MALARIA: 30 YEARS OF EXPERIENCE AT A NEW YORK CITY TEACHING HOSPITAL

CHRISPIN KAMBILI, HENRY W. MURRAY, AND LINNIE M. GOLIGHTLY

Division of International Medicine and Infectious Diseases, Department of Medicine, Weill Medical College of Cornell University and New York-Presbyterian Hospital, New York, New York

Abstract. Two previous reviews summarized the New York Hospital experience with 110 cases of malaria from 1968 to 1990. We have extended these studies to include 59 cases of malaria seen from 1991 to 1999 and analyze trends over the past 30 years. Plasmodium falciparum remains the most common species, 38 (64%) of the 59 cases, with the majority of them, 34 (89%) of 38 cases, being acquired in Africa. Of the 59 cases, 22 (37%) were immigrants living in the United States who had visited their countries of origin. Only five (8%) of 59 patients reported using chemoprophylaxis. This represents a marked decrease from the previous reviews. None of the immigrants or their children used chemoprophylaxis. Diagnosis was prompt, and patients responded well to therapy. Complications of malaria were low and no deaths were reported, as was the case in the previous reviews. The low use of chemoprophylaxis, particularly among immigrants, is a major concern.

INTRODUCTION

Rates of imported malaria have been increasing both in Europe and in North America.1,4 The U.S. Centers for Disease Control and Prevention (CDC) reported a 25% increase in reported cases of malaria among persons in the United States from 1998 to 1999.1 The rising rates of imported malaria have been attributed mostly to increased travel to and from malaria-endemic areas.1,4 The U.S. Department of Transportation reported a 30.5% increase in international travel originating from the United States between 1990 and 2000 with an 86% increase in travel to Africa,5 where the risk of acquiring imported malaria is greatest.1 With these trends, we felt compelled to follow up on two reviews on the clinical and epidemiologic features of imported malaria that have been published from our hospital in the last quarter century.6,7

We therefore have extended these studies to include the years 1991–1999 and report on the demographic and epidemiologic features of patients with imported malaria at our hospital. We explore trends in these features over the quarter century that these reviews span and we briefly review the clinical characteristics of the disease in our cohort of patients.

MATERIALS AND METHODS

The clinical parasitology laboratory at The New York-Presbyterian Hospital-Weill Cornell Medical Center (formerly The New York Hospital) maintains a registry of all positive malaria smears. We reviewed cases that were recorded for the nine-year period from January 1, 1991 to December 31, 1999. The study was reviewed and approved by the Weill Medical College of Cornell University Institutional Review Board (protocol no. 1203-077).

There were 82 positive smears for Plasmodium species during the study period. Nineteen of these patients were referrals from outside practitioners or other hospitals for review and confirmation, and did not have corresponding patient charts at our hospital. Therefore, 63 smears from 61 patients had corresponding charts in our hospital. (Two patients had two smears each so only their first presentation has been included for analysis, since any subsequent presentation may represent a recrudescence or recurrence of the first presentation.) Charts belonging to two patients could not be located despite an extensive search. Fifty-nine patient charts were therefore available for review. Information on demographics, area(s) of travel, species of Plasmodium, use of chemoprophylactic agents, and clinical course were extracted from the charts and analyzed.

RESULTS

Demographic and epidemiologic features. The 59 patients included 39 (66%) males and 20 (34%) females for the period 1991–1999 (Table 1). The mean age was 31 years with a range of 2 to 74 years. Seventeen patients (29%) were under the age of 15, including three pairs of siblings. (Table 1 also shows data for the periods 1968–1975 and 1975–1990 for comparison).

Twenty-seven patients (46%) were non-immune travelers (individuals born and residing in non-endemic countries), 23 of the 27 being born in the United States (Table 1). Thirty-two patients (54%) were born in or were residents of malaria-endemic areas. Twenty-two of these patients (37%) were immigrants (natives of malaria-endemic areas) living in the United States and their children (three of the children were born in the United States) who were visiting their countries of origin. All but one of these immigrants were of African origin. Ten patients (17%) were natives of malaria-endemic areas who were visiting the United States when malaria was diagnosed; three were from Asia and seven were from Africa.

Table 2 shows the regions where the patients had last traveled before malaria was diagnosed, comparing the three periods. These areas were presumed to be the areas where malaria was acquired. The majority (73%) of the cases were acquired in Africa during 1991–1999. There were 38 patients (64%) with P. falciparum, making it the most dominant species, and 89% of these were acquired in Africa. Plasmodium vivax was the second most common species with 14 cases. Two smears had mixed P. falciparum and P. vivax infections, and one smear had mixed P. falciparum and P. ovale infection. The species of Plasmodium could not be determined on nine smears because the parasitemia was too low. There were no cases of P. malariae. Table 2 shows comparisons with the previous two study periods.

