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Case report

A depiction of imported malaria in Connecticut

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ABSTRACT

In 2010, there were roughly 219 million cases of malaria reported worldwide resulting in an estimated 660,600 deaths [1]. In contrast, the total number of cases according to the Centers for Disease Control and Prevention (CDC) in the United States (USA) was only 1691 [2]. Of those, 1688 were cases of imported malaria [2]. This is the highest number of cases reported in U.S. since 1980 [2]. Here, we describe a case of imported malaria and conduct a retrospective case series at four Connecticut (CT) hospitals in order to describe the demographics of imported malaria and to identify potential barriers to timely diagnosis and treatment.

Introduction

In 2010, there were roughly 219 million cases of malaria reported worldwide resulting in an estimated 660,600 deaths [1]. In contrast, the total number of cases according to the Centers for Disease Control and Prevention (CDC) in the United States (USA) was only 1691 [2]. Of those, 1688 were cases of imported malaria [2]. This is the highest number of cases reported in U.S. since 1980 [2]. Here, we describe a case of imported malaria and conduct a retrospective case series at four Connecticut (CT) hospitals in order to describe the demographics of imported malaria and to identify potential barriers to timely diagnosis and treatment.

Case report

A 24-year-old African-American female college student with no significant past medical history presented to the emergency room with fever, lower abdominal pain and nausea without vomiting starting the day prior to admission. She noted that her menstrual period was slightly late, but otherwise the history obtained was non-contributory.

In the ED, she was found to be febrile (102 F) and tachycardic. She had an episode of vaginal bleeding while being evaluated. As a result, a pelvic examination was performed, which was unremarkable aside from scant blood in the vaginal canal and a closed cervix. Beta-HCG was obtained and was elevated at 784. Ultrasound of the abdomen and pelvis demonstrated a fetal sac in the uterus, but was otherwise within normal limits. Routine diagnostic testing was notable for a normal white blood count, normal hemoglobin, low platelets (92,000), normal kidney function (Cr 0.6), mild transaminitis (ALT 84, AST 72) and an indirect hyperbilirubinemia (TB 1.4, DB 0.3). Urinalysis demonstrated 5–6 WBCs, 9–10 RBCs, 10–12 epithelial cells, 1+ bacteria and trace leukocytes.

She was subsequently admitted to the medical service with the diagnosis of UTI and threatened abortion and was started on nitrofurantoin and IV fluids. Overnight, she spiked a high fever (104 F) with rigors. Morning laboratory investigations revealed a new leukopenia (WBC 2.8) and worsening thrombocytopenia (Plt 66,000). As a result, OB/Gyn was consulted for concern for possible septic abortion. They determined that it was an inevitable abortion and antibiotics were broadened. Given her worsening septic picture, infectious disease was consulted, a peripheral blood smear sent and doxycycline started for concern of ehrlichiosis. During the infectious disease evaluation, it is discovered that both the patient and her husband had recently traveled to Nigeria, her husband had been infected with malaria during their visit there, and she herself

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had developed a fever a day prior to returning to the USA and had become so ill en route that she presented to the emergency room directly from the airport.

Subsequently, the peripheral smear was reviewed by the ID attending in the laboratory and intracellular 'ear muff' shaped parasites consistent with *Plasmodium falciparum* were seen. As a result, the patient was diagnosed with uncomplicated malaria given no evidence of complications meeting criteria for severe malaria (namely, severe anemia, renal failure, ARDS, and hyperparasitemia) [3]. The CDC was contacted with respect to Artemisinin-based combination treatment. However, the decision was made to treat immediately with atovaquone/proguanil given that it was more readily available from an outside pharmacy than waiting for Artemisinin-based medication sent directly from the CDC. It was not until the third day of hospitalization that she received appropriate treatment. With anti-malarials, her clinical condition improved and she defervesced over the next 48 h. She was eventually discharged home after a six-day admission.

Retrospective case series

We conducted a retrospective case series of all patients with confirmed diagnosis of malaria from 2001 to 2012 at four Connecticut teaching hospitals (Waterbury Hospital, St. Mary's Hospital, Hospital of St. Raphael, & Griffin Hospital) in order to describe the demographics of imported malaria and to identify potential barriers to timely diagnosis and treatment.

