Case Report

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Seven cases of imported malaria with recurrence

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ABSTRACT

Malaria is an infectious disease caused by Plasmodium species parasites and transmitted to humans by the Anopheles mosquito. The malaria parasites responsible for infection in humans are *Plasmodium vivax*, *Plasmodium ovale*, *Plasmodium falciparum*, *Plasmodium malaria*, and Plasmodium knowlesi. Although malaria cases originating from Turkey no longer occur, cases originating from abroad are still seen. This report evaluates the epidemiological and clinical characteristics and histories of seven imported malaria cases. All seven cases in this report had a history of travel to African countries together with fever (>39°C), weakness, headache, tremor, sweating, cough, general body pain, and severe shortness of breath. Appropriate treatment was arranged once the necessary examinations had been performed. All patients but one responded to treatment. The non-responsive patient re-presented after 15 days with similar complaints. Primaquine therapy at 15 mg tablet 2×1 was administered, and that patient was discharged after 14 days. The most effective means of bringing malaria under control involves rapid diagnosis and effective treatment. We wish to emphasize that imported cases may be seen in non-endemic regions due to international travel. The travel history of patients in sporadic regions should be investigated, and malaria should be considered in the presence of fever in order to ensure early diagnosis and treatment.

Keywords: Malaria, fever, *Plasmodium falciparum*, infectious disease

INTRODUCTION

Malaria remains a common infectious disease in much of the world. The agent is protozoan parasites from the family *Plasmodidae*. The disease is transmitted to humans by the Anopheles mosquito (1).

The World Health Organization (WHO) World Malaria Report for 2017 stated that 237 million cases were seen in 2010, decreasing to 216 million in 2016. In addition, 445,000 individuals died from the disease (2). Symptoms include periodic fever, shivering, anemia and splenomegaly. Diagnosis is based on the presence of Plasmodia at thick drop and thin smear tests. Where the disease was contracted, and its resistance, are important factors in terms of treatment (1).

Although the numbers of malaria cases are decreasing as a result of measures being adopted worldwide, sporadic cases can still be seen in non-endemic regions for reasons such as migration and seasonal labor. We describe seven cases presenting with histories of travel and fever in which malaria needed to be considered at differential diagnosis.

CASE REPORT

Seven male patients, aged 22-56 years, were admitted to our outpatient clinic between June and September. These had complaints of fever (>39°C), weakness, headache, chills, chills, sweating, coughing, generalized body pain, and severe shortness of breath. All patients had a history of stays of 1-6 months in African countries. No drugs had been used for prophylaxis before travel, although they had employed unknown medicines for these complaints while in Africa. The seven cases' laboratory tests were examined (**Table**). Hepatosplenomegaly was present in all patients. Thick drop and thin smear methods were applied to blood samples. Giemsa staining was applied, and a signet ring-shaped plasmodium trophozoite was observed (**Figure**). In the light of the region from which the patients had arrived, *Plasmodium falciparum* (*P. falciparum*) was suspected as the cause of malaria. This was regarded as resistant to chloroquine, and treatment with Artemether (20 mg)-lumefantrine (120 mg) 2×4 tablets was initiated (three days). Tetracycline was also given (4×500 mg/day for seven days). One

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Table. Laboratory findings of cases before treatment

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
WBC K/mm³	10340	3400	6400	5200	4900	4400	5100
Hemoglobin g/dL	11.3	11.2	10.2	10.4	11.3	10.4	11.5
PLT /L	148000	113000	26000	76000	134000	39000	120000
AST U/L	43	37	55	56	35	43	30
ALT U/L	53	45	61	33	37	56	52
LDH U/L	336	303	208	649	276	439	253
Total bilirubin µmol/L	1.0	1.2	1.1	5.4	0.9	0.7	0.8
Creatinine µmol/L	0.8	0.9	1.0	1.2	0.7	0.8	0.5

WBC: White blood cell count, ALT: Alanin aminotransferaz, AST: Aspartat aminotransferaz

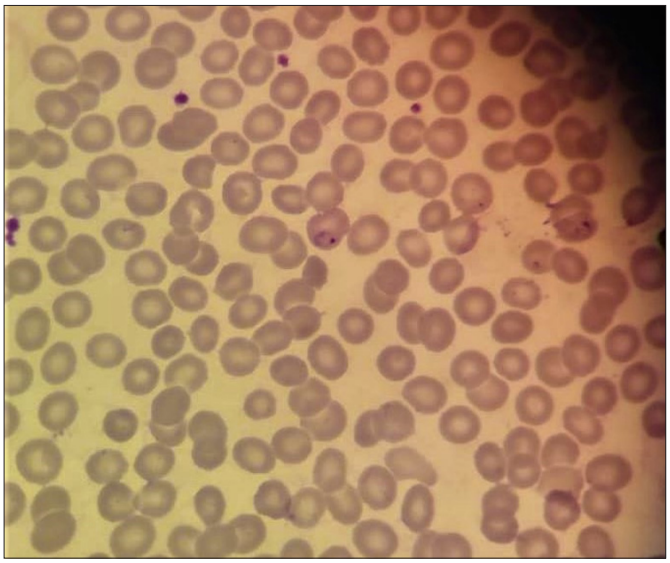

Figure. Signet Ring Shape *Plasmodium trophozoite*
* It was stained with Giemsa paint and a signet ring shape plasmodium trophozoite was seen.

patient (Case 4) again reported chills, high fever and nausea, vomiting, and dizziness 15 days after discharge. Trophozoites were observed at smear preparation examination, and mixed type malaria was suspected. Primaquine therapy was initiated at 15 mg tablet 2×1 (14 days). Patients with clinical and laboratory improvement were discharged, and no relapse was observed at six-month follow-up.

