Malaria – Eight Years of Experience in a Tokyo Metropolitan Hospital

Kenji OHNISHI and Misako MURATA

Malaria patients who were admitted to the Department of Infectious Diseases of the Tokyo Metropolitan Bokutoh General Hospital during the past 8 years are reviewed. Cases included 17 patients infected with *Plasmodium falciparum* (14 Japanese), 13 patients infected with *P. vivax* (9 Japanese), 3 patients infected with *P. ovale* (2 Japanese) and 1 Chinese patient with a mixed infection of *P. falciparum* and *P. vivax*. About 70% of Japanese patients infected with *P. falciparum* contracted the disease in Africa, about 90% *P. vivax*-infected Japanese patients contracted the disease in Asia and all *P. ovale*-infected patients contracted the disease in Africa. Only 13% of all (17% of Japanese) patients infected with *P. falciparum* who initially contacted doctors of other Japanese hospitals were correctly diagnosed, but 78% of all (67% of Japanese) patients infected with *P. vivax* who initially contacted doctors of other Japanese hospitals were correctly diagnosed. At present, malaria is not a rare disease in Tokyo among travelers to or from Africa or Asia. (Internal Medicine 35: 111–114, 1996)

Key words: falciparum malaria, vivax malaria, ovale malaria

Introduction

Malaria is one of the most predominant infectious diseases in tropical or subtropical areas and it remains a major public health problem in the world. In Japan, most of the people afflicted with malaria are people who travel to or from tropical or subtropical areas where the disease is endemic. This protozoan infection is supposed to be reported to the government in Japan, however it is thought that more than half of the cases are not reported, and that the true numbers, and the clinical and epidemiological aspects of the present malaria patients are not fully known in this country. At the Tokyo Metropolitan Bokutoh General Hospital in Sumida-ku, Tokyo, the Department of Infectious Diseases admits patients with tropical diseases every year. We reviewed the cases with malaria in this department.

Patients and Methods

Charts of all malaria patients admitted to the Department of Infectious Diseases of the Tokyo Metropolitan Bokutoh General Hospital from April 1987 to March 1995 were available for review.

All but one diagnosis was made by positive blood smear; the remaining 1 patient was diagnosed by high antibody titer by the

indirect fluorescent antibody test (IFAT).

Results

Seventeen cases of falciparum malaria, 13 of vivax malaria, 3 of ovale malaria and 1 case with a mixed infection of *P. falciparum* and *P. vivax* were identified, but no patient infected with *P. malariae* was found. All patients were infected with the disease while outside Japan. There were no cases of transfusion-induced infection or associated drug abuse.

Falciparum malaria

Population

Nine patients were Japanese males, 5 were Japanese females, 1 was a French male, 1 was a Tunisian male, and 1 was an Indian male. The ages ranged from 22 to 64 years (mean 36.2 years).

Chemoprophylaxis

Nine Japanese and 2 foreign patients had taken no chemoprophylaxis agents. Two Japanese and 1 French patients had taken inadequate doses of sulfadoxine-pyrimethamine (S-P), and 1 Japanese patient, inadequate doses of chloroquine and proguanil: they discontinued the medication. One Japanese had taken the recommended doses of S-P and another Japanese

From the Department of Infectious Diseases, Tokyo Metropolitan Bokutoh General Hospital, Tokyo

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Reprint requests should be addressed to Dr. Kenji Ohnishi, the Department of Infectious Diseases, Tokyo Metropolitan Bokutoh General Hospital, 4-23-15 Kohtohbashi, Sumida-ku, Tokyo 130

patient had taken the recommended doses of chloroquine.

Presumed country of contraction and duration of stay

Presumed countries of contraction are shown in Table 1. Ten Japanese patients contracted malaria in Africa (71.4%). The duration of stay in the contracting country of the Japanese patients is shown in Table 2.

Physical contact

The results of initial doctor contacts with presenting symptoms are shown in Table 3. Four Japanese and no foreign patients had had a history of being treated for malaria in overseas countries or in Japan. The initial diagnoses of 8 patients attending other hospitals in Japan were as follows; 3 were common cold, 2 were fever of unknown origin, 1 was hepatitis, 1 was dysentery and 1 was falciparum malaria.

