

## HIDDEN ENEMY BEHIND FEVER

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### ABSTRACT

This study aimed to raise awareness about autochthonous malaria caused by *Plasmodium vivax* which is increasing day by day in Türkiye and could be fatal if not treated in time. The patient, a 25-year-old man was admitted to the hematology division of Trakya University Hospital with the symptoms such as fever, chills, cough, headache, and drenching night sweats. After a delay of 10 days, he was diagnosed with *Plasmodium vivax* malaria and then treated with primaquine. The diagnosis of malaria is challenging in areas where malaria is not widespread, but clinicians must keep differential diagnoses of fever, cytopenia, and splenomegaly in mind, especially in times of globalization in the world.

**Keywords:** *Plasmodium vivax*, malaria, autochthonous transmission

### INTRODUCTION

Malaria is an important public health problem with about 241 million cases, which accounts for 627 thousand deaths in 2020 globally (1). There are five *Plasmodium* species [*Plasmodium vivax* (*P. vivax*), *Plasmodium malariae*, *Plasmodium ovale*, *Plasmodium falciparum*, *Plasmodium knowlesi*] that infect humans and are transmitted by the bites of infected female *Anopheles* mosquitoes (2). Türkiye, a part of the WHO European Region is a malaria-free country. The European Region has been malaria free since 2015 (1, 3). According to the annual health statistics, autochthonous cases have not been seen in recent years, but 279 imported cases were reported in 2019 (1, 3, 4). For these reasons, malaria is not considered in the differential diagnosis in patients without a travel history. This study aimed to raise awareness about autochthonous malaria caused by *P. vivax* which is increasing day by day in Türkiye and could be fatal if not treated in time (4).

### CASE REPORT

A 25-year-old male patient was admitted to the hematology division of Trakya University Hospital with a 10-day history of fever, chills, cough, headache, and drenching night sweats. He

had never traveled outside of Türkiye and had no history of blood transfusion, organ transplantation, or intravenous drug use. The patient works in Kapıkule which is the name of the border crossing station in Edirne province on the border of Türkiye and Bulgaria. The temperature of the patient was 38.9 °C, the blood pressure was 110/60 mm Hg, and the pulse was 90 beats per minute. Splenomegaly was detected in his physical examination, but hepatomegaly was not present. The results of routine blood tests revealed that the erythrocyte count was 2.95 million cells/mcL, hemoglobin was 7.8 g/dL, red blood cell distribution width was 15% and white blood cell count was 3680/uL, with 61.7% neutrophils, 20.1% lymphocytes, 2.7% eosinophils, and 15.2% monocytes. The platelet count was 45000/uL. The patient's blood tests showed the following: C-reactive protein of 54.4 mg/L, lactate dehydrogenase of 475 U/L, alanine aminotransferase of 36 U/L, aspartate aminotransferase of 28 U/L, total bilirubin of 1.1 mg/dL, conjugated bilirubin of 0.7 mg/dL. The creatinine level of the patient was slightly decreased (1.7 mg/dL). Prothrombin time was measured as 13.4 sec, international normalized ratio was 1.14, and activated partial thromboplastin time was 22.5 sec. The level of serum ferritin was 954 ng/mL. Urine and blood cultures were negative.



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Examination of the peripheral blood smears showed the presence of atypical lymphocytes and poikilocytosis. Due to an enlarged spleen, and abnormal hematologic findings, a bone marrow biopsy was requested for further examination and to rule out hematological malignancies such as lymphoma or leukemia. Bone marrow aspirations showed normal cellularity without any pathological findings. The reverse transcription-polymerase chain reaction test for severe acute respiratory syndrome coronavirus 2 was negative. Brucella, hepatitis B, hepatitis C, Epstein-Barr virus, cytomegalovirus, and syphilis were excluded from serological evaluation. The culture of *Leishmania* was negative. Due to the relapsing fever episodes, the peripheral blood smears were repeated and stained with Giemsa and the presence of trophozoites and gametocytes was shown (Figure 1). The definitive diagnosis was *P. vivax* infection, and the patient was treated with primaquine. No parasites were observed in the peripheral smear after three days of treatment. The patient, whose general condition improved on the seventh day of his hospitalization, was discharged and routine check-ups were recommended after discharge. No parasites were observed in the peripheral smear after three days of treatment. The patient, whose general condition improved on the seventh day of his hospitalization, was discharged and routine check-ups were recommended after discharge. No parasites were observed in two peripheral smears which were performed one week and two weeks after the start of treatment to check the effectiveness of the treatment. An informed verbal consent form was obtained from the patient to publish the paper.