DISCUSSION

Thanks to its effective malaria control program, Turkey was included in the elimination phase by the WHO, reducing its case numbers from 11,381 in 2000 to 90 in 2010 (2). While a major decrease has occurred in local malaria cases, 251 cases of malaria imported from abroad were reported in 2013, 249 in 2014, 221 in 2015, and 209 in 2016 (2). Imported cases are seen in Turkey due to increased travel, international workforce mobility, and migration, and malaria remains an important health problem (1,3). For climatic reasons, malaria in our region assumes the form of sporadic cases. The majority of cases are imported from abroad, and the most important problems are experienced in diagnosis and treatment. Malaria is most commonly seen between June and October (3). In Turkey, the disease exhibits travel-related seasonal variation. Travelers to endemic regions must be started on chemoprophylaxis, and this must be maintained for four weeks after their return. None of our cases had employed chemoprophylaxis before traveling (4).

The characteristic feature of malaria is that it emerges in the form of rising body temperature with chills and episodes. Febrile episodes occur regularly once every 48 h in *Plasmodium vivax* (*P. vivax*) and *Plasmodium ovale* (*P. ovale*) infections, once every 72 h in *Plasmodium malaria* (*P. malaria*), and irregularly once every 36-48 h in *P. falciparum* (1). Fever exhibited an intermittent irregular pattern in all our cases. Shivering, fever, sweating, headache, fatigue, listlessness, and joint and skeletal pain were also present in all seven patients. Accompanying shortness of breath and cough were also present in four patients. Anemia, thrombocytopenia, splenomegaly, hepatomegaly, jaundice, petechiae, conjunctival bleeding, and herpes labialis can also be seen in cases of malaria (5). Hepatosplenomegaly, anemia, mild hepatic enzyme elevation, and thrombocytopenia were present in our cases. Bilirubin elevation and icterus were also observed in Case 4. No cutaneous lesions were detected, but vesicular eruptions, which are uncommon in malaria, were observed in the febrile period in one patient.

Histories of travel to African countries have been determined in cases of imported malaria previously reported from Turkey, and as in the present cases, no history of prophylaxis use prior to travel was present in those cases. Patients had similarly previously presented with fever, shivering, nausea, vomiting, and headache. Quinine-sulfate and tetracycline therapy was administered in the light of the possibility of resistance in cases thought to be caused by *P. falciparum* based on the regions of travel involved and Giemsa staining. Primaquine, effective against the hypnozoite form seen in *P. vivax* and *P. ovale*, was also given in cases thought to be mixed type, as in our case. The importance of considering malaria in individuals traveling to endemic regions was also emphasized (3,8).

Microscopic examination of peripheral blood specimens is still the gold standard for the diagnosis of malaria. Diagnosis is based on the presence of the parasite in thick drop and thin smear preparates from peripheral blood (6). Diagnosis was based on observation of trophozoites in all our cases. All seven patients had used unidentified medications due to similar symptoms while in the African countries where they were working. All presented to our clinic with recurrence of infection.

Manifestations of reinfection despite appropriate treatment or recrudescence (unsuccessful treatment) can be seen in *P. falciparum malaria*. Failure of treatment may be associated with various factors, such as drug resistance, weak medication passage into the body or dosages being below the requisite levels, vomiting, and inappropriate drug pharmacokinetics (4). Artemisinin performs an important function in the rapid reduction of the parasite burden, immediate improvement of symptoms, and prevention of resistance to other drugs (5). Artemisinin combination therapy is recommended by the WHO. Artemisinin/lumefantrine is well tolerated and highly effective. This was used in all our patients, and responses to treatment were achieved in all cases (4,7).

Lumefantrine, artemisinin and tetracycline were used in the treatment of our patients. Since the patients had been treated in various different countries, tetracycline was added to the artemisinin regimen. Smears were repeated due to recurrence of fever and vomiting after 15 days in only one case. Trophozoites were observed at examination, and mixed type malaria was suspected.

Primaquine therapy, which is effective in the hypnozoite form seen in *P. vivax* and *P. ovale*, was started in the form of 15 mg tablet 2×1. No recurrence or relapse was observed in our patients at six-month follow-up.

CONCLUSION

Malaria is one of the diagnoses requiring primary consideration in case of fever in individuals traveling from countries where the disease is endemic. The most effective means of bringing malaria under control is rapid diagnosis and effective treatment. Individuals due to travel to endemic regions must be given chemoprophylaxis, and presenting cases must be treated in the light of the drug-resistance status of the region in question. Finally, we wish to emphasize that imported cases may be seen in non-endemic regions due to international travel

ETHICAL DECLARATIONS

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Referee Evaluation Process: Externally peer-reviewed.

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