Table 1. Presumed Countries of Contraction

Species (No. of patients)	Country-No. of patients (No. of Japanese)
<i>P. falciparum</i> (17)	Mozambique-2(2), Benin-1(1), Central Africa Rep.-1(1), Niger-1(1), Tanzania-1(1), Tunisia-1(0), Nigeria-1(1), Tunisia or Zambia-1(1), Kenya or Uganda-1(1), Kenya or Tanzania-1(1), Indonesia-1(1), India-1(0), Malaysia-1(1), Thailand or India-1(0), Indonesia or Singapore or Malaysia or Thailand-1(1), Papua New Guinea or Indonesia-1(1).
<i>P. vivax</i> (13)	India-5(2), Indonesia-4(4), Malaysia-1(1), Pakistan-1(0), Papua New Guinea-1(1), Sri Lanka or Thailand-1(1).
<i>P. ovale</i> (3)	Ghana-1(0), Tanzania-1(1), unknown African country-1(1).
Mixed infection with <i>P. falciparum</i> and <i>P. vivax</i> (1)	
<i>P. falciparum</i>	Thailand
<i>P. vivax</i>	China

Table 2. Duration of Stay of the Japanese Patients in the Country of Contraction

	Duration					
	<2wk	2wk≤ ~ <1mo	1mo≤ ~ <3mo	3mo≤ ~ <1yr	1yr≤ ~ <4yr	4yr≤
Falciparum malaria	2	6	1	3	2	0
Vivax malaria	0	3	2	1	1	2

wk: week, mo: month, yr: year.

Fever, diarrhea and disturbed consciousness

All patients had a history of fever. Thirteen patients were febrile over 37.5°C at presentation or after admission to our hospital; 4 patients had a maximum temperature of over 40°C, and 7 patients had maximum temperatures of 39–40°C. Watery or mud-like diarrhea was found in 6 of 12 Japanese patients (50.0%) and in 1 French patient. No cases showed disturbed consciousness at the time of admission to our hospital, but disturbed consciousness was observed in 2 patients soon after the start of therapy.

Treatment and outcome

Fourteen patients were treated with anti-malarial drugs in our hospital. Three patients were treated with oral administration of S-P, 4 patients with oral administration of mefloquine, 3 patients with drip intravenous administration of Quinimax® (Quinimax® corresponds to quinine base, quinidine base, cinchonine base and cinchonidine base) and oral mefloquine, 2 patients with drip intravenous administration of Quinimax® and oral S-P and chloroquine, and 2 patients with drip intravenous Quinimax® and oral S-P and mefloquine. All patients recovered completely with therapy.

Vivax malaria

Population

Six patients were Japanese males, 3 were Japanese females, 2 were Indian males, 1 was a Pakistani male and 1 was an Australian female. Ages ranged from 21 to 57 years (mean 31.1 years).

Chemoprophylaxis

No patients had taken adequate chemoprophylaxis agents. Three of the Japanese patients had taken inadequate doses of drugs of unknown names which they had bought in countries they had visited; they discontinued the medication.

Presumed country of contraction and duration of stay

Presumed countries of contraction are shown in Table 1. Eight Japanese patients contracted malaria in Asia (88.9%).

Table 3. Initial Patient Visit of Falciparum Malaria Patient Presenting Symptoms

	No. of patients	Malaria initially diagnosed or suspected
Physician in endemic area	1 (0)	1 (0)
Other hospital in Japan	8 (2)	1 (0)
Tokyo Metro. Bokutoh General Hospital	7 (1)	7 (1)
Other hospital in Europe	1 (0)	1 (0)

() = number of foreign patients.

Table 4. Initial Patient Visit of Vivax Malaria Patient Presenting Symptoms

	No. of patients	Malaria initially diagnosed or suspected
Physician in endemic area	1 (0)	0 (0)
Other hospital in Japan	9 (3)	7 (3)
Tokyo Metro. Bokutoh General Hospital	3 (1)	3 (1)

() = number of foreign patients.

The duration of stay in the country of Japanese patients is shown in Table 2.

Physical contact

Results of initial doctor contacts with presenting symptoms are shown in Table 4. Three Japanese and 3 foreign patients had had a history of being treated for malaria in countries they had visited or home countries. The initial diagnoses of 9 patients attending other hospitals in Japan were as follows; 7 were malaria (3 patients were diagnosed as vivax malaria), 2 were fever of unknown origin.

Fever, diarrhea and disturbed consciousness

All patients had a history of fever. Eleven patients were febrile over 37.5°C at presentation or after admission to our hospital; 2 patients had maximum temperatures of over 40°C, and 4 had maximum temperatures of 39–40°C. No patients complained of watery or mud-like diarrhea. No cases showed disturbed consciousness.

Treatment and outcome

Eleven patients were treated with oral administration of chloroquine and primaquine, 1 patient with oral administration of mefloquine and primaquine, and 1 patient with oral administration of S-P and primaquine. All patients recovered completely with the therapy.

Ovale malaria

Population

One 55-year-old American male, 1 27-year-old Japanese female and 1 23-year-old Japanese male.

Chemoprophylaxis

The American patient had taken adequate doses of chloroquine, but the other 2 patients had taken no chemoprophylaxis agents.

Presumed country of contraction and duration of stay

Presumed countries of contraction are shown in Table 1. The respective duration of stay in the country was as follows; 5 years, 1 year, 6 months.