Use of chemoprophylaxis. Only five patients, all of whom were United States–born travelers, reported using chemoprophylaxis during their most recent travel to a malaria-endemic
area. None of these patients used a CDC-recommended drug regimen for the area of travel. One patient, traveling to East Africa, an area known to have high levels of chloroquine resistance, had taken only chloroquine. Another patient, with a three-month stay in west Africa, had stopped taking prophylaxis in the second month because “none of his friends was getting sick despite not being on prophylaxis.” A third patient stopped taking his mefloquine prophylaxis one week before he left the malaria-endemic area. Two patients did not remember the name of the drug they had taken and their compliance with the regimens was questionable. None of the immigrants from malaria-endemic areas living in the United States (or their children) who traveled to an endemic area reported any use of chemoprophylaxis. Use of bed nets and insect repellants was not documented for any of the patients.

**Disease among children of immigrants.** Seventeen (29%) of the patients were children less than 15 years of age. All were children of immigrants who had traveled with their families to Africa, including three pairs of siblings with malaria. In one family, the father and two young children had symptomatic malaria. In another family, one child was diagnosed with malaria when he presented with a febrile illness, at which point the parents requested that their other child be screened for malaria, and indeed, the child had *P. falciparum* parasitemia although he was completely asymptomatic. In the third pair of siblings, the children presented with fever two weeks apart; one child had *P. falciparum* and the other had an indeterminate species.

**Clinical features and accuracy of clinical diagnosis.** The time interval from arrival in the United States to presentation at the hospital varied from as little as 24 hours to as long as 15 days for all patients, except for one patient who became ill with fevers four months after his arrival in the United States. He was diagnosed as being infected with *P. vivax*, which he had acquired in India.

Diagnosis was prompt for most of the patients; 97% of the patients were diagnosed with malaria within 24 hours of being evaluated by a physician at our hospital. The two patients whose diagnosis was delayed were in the hospital for five and seven days, respectively, with fever before a diagnosis was made. Both were United States–born men in their thirties who had traveled to South America; travel history was not elicited in either case until after the diagnosis was established. They both were infected with *P. vivax*. Two other patients (children four and six years old) had been seen by their local physicians, and had been diagnosed as having viral gastroenteritis and bacterial otitis media respectively prior to presenting at our hospital, where malaria was promptly diagnosed.

Clinical manifestations were protean and nonspecific but fever was present in 58 of 59 patients (98%). There were two cases of severe *P. falciparum* malaria as defined by the World Health Organization. The first was a 40-year-old businessman from Africa who was visiting New York when he presented with fever and confusion. He had a parasitemia of 8%. This patient required a short stay in the intensive care unit because of pulmonary edema that was noted on his chest radiograph on his second day of admission. The second case of severe disease was a six-year-old United States–born daughter of African immigrants who presented with fever and acute renal failure requiring dialysis, and had a parasitemia of 18%.

**Treatment and clinical response.** All patients responded well to treatment, including the ones with severe malaria. Treatment consisted of quinine with or without doxycycline in adults or sulfadoxine/pyrimethamine in children for *P. falciparum* malaria. Chloroquine plus primaquine was given in cases of *P. vivax* malaria. There were no deaths in our series.

**DISCUSSION**

Despite the availability of effective preventive regimens for malaria, including drugs effective against chloroquine-resistant *P. falciparum*, the rates of imported malaria have continued to rise in many non-endemic temperate areas, with immigrant populations contributing to the increasing rates. Recent data from the CDC has shown increases in the number of reported cases of malaria. Some areas of the United States have experienced large increases in the number of malaria cases due to changing immigration patterns. Malaria cases reported to the Minnesota Department of Health increased from 5 in 1988 to 76 in 1998, an increase of more than 1,400%. In addition to increased travel, lack of preventive measures used by travelers may also be an important contributing factor to this trend. Increased numbers of immigrants (both former residents of malaria-endemic areas visiting their countries of origin and new arrivals) seem to play a significant role. However, data from our hospital do not show a difference in the proportions of immigrants between the periods 1975–1990 and 1991–1999. In a review of imported malaria at our hospital for the period 1975 to 1990, Winters and Murray found that 42 of 86 cases (49%) were non-immune (United States–born) travelers, 28 (33%) of 86 were immigrants (natives of malaria-endemic areas who had resettled in the United States), and 16 (19%) of 86 were people visiting the United States when malaria was diagnosed. These proportions are similar to those found in the current study, perhaps due to stable trends in immigration from malaria-endemic areas to New York City over the past 25 years. In contrast, European studies and a study from Minnesota have demonstrated very substantial increases in the proportions of immigrants among patients diagnosed with imported malaria over the last quarter century. Recent changes in immigration patterns to those locales may explain this observation.

One notable finding in our series was the occurrence of malaria among young siblings. Given the devastating nature of this disease in young children, it might be prudent to screen for malaria among young children. Given the devastating nature of this disease in young children, it might be prudent to screen...
young siblings for malaria if one child is diagnosed with the disease after traveling to malaria-endemic areas. Others have advocated screening immigrants, particularly refugees, from malaria-endemic areas for asymptomatic parasitemia.\textsuperscript{4,13} The effectiveness of this practice has yet to be established. Practitioners giving pre-travel counseling should inquire if the travelers are bringing children or others with them on their journeys and appropriate measures should be taken to protect the children from malaria and other health problems.

In this series, the use of chemoprophylaxis was only 8%. This is much lower than the percentage reported by our predecessors. In the reviews by Kean and Reilly\textsuperscript{6} and Winters,\textsuperscript{7} the overall percentages of people using chemoprophylaxis were 45% and 36%, respectively. This suggests that there may be lower rates of chemoprophylaxis use; however, since this is a case series this conclusion cannot be made. A cohort study is needed to quantify the extent of the problem and if there are truly lower rates of chemoprophylaxis use.

However, some European studies have shown lower rates of chemoprophylaxis use among immigrant groups compared with non-immigrants.\textsuperscript{10} There are several potential reasons for this. For example, there is a misconception among immigrants that they are immune to the disease when they return to their native countries. The exact duration of such acquired immunity is not known. In addition, some immigrants may not seek pre-travel advice due to a lack of resources or they may be misinformed about preventive measures against malaria. Similarly, individuals from malaria-free countries might discontinue their chemoprophylaxis after an extended stay in endemic areas believing that their residence in a malaria-endemic area has afforded them adequate immunity to the disease. According to the CDC, malaria-related deaths among United States citizens are attributable mainly to non-use or inappropriate use of chemoprophylaxis.\textsuperscript{14} Patient education is therefore vital. Clinicians should impress upon travelers the need for preventive regimens against malaria. The CDC considers immigrants visiting their homelands at high risk for infection, and advises that this be recognized when providing them with pre-travel counseling.\textsuperscript{14} If necessary, travelers should be referred to specialized travel clinics to get the most up-to-date recommendations.

The need for prompt diagnosis, especially with \textit{P. falciparum} malaria, cannot be overemphasized. In our group of patients, diagnosis was rendered swiftly in most cases, owing largely to an accurate travel history. This was also the case in the previously published series.\textsuperscript{6,7} Fewer patients were seen by outside practitioners before coming to the hospital in this series than in the study by Murray and Winters.\textsuperscript{7} In that study, many patients had been seen by community physicians, and malaria was not initially considered by the community physicians.\textsuperscript{7} Only two patients, both of them children, had been seen by their private physicians prior to presenting to our hospital. It is not entirely clear why most of our patients had not consulted community physicians prior to presenting to our hospital. Delay in the diagnosis of imported malaria is due either to lack of familiarity with the symptoms of malaria by the treating practitioner or failure to elicit a pertinent travel history. Several studies have confirmed that a more timely diagnosis of malaria in non-endemic areas occurs in centers that specialize in travel medicine and/or tropical diseases.\textsuperscript{3,6,7}

As travel and migration between malaria-endemic areas and temperate countries increase, imported malaria will remain a public health priority. Although we have highlighted malaria among immigrants living in the United States who have visited their countries of origin, a high proportion of our cases occurred in United States–born travelers (46%). A concerted effort is needed to disseminate knowledge about the dangers of malaria and the need for pre-travel counseling to all visitors to malaria endemic areas. However, immigrants living in the United States may be at a particularly high risk of acquiring malaria when they visit their countries of origin. Several factors including lack of resources, cultural beliefs and lack of knowledge, may contribute to their increased risk.

\begin{table}[h]
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\begin{tabular}{|c|c|c|c|c|c|c|c|c|c|}
\hline
& Africa & Asia & America & Africa & Asia & America & Africa & Asia & America \\
\hline
\textit{P. falciparum} & 34 & 2 & 1 & 45 & – & 8 & 14 & 1 & 1 \\
\textit{P. vivax} & 4 & 5 & 5 & 5 & 13 & 3 & 4 & 3 & – \\
\textit{P. malariae} & – & – & – & 2 & 1 & 1 & 1 & – & – \\
Indeterminate* & 6 & – & – & 1 & – & 1 & – & – & 6 \\
Total† & 45 & 7 & 6 & 62 & 14 & 13 & 20 & 4 & 1 \\
\hline
\end{tabular}
\caption{Region where malaria was acquired\textsuperscript{*} and \textit{Plasmodium} species for each of the three periods}
\end{table}

\textsuperscript{a} The most recent place known to be endemic for malaria where the patient traveled is presumed to be the place where malaria was acquired. America includes South and Central America, and Haiti. Asia includes New Guinea.

\textsuperscript{b} For the period 1991–1999, the total number of species exceeds the number of patients given in the text because two patients had mixed \textit{P. falciparum}/\textit{P. vivax} infections and one patient had \textit{P. falciparum}/\textit{P. ovale} infection; one case of \textit{P. falciparum} and three cases of indeterminate species did not have a documented region of travel. For the period 1975–1990, three patients had mixed \textit{P. falciparum}/\textit{P. ovale} infections and one patient had a mixed \textit{P. vivax}/\textit{P. malariae} infection; one case of \textit{P. malariae} had an unknown area of travel. For the period 1968–1975, one patient had a mixed \textit{P. falciparum}/\textit{P. vivax} infection.\textsuperscript{11}

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Reprint requests: Linnie M. Golightly, Division of International Medicine and Infectious Diseases, Weill Medical College of Cornell
REFERENCES