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Case Report

Two unfavorable cases of *Plasmodium falciparum* infection returning from Tanzania

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Abstract

Introduction: Malaria has been eradicated in China; however, with the expansion of international trade in recent years, imported malaria cases have become non-negligible.

Case presentation: We report two cases of patients infected with *Plasmodium falciparum* who returned from Tanzania to Yunnan, China. The patients sought treatment at different hospitals after developing symptoms, mainly fever. However, the exact cause was not identified in time, and the patients' condition worsened progressively. Although the patients were finally diagnosed with malaria infection and received specific antimalarial drugs in our hospital, both died because of missing the optimal treatment window.

Conclusions: Chinese doctors should enhance their awareness of *Plasmodium* detection and receive professional training for timely diagnosis of malaria patients who return home after being infected abroad.

Key words: *Plasmodium falciparum*; malaria; Tanzania.

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Introduction

Malaria is a widespread insect-borne infectious disease that is mainly distributed in tropical and subtropical regions of South America, Africa, and Asia [1]. Changes in temperature, humidity, and rainfall affect the behavior and survival of the malaria-carrying *Anopheles* mosquitoes [2]. In addition, numerous factors such as the coronavirus disease 2019 (COVID-19) pandemic and flooding affect malaria transmission [3,4]. It has been reported that the total number of malaria cases worldwide reached 249 million in 2022, far higher than pre-COVID-19 estimates and 5 million more than in 2021 [5]. Meanwhile, catastrophic floods in Pakistan in 2022, led to over 44,832 malaria cases in the country [6]. The 5.4 million cases in the South-East Asia region contributed 2% of the burden of malaria cases globally in 2021 [7]. Thus, malaria is still a serious threat to human health in the early 21st century.

China cannot ignore malaria prevention and control work because there is severe malaria epidemic in the neighboring countries. Myanmar, Laos, and Vietnam are high malaria incidence areas and share borders with Yunnan. For instance, Myanmar accounts for 95% of the local malaria cases in the Greater Mekong sub-region and has the problem of artemisinin resistance [8].

The last indigenous malaria case in Yunnan province was reported in 2016 [9]. The World Health Organization (WHO) confirmed that China is malaria-free in 2021 [5]. However, with the in-depth development of international trade, the number of people traveling to and from Africa, Southeast Asia, and other malaria-endemic areas in Yunnan is increasing [10]. In recent years, there have been severe, critical, and even fatal imported cases of *Plasmodium* infection in Yunnan, some of which have led to illness or death. [11].

Case presentation

A couple, male and female in a relationship, both 32 years old, were admitted to our hospital simultaneously on 21 December 2023. We named them Patient A and Patient B respectively. We obtained the medical history from Patient A's relatives due to his clouded consciousness. Patient A developed fever on 15 December, with a maximum temperature of 40 ℃; accompanied by chills, muscle aches, cough, and expectoration. Patient A went to Kunming Hospital of Traditional Chinese Medicine for treatment. Patient A's blood work analyses were as follows: leukocytes 11.24 × 10^9/L, neutrophils 83.5%, lymphocytes 9.3%, and C reactive protein (CRP) 28.7 mg/L. Accordingly, Patient A received infusion therapy with cefazolin sodium and vitamin C. However, at 19:00 on 21 December, Patient

Table 1. Blood work analysis results of Patients A and B upon hospital admission.