Of a total of the fourteen patients, 54% were African, 23% American, 16% South Asian and 8% Hispanic. Most patients were foreign residents visiting the USA (54%), while the rest were USA citizens. A vast majority of patients were traveling in sub-Saharan Africa (73%, 9% India, 9% Pakistan, 9% Dominican Republic). Only a minority of patients took anti-malarial prophylaxis (22%). Symptoms began on average 3.1 days (range 1–8, SD 2.8) after arrival to the USA and patients presented to a healthcare provider on average 4.7 days (range 0–37, SD 12.1) after onset of symptoms. At the time of presentation, malaria was on the differential diagnosis in only half of cases and travel history was documented in only 69% of cases. Mean time to diagnosis was 2.9 days (range 0–12, SD 3.6). The vast majority of cases were due to *P. falciparum* (92%), while the remaining case was due to *Plasmodium vivax*. In general, parasite burden was low with 75% of cases with $\leq$2% parasitemia.

Appropriate treatment was initiated in 93% of cases and mean time to treatment from time of presentation was 3.0 days (range 0–12, SD 3.6). Anti-malarial medications were available in the hospital pharmacy for only half of the cases. For these patients, treatment was administered promptly (mean 2.2 h, range 1–3 h). In cases where medications were not available in the hospital, there was a significant time delay between when the drug was ordered and when it was administered with 75% of patients receiving treatment $\geq$8 h (mean 10.3 h, range 7–12 h) after it was ordered. In general, patients responded well to treatment. 71% were admitted to the hospital and only one case required ICU admission. Patients requiring inpatient admission were hospitalized on average for 3.2 days (range 1–7, SD 1.9).

Discussion

Internationally, malaria is a life-threatening infectious disease resulting in as many as 500 million estimated cases annually [4]. In contrast, domestically, malaria is no longer endemic and instead is imported via international travel and immigration from afflicted parts of the world. According to Department of Homeland Security, about 12,000 people obtained legal residence in Connecticut during 2011. In comparison, the bordering state of New York had close to 150,000 legal immigrants out of a total of just over 1 million for the US as a whole [5]. With regards to malaria, Connecticut had a total of 21 reported cases compared to the 1691 nationwide in 2010 [2]. The incidence of malaria in Connecticut is comparable to that of the US (0.6 vs. 0.5 cases of malaria per 100,000 people, respectively) [2,6,7]. Given the rise of globalization, the number of cases of malaria has increased proportionally in the US. According to the CDC, the number of cases of malaria in 2010 was a 30% increase compared to 2008 and a 14% increase compared to 2009 [2]. Similarly, the United Kingdom reported a 29% increase of malaria cases from 2008 to 2010 [2].

Several possible factors have been identified for the delay in diagnosis and treatment of imported malaria. In 2000, Dorsey et al. reviewed 121 confirmed cases of malaria over a 10-year period in San Francisco, California and found that in 19 (16%) of these cases the initial physician missed the diagnosis of malaria [8]. The authors suggested the delayed diagnosis might be attributed to an incomplete travel history. Similarly, our analysis determined that in 31% of imported malaria cases a travel history was not documented and in half of the cases malaria was not considered on the differential diagnosis. In 1998, Kain et al. performed a prospective analysis of the diagnosis and treatment of malaria in Toronto, Canada [9]. In that study, the correct initial diagnosis was not made in 59% of cases and there was a delay in treatment for cases of *P. falciparum* by about 7 days [9]. In our series, the mean time to treatment was also delayed until approximately 3 days after presentation to a healthcare provider. Furthermore, these treatment delays were often exacerbated by the unavailability of anti-malarials in hospital pharmacies. Lastly, the CDC has long recommended chemoprophylaxis against malaria. However, only a minority of travelers is compliant with prophylactic medications [4,8,9]. Similarly, in our results, only about one-fifth of the patients took anti-malarial prophylaxis.

In conclusion, imported malaria is relatively uncommon in the US, but each year the number of cases continues to rise given trends in globalization and international travel [8]. However, when these cases presented to the healthcare system, malaria was not entertained on the differential diagnosis, travel history was not obtained, chemoprophylaxis was underutilized, and anti-malarials were not available in hospital pharmacies in substantial proportion of these cases resulting in possible delays in diagnosis and treatment. Based on these findings, we wish to re-emphasize and recommend that:

1. All individuals traveling to malaria endemic parts of the world be evaluated by a travel clinic prior to departure and to stress the importance of anti-malarial prophylaxis;
2. All healthcare providers must maintain a broad differential diagnosis and take a thorough travel history given that imported tropical diseases will become more commonplace in the setting of globalization in order to prevent delays in diagnosis;
3. All healthcare provides should be familiar with trends in global health in order to be informed of the growing mobility and the evolving epidemiology of infectious diseases;
4. All hospital pharmacies should have anti-malarial medications stocked to allow for prompt treatment of this life-threatening infectious disease.

Conflict of interest statement

The authors declare that there are no conflicts of interests.

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