5-2019

Malaria in Macomb, Michigan

Justin Gardner
Henry Ford Health System

Keith Cronovich
Henry Ford Health System

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Justin Gardner DO, Keith Cronovich, DO.
Emergency Medicine, Henry Ford Health System, Detroit, Michigan

Tropical Diseases – Central Africa

Evaluation of a patient in whom you suspect a tropical disease requires a thorough history. You must determine the timeline of travel as well time course of symptom onset and progression. Ask about geographical region of travel, mode of transport, human sick contacts, animal exposure, insect bites, water sources, sexual contact, vaccine history, and prophylactic medications. There are specific diseases of concern in patients traveling to Central Africa, including: Malaria, Dengue fever, Chikungunya fever, Ebola virus, Marburg virus, Crimean-Congo hemorrhagic fever, Yellow fever, Zika virus, Leishmaniasis, Trypanosomiasis, Onchocerciasis, Schistosomiasis. Central Africa is also the region most heavily affected by HIV/AIDS as well as Plague. What follows is a case report of a patient diagnosed with Malaria as well as pertinent information regarding this disease.

Initial Presentation

27yo male presents to the ED complaining of fever/chills, body aches and headache that began in the evening two days ago, worsening in severity since onset. Fever and body aches are more severe at night. He has had 2 episodes of diarrhea which started today. Denies any vomiting, cough, abdominal pain, vision changes, or sore throat. He went on a mission trip to Nigeria and Zambia for 8 days, returning 15 days ago. He did not take his prophylactic malaria medications nor use a mosquito net, although he did receive his Hepatitis A vaccinations. Denies contact with anyone ill, however, he did visit a hospital in Africa.

- ROS: Positive for Chills, Fever, Weakness, Fatigue, Headache, Body Aches.
- PE: HR 67 RR 18 T 98.6F SPO2 99% BP 113/75
  Patient is Oriented x4. Fatigued appearing. No meningeal signs. Neck full ROM. RRR, no murmurs. Lungs clear in all fields. Abd non tender. GCS 15. No rashes.
- Results: Chest xray negative. Influenza negative. Malarial Smear sent
  Na 135 K 3.6 Cl 99 CO_2 27 BUN 14 Cr 1.45 Gluc 107 ALT 49 AST 41 $Bili_T$ 1.8 $Bili_D$ 0.4
  WBC 2.8 Hgb 16.4 Plt 113 Hct 46.0. INR 1.16 PT 15.1 PTT 26

Consulted ID, who recommended Discharge with prescription for Mefloquine and outpatient follow with ID within 3 days. Spoke with pharmacy, Mefloquine not available in Henry Ford Health System nor nearby pharmacies. Hydroxychloroquine given in ED, and discharge prescription given.

Return to the ED

Patient returned 7 days later, stating that he had been feeling better since discharge but fevers, chills, malaise, body aches, nausea, vomiting, diarrhea, returned 2 days ago. Associated 10lb weight loss since initial symptom onset. Patient has not followed up with ID. Completed course of Hydroxychloroquine from prior visit. Denies chest pain, cough, SOB, abdominal pain, neck stiffness.

- PE: HR 103 RR 16 T 100.9F SPO2 100% BP 111/63
- Oriented x 4. Fatigued appearing. Scleral icterus. No meningeal signs. Tachycardia. Nontender abdomen. Lungs clear in all fields.
- Results: Na 134 K 3.7 Cl 97 CO_2 26 BUN 10 Cr 1.51 Gluc 110 ALT 58 AST 37 $Bili_T$ 1.7 $Bili_D$ 0.4 LA 1.1 WBC 5.1 Hgb 15.7 Plt 231 Hct 45.2. INR 1.34 PT 16.9 PTT 35. Urinalysis negative.
  Malaria smear from prior visit negative. Repeat Malaria smear sent. Viral panel, Hepatitis panel, Dengue and chikungunya antibody assays sent.
  ID consulted. Patient received Yellow Fever vaccine 1 day prior to trip to Africa, did not take Malaria prophylaxis and did not use mosquito nets. Drank only bottled water during his trip. Patient transferred to HF Detroit, as recommended by ID, with high concern for tropical disease.