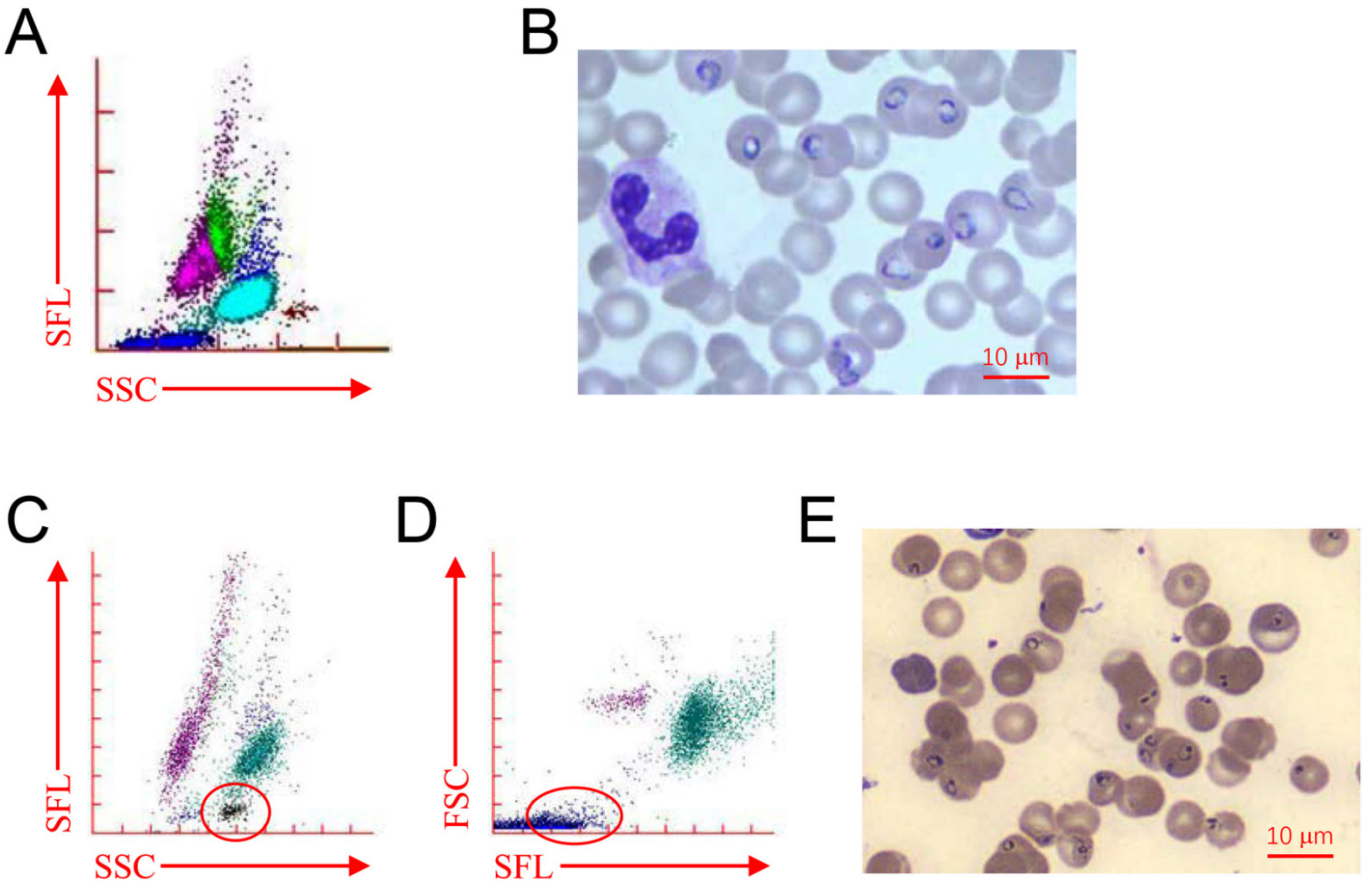
Item	Patient A	Patient B	Reference value	Unit
White blood cell	19.12	6.45	3.5–9.5	10^9/L
Neutrophil	14.58	4.18	1.8–6.3	10^9/L
Lymphocyte	2.55	1.74	1.1–3.2	10^9/L
Red blood cell	4.71	1.4	3.8–5.1	10^{12}/L
Hemoglobin	150	131	115–150	g/L
Platelet	24	22	125–350	10^9/L
Blood pH	7.43	7.48	7.35–7.45	None
Procalcitonin	4.73	5.26	0–0.052	ng/mL
C-reactive protein	28.7	175.9	0–10	mg/L

Indicators above the reference range are displayed in red font, while those below are in blue font.