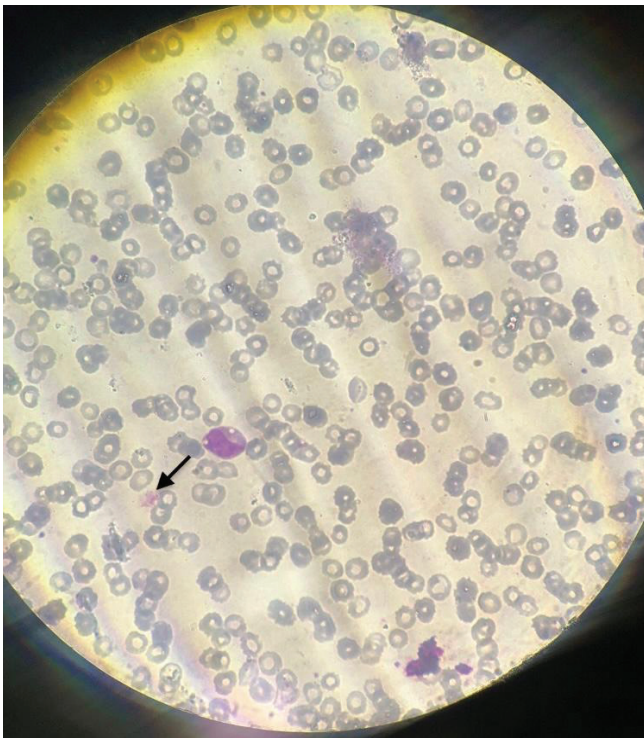


Figure 1: Peripheral blood smear, thin region (Giemsa stain, x1000 magnification). Intraerythrocytic trophozoite, and gametocytes of *Plasmodium vivax* (black arrow).

## DISCUSSION

Autochthonous malaria refers to local transmission by the bite of a vector. This could either be introduced (with strong epidemiological evidence linking to a known imported case) or indigenous (without direct proof of transmission from an imported case) (5, 6). Other circumstances must also be ruled out, whether they arise naturally (such as congenital malaria), through blood transfusions, or another type of parenteral contagion (induced malaria) (6).

Since the elimination of malaria, autochthonous malaria cases have not been reported anywhere else in Türkiye and there have been no imported cases in the region where the patient lives (1, 3, 4). The patient had not traveled abroad to a malaria-endemic country and his home was 200 km from the nearest airport and 100 km from the seaport. Besides, and had no previous history of malaria. All this led to the conclusion that the patient acquired the infection at the border-cross station Kapıkule. After Türkiye opened its border gates in February 2020 (27 February), immigrants from many provinces of Türkiye who wanted to cross into European Union countries came to the border gates. Immigrants from Syria, Iran, Afghanistan, Morocco, and North Africa gathered in Edirne, the border gates with Europe (7). Immigrants are often coming from malaria-endemic countries, transporting malaria with them as they cross borders. Swamps caused by Meriç, Tunca, Arda, and Ergene Rivers flooding and rice farming used to provide ideal conditions for *Anopheles* breeding (8). Prior to eliminating malaria, *P. vivax* was the only reported species from autochthonous cases and other *Plasmodium* species are reported as imported cases of malaria in Türkiye (9). Migrants from malaria-endemic countries, *Anopheles* populations, and climate played an important role in the transmission of malaria.

There was a delay of 10 days from the first development of febrile symptoms to the time that malaria was diagnosed. One of the main challenges in the post-elimination phase of malaria is that it tends to be overlooked as a cause of fever by clinicians (10). However, in this case, the reason for the delay in the diagnosis of malaria may be that the patient did not give a history of traveling abroad and presented with pancytopenia (10, 11). Pancytopenia is a condition that is frequently observed in clinical practices. Megaloblastic and aplastic anemia is a finding that can also result from other several diseases such as hematological malignancies, metastatic cancer, infection, and/or inflammation. These diseases may affect the bone marrow, either primary or secondary, and result in manifestations of pancytopenia that predispose the patient to anemic symptomatology, infections, and hemorrhagic diathesis (12). Pancytopenia due to *P. vivax* malaria is extremely rare (11).

*Plasmodium vivax* infection is known to be a prevalent illness in several parts of the world and characteristically presents with fever, chills, and rigors (12). The clinical presentations of malaria are non-specific, but malaria should be suspected in patients with unexplained fever and an abnormal white blood cell scattergram with thrombocytopenia and/or anemia, and a

blood smear test must be performed (12). If the treatment is delayed, disrupted, or not followed up, it can have serious clinical consequences such as acute respiratory distress syndrome, cerebral malaria, multiple organ dysfunction syndrome, dyserythropoiesis, anemia, other hematological complications, and death (12, 13). Malaria has become an emerging infection in Türkiye, which is caused by thousands of immigrants, global warming, and Türkiye's location in the subtropical region where malaria can spread. Therefore, clinicians should be aware of considering malaria early in their differential diagnosis of fever, cytopenia, and splenomegaly. Especially in times of poverty, immigration, and globalization of the world.

**Ethics Committee Approval:** N/A

**Informed Consent:** Verbal consent has been obtained from malaria case to publish the paper. The patient has given his consent for his images and other clinical information to be reported in the journal. The patient has not been identified in any manner.

**Conflict of Interest:** The authors declared no conflict of interest.

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