Hospital Course

- Day 1: Patient admitted to HF Detroit to the ID service. Dengue RT-PCR, Chikungunya RT-PCR, Zika urine and serum PCR, EBV, HIV, CMV, Quantiferon Gold, stool cultures for typhii and paratyphii sent. Smear positive for Plasmodium falciparum (0.1% parasites). Atovaquone and Chloroguanide begun.
- Day 2: HIV negative, CMV negative, typhii and paratyphii negative. Smear again positive for Plasmodium falciparum (0.1% parasites). Liver function tests returned to normal limits.
- Day 3: Smear again positive for Plasmodium falciparum. (0.1% parasites). Course of Atovaquone and Chloroguanide completed.
- Day 4: Parvovirus IgM (2.61) positive (reference range <0.9). EBV negative, Quantiferon Gold negative, Giardia negative. Repeat Malaria smear pending. Dengue, Chikungunya, and Zika PCR pending. Leukopenia suspected to be due to Acute Malaria vs Hydroxychloroquine induced vs Parvovirus coinfection. Patient discharged with plan to call patient if tests return positive.
  Results: Na 139 K 4.4 Cl 104 CO_2 29 BUN 10 Cr 1.23 Gluc 98 WBC 2.6 Hgb 13.7 Plt 248 Hct 39.3
- Repeat Malarial smear negative. Zika PCR negative. G6PD negative. Hepatitis viral panel negative. Chikungunya RT-PCR and Dengue RT-PCR negative. Malaria PCR returned positive only for Malaria Falciparum. Patient did not require further treatment.

Malaria - Epidemiology

Malaria occurs throughout most tropical regions and consists of multiple species: P. falciparum (sub-Saharan Africa, New Guinea, Haiti, Dominican Republic), P. vivax (Americas and western Pacific), P. knowlesi (Malaysia, Thailand, Myanmar, Philippines, Thailand). P. ovale and P. malariae also occur in Africa. More than 216 million people develop symptomatic infections annually, approximately 90% of infections are caused by P. falciparum. Annual worldwide Malaria deaths peaked at 1.82 million in 2004, and have declined to 445,000 as of 2016. More than 90% of deaths occur in children in sub-Saharan Africa. In a sample of 7,000 returned travelers presenting with fever, between 1997 and 2006, 21% were found to have Malaria, with more than 50% of these cases being P. falciparum. More than 70% of cases of imported Malaria are in Americans born in endemic countries and who later return home to visit friends and relatives. These travelers may not appreciate the risk or severity of infection once their immunity has waned.

Malaria - Prevention

Malaria is spread through the bite of a female Anopheles mosquito. Prevention of a mosquito bite is a key means of reducing transmission of Malaria. The most basic measures include staying indoors from dusk to dawn, wearing clothes that minimize exposed skin, and using well sealed screens in every window and doorway. Insect repellent (Picardin or DEET) should be worn, applied to the skin, at all times, and they have comparable efficacy for up to 8 hours. Clothing and bed netting treated with Permethrin aerosol spray effectively repel mosquitos for more than 1 week. Long-lasting insecticide impregnated nets (LLINS) can remain effective for up to 3 years.

- **For travelers to areas of low risk for malaria**
  - Mosquito prevention methods only. No need for chemoprophylaxis.
- **For travelers to areas where Chloroquine-resistant P. falciparum is present:**
  - Africa, Asia, Oceania.
  - Atovaquone-proguanil, Mefloquine, or Doxycycline.
  - Pregnant women should be given Mefloquine
- **For travelers to areas where Chloroquine-sensitive P. falciparum is present:**
  - Caribbean, Central America, Middle East, China.
  - Chloroquine, Hydroxychloroquine, Atovaquone-proguanil, Mefloquine, or Doxycycline.
  - Pregnant women should be given Chloroquine or Mefloquine.
- **For travelers to areas where P. vivax is present:**
  - Mexico and Central America.
  - Primaquine, Chloroquine, