNOWlesi MALARIA WITHOUT PCR CONFIRMATION

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Abstract. Plasmodium knowlesi morphologically resembles P. malariae; PCR assays are able to differentiate between the 2 species correctly. However, PCR is not available in many hospitals in P. knowlesi endemic areas, particularly in Southeast Asia. In places where PCR is not available, anti-malarial drugs for P. malariae or other non-P. falciparum or P. falciparum species are effective against P. knowlesi. Even with a wrong diagnosis of another malaria species by light microscopy instead of P. knowlesi, the antimalarial drugs given are still effective for treating P. knowlesi infection.

Key words: Plasmodium knowlesi, management, PCR

Plasmodium knowlesi, a fifth known cause of human malaria, naturally occurs among long-tailed and pig-tailed Southeast Asian monkeys. There have been many cases reported from Malaysian Borneo (Singh et al., 2004), and reports of human cases from Myanmar, the Philippines, Singapore, and Thailand (Jongwutiwes et al., 2004). Cox-Singh et al. (2008) showed that by using PCR, P. knowlesi was misdiagnosed by light microscopy to be P. malariae, P. falciparum, and P. vivax in 69% (216/312 cases), 5% (11/216 cases), and 4% (16/428 cases), respectively. For the 4 human malaria species (P. falciparum, P. vivax, P. ovale, and P. malariae) light microscopy is the gold standard for diagnosis of malaria species but light microscopy results in a high rate of misdiagnosis for P. knowlesi.

White (2008) determined some factors for the diagnosis of P. knowlesi: (1) febrile patients with travel history to a P. knowlesi endemic area, such as Southeast Asia or Borneo; (2) a blood smear showing early trophozoites, similar to P. falciparum and late trophozoites, similar to P. malariae; (3) P. malariae multiplies every 3 days (quartan cycle) and never reaches hyperparasitemia, whereas P. knowlesi has a daily (quotidian) cycle and can rapidly reach potentially lethal densities. In clinical practice, hyperparasitemic P. malariae is unusual and life-threatening P. malariae is rare.
Therefore, if light microscopy morphologically appears to show *P. malariae* in a patient with an unusual clinical presentation of *P. malariae*, or a patient with morphologically appearing *P. malariae* on blood smear has severe malaria, then the correct diagnosis is most likely *P. knowlesi* rather than *P. malariae*.

Molecular techniques, such as PCR, are useful in confirming the diagnosis of *P. knowlesi* for epidemiological reasons and in characterizing mixed infection. Recently, a rapid diagnostic test using pLDH was positive for *P. falciparum*, *P. vivax* and *P. knowlesi* (McCutchan et al, 2008). Whether commercially available rapid diagnostic test can detect *P. knowlesi* infections in larger patient samples remains to be determined.

*P. knowlesi* is sensitive to chloroquine, quinine, mefloquine and other conventional antimalarials (Singh et al, 2004; Bronner et al, 2009). Primaquine is not necessary for treatment since *P. knowlesi* has no hypnozoite. Therefore, the treatment of uncomplicated *P. knowlesi* infection is similar to *P. malariae* (eg, chloroquine without primaquine). In severe infections due to *P. knowlesi*, the treatment is quinine. Intravenous quinine cleared *P. knowlesi* parasitemia in 2.4±0.97 days (range 1-5 days) (Singh et al, 2004). Although there have been no clinical studies of the use of parenteral artemisinin derivatives for the management of severe *P. knowlesi* malaria in humans, a previous study found artemisinin derivatives had antimalarial activity against *P. knowlesi* in rhesus monkeys (Li et al, 2003).

PCR is not a rapid detection method and is not available option for diagnosis in many hospitals in Southeast Asia. Confirmation of all suspected *P. malariae* cases by PCR may not be possible in many malaria endemic areas. Studies of the use of a rapid diagnostic test specific for *P. knowlesi* have been limited and are not widely available. Light microscopy is more available than PCR. However, light microscopy in *P. knowlesi* infection may lead to a misdiagnosed of *P. malariae* or another malaria species, and treatment may be given accordingly: chloroquine for *P. malariae*, chloroquine plus primaquine for *P. vivax*, or quinine plus doxycycline or artesunate plus mefloquine for *P. falciparum*. *P. knowlesi* is sensitive to those antimalarial drugs even with a wrong diagnosis of non-*P. knowlesi* species. Therefore, even with a misdiagnosis by light microscopy, treatment is still effective against *P. knowlesi*.

In conclusion, although a confirmative diagnosis of *P. knowlesi* by PCR is often not available, the treatment of uncomplicated *P. knowlesi* with anti-malarial regimens against *P. malariae*, other non-*P. falciparum* malaria or uncomplicated *P. falciparum* malaria is effective; the treatment of severe *P. knowlesi* with the antimalarial regimens against severe *P. falciparum* malaria (such as with intravenous quinine) is also effective.

REFERENCES