A suddenly developed convulsions during the infusion, characterized by upward deviation of the eyes, frothing at the mouth, nausea, vomiting, and incontinence. After receiving treatment with sedative drugs (specific drug unknown), Patient A was transported to the emergency department of our hospital by ambulance. Patient A was immediately admitted to the intensive care unit (ICU) of The First People's Hospital of Yunnan Province, presenting with fever, unexplained convulsions, and confusion. Upon inquiry, we found that Patient A was in good general health prior to this episode and he denied any past medical history. However, Patient A and Patient B traveled to Tanzania two weeks before, and they stayed there for approximately one week.

Patient B developed recurrent, irregular fever with a maximum temperature of 40 ℃ after returning from Tanzania with Patient A on 6 December. She presented with body aches, fatigue, dyspnea, dry cough, chills, headache, dizziness, and pink frothy sputum. Patient B sought treatment at Yunnan Provincial Hospital of Traditional Chinese Medicine where she received symptomatic management (details unknown), but her

Figure 1. Blood work analysis results of Patient A and Patient B.



A: Five-part differential scatter plots of Patient A. **B:** Malaria parasites in red blood cells under microscopy of Patient A. Scale bar 10 μm. **C:** Five-part differential scatter plots of Patient B. **D:** Basophilic granulocyte channel view of Patient B's blood work analysis result. **E:** Malaria parasites in red blood cells of Patient B under microscopy.

condition failed to improve. As a result, she presented to the Emergency Department of our hospital on 21 December with an undiagnosed condition. Subsequently, Patient B was admitted to the Department of Infectious Diseases and Hepatology on 22 December.

Blood work analysis of Patient A showed elevated white blood cells and neutrophils, whereas his platelets were decreased (Table 1). In contrast, both red blood cells and platelets of Patient B were decreased, accompanied by an acid-base imbalance (Table 1). Furthermore, procalcitonin as well as C-reactive protein was elevated in both patients, indicating underlying infection and inflammation (Table 1).

Blood work analysis of Patient A showed an abnormal scatter pattern, indicating that lymphocytes and monocytes could not be clearly grouped and naive granulocytes were present (Figure 1). Accordingly, Giemsa-stained blood smears were microscopically examined in the laboratory. Eventually, *Plasmodium* with a typical early asexual stage ring structure was detected in red blood cells on 23 December 2023 (Figure 1). More obvious abnormal scatter plots were observed in Patient B's peripheral blood on the same day, indicating a blood parasite infection (Figure 1). Similarly, *Plasmodium* ring structure was also identified upon microscopic reexamination (Figure 1). Subsequently, both infections were confirmed as *Plasmodium falciparum* via MetaCAP™ pathogenic microbial nucleic acid high-throughput sequencing, an advanced molecular diagnostic technology based on next-generation sequencing (NGS). These results were highly consistent with the above-mentioned travel history to the epidemic area of Tanzania, Africa.

Artemether was administered after the patients were diagnosed with malaria. However, since the patients had not received proper medical treatment in the early stage of the disease, their condition did not improve. Patient B died on 25 December as her condition severely deteriorated. Diagnoses at the time of death of Patient B were as follows: 1. sepsis; 2. *Plasmodium falciparum* malaria with cerebral complications; 3. acute respiratory failure; 4. thrombocytopenia; 5. severe anemia; 6. metabolic acidosis; 7. azotemia stage of acute renal insufficiency; 8. circulatory failure.