Physical contact

All patients initially contacted our hospital because of the presenting symptoms and they were diagnosed as ovale ma-

laria. Two Japanese patients had had a history of being treated for malaria in the countries they had visited.

Fever, diarrhea and disturbed consciousness

All patients had a history of fever. The maximum temperatures on admission or after admission were as follows; 40.2°C, 38.0°C and 37.0°C. One patient complained of diarrhea; no cases with disturbed consciousness were observed.

Treatment and outcome

All patients were treated with oral administration of chloroquine and primaquine, and they recovered completely with therapy.

Mixed infection with *P. falciparum* and *P. vivax*

Patient

One 35-year-old Chinese male.

Presumed country of contraction

The presumed country of contraction is shown in Table 1.

Physical contact

The initial diagnosis of the patient by a doctor from another hospital in Japan was fever of unknown origin.

Treatment

The patient was treated with oral administration of mefloquine and primaquine, and recovered completely.

Drugs

Chloroquine, primaquine, mefloquine and Quinimax® were provided by the Research Group on Chemotherapy for Tropical Diseases (President Prof. H. Ohtomo, Department of Tropical Medicine, Jikei University School of Medicine, Tokyo), and the drugs were used with the consent of patients.

Discussion

In the 1960s and 70s, malaria in Japan had been thought to be a very rare disease imported from tropical or subtropical areas. Recently, not only young, but also middle-aged and elderly Japanese have begun travelling to tropical and subtropical countries with greater frequency. The fact that middle-aged and elderly Japanese patients were identified in this study along with young patients reflects the recent tendencies of Japanese travelers outside Japan. More than half of the total and the majority of Japanese patients infected with *P. falciparum* contracted the disease in Africa. It is well known that some non-immune patients infected with *P. falciparum* do not survive without adequate therapy, so Africa may be the greatest threat to Japanese travelers in terms of malaria.

Many Japanese travelers are unaware of diseases in the countries they visit, and do not adequately protect themselves. Careful attention to avoid contact with mosquitos is very important to avoid malaria infection, but difficult. No practical method of immunization is available to date. Various types of chemoprophylaxis agents for malaria have been used for a long time. The usefulness of chemoprophylaxis agents for travelers visiting malaria endemic areas is still debatable. Although no available regimen of chemoprophylaxis is completely effective due to drug-resistant malaria and the lack of compliance among

travelers, the proper chemoprophylaxis is recommended for non-immune travelers to malaria endemic areas (1–3). Three patients of the present study contracted malaria in spite of having taken the recommended dose of chemoprophylaxis agents. If more patients had taken the adequate chemoprophylaxis, however, the number of malaria patients might have been decreased.

There is no sign or symptom specific to malaria, but fever is the most important symptom among those shown in malaria patients. It is reported that diarrhea is also one of the common symptoms of malaria in USA (4). No patients infected with *P. vivax* complained of diarrhea in our study, but half of the Japanese patients infected with *P. falciparum* complained of diarrhea accompanied with fever. These results indicate that diarrhea is a common symptom in Japanese patients infected with *P. falciparum*. Disturbed consciousness was identified in 2 patients infected with *P. falciparum* after admission. We feel it is important to immediately hospitalize non-immune patients infected with *P. falciparum* because without adequate antiparasitic and supportive therapy, their condition can deteriorate dramatically over a short period, sometimes resulting in death. Malaria should be one of the diagnostic diseases and a malaria blood smear should be made in febrile patients associated with malaria endemic areas. The species of *Plasmodium* present in an infection should be identified as soon as possible because the therapy differs depending on the species.

In the present study, only 14.3% of Japanese patients infected with *P. falciparum* and no Japanese patients infected with *P. vivax* stayed less than 2 weeks outside Japan. It has been reported, however, that a patient contracted malaria after a stay of only several hours in a malaria-endemic country (5). Therefore, physicians must be aware of the possibility of malaria in febrile patients returning or coming from malaria-endemic

areas regardless of their duration of stay.

There is presently no indigenous malaria in Japan, and there is little attention to the disease. Moreover, blood film is checked automatically by machine in most Japanese hospitals and clinics, and such equipment does not recognize *Plasmodia*. Therefore, many Japanese doctors overlook the diagnosis. Initially attending doctors of other Japanese hospitals correctly diagnosed only 12.5% of all and 16.7% of Japanese patients infected with *P. falciparum*. On the other hand, 77.8% of all and 66.7% of Japanese patients infected with *P. vivax* were diagnosed correctly. This discrepancy may be attributed to the fact that patients infected with *P. vivax* tend to know much more about malaria than patients infected with *P. falciparum* because they stayed in the endemic area for a much longer time period, and as a result, they requested to be checked for malaria.

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