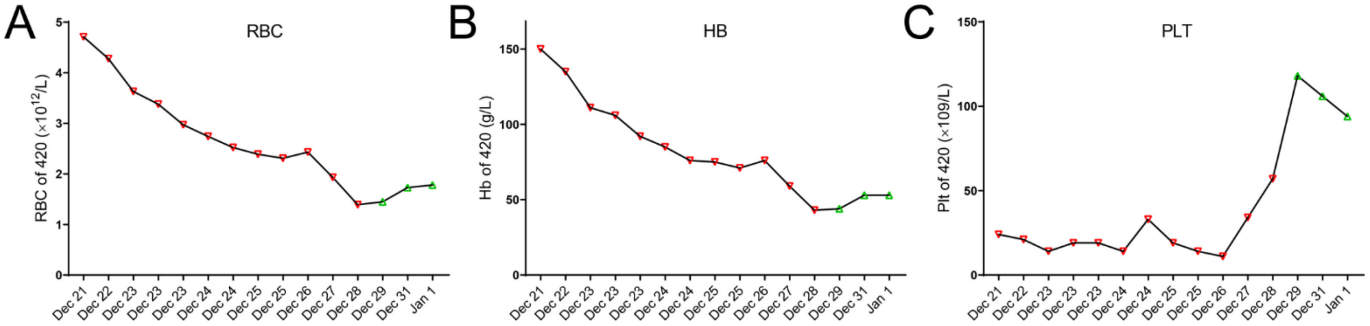
As shown in Figure 2, the red blood cells and hemoglobin of Patient A continued to decrease until blood transfusion therapy was administered on December 28. Additionally, the platelet count remained consistently below the normal range (Figure 2). During treatment, cytokines such as IL-6, IL-8, IL-10 and TNF were upregulated to varying degrees in Patient A. Eventually, following 38 days of ICU treatment, the treatment was terminated with consent of the Patient A's family. Patient A succumbed to malaria, and the diagnoses were as follows: 1. *Plasmodium falciparum* malaria; 2. cerebral malaria; 3. septic shock; 4. diffuse intravascular coagulation; 5. respiratory failure; 6. circulatory failure; 7. acute renal failure; 8. acute heart failure; 9. liver insufficiency.

Discussion

Malaria remains the most significant infectious disease of the modern world, continuously emerging or re-emerging due to climate change or cross-regional human mobility [12]. This case highlights the significant impact of personnel mobility on the resurgence of malaria. Meanwhile, cases of malaria occurring in countries and regions such as China, where it has been eradicated for years or even decades, emphasize the necessity of constant alertness for prompt diagnosis and efficient treatment.

These two patients who returned from Tanzania went to several different hospitals after showing symptoms, but the exact cause of *Plasmodium* was not detected in these hospitals. Obviously, this is related to

Figure 2. Trends in red blood cells, hemoglobin, and platelets in Patient A.



A: red blood cell, RBC; **B:** hemoglobin, HB; **C:** platelet, PLT, trends from December 21 to January 1.

clinicians' inadequate awareness of malaria. Finally, the patients were diagnosed in our hospital, a finding that reflects the differences in diagnostic capabilities for malaria among hospitals in Yunnan Province. Of course, this may be related to differences in the performance of blood work analysis equipment used in different hospitals. Advanced instruments can detect abnormalities and trigger an alarm indicating the possible presence of blood parasites. Meanwhile, the professional knowledge and skills of the laboratory doctors, as well as their rich clinical diagnostic experience, also play a crucial role in the correct diagnosis of patients.

Numerous studies have shown that Chinese herbal medicine has certain therapeutic effects on tropical infectious diseases including malaria and dengue fever [13,14]. However, we contend that due to the absence of a clear etiology, traditional Chinese herbal medicine administered to Patient A in this case provided no substantial therapeutic benefit. Therefore, exploring new diagnostic and treatment technologies is urgently needed to eliminate malaria [15]. For example, nanomedicine delivery systems hold significant promise in malaria treatment [16].

Although few malaria vaccines have been developed and proven to have some protective effect in African children [17], it is not a feasible solution to protect against malaria through mass vaccination in a non-endemic region such as China. We recommend that all travelers to malaria-endemic regions adopt mosquito avoidance measures and take prescribed prophylaxis [18]. Febrile travelers who have recently returned from a malaria-endemic area should be evaluated for malaria.

At the same time, travel medicine should be strengthened to improve the capacity and accessibility of pre- and post-travel services, including malaria prevention and timely diagnosis of the disease for returning travelers [19]. This means clinical and laboratory doctors in non-endemic regions should improve their malaria detection awareness and capacity for patients returning from malaria-affected areas. This is the only way for us to avoid the tragedy reported herein.

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Conflict of interest

No conflict of interest is declared.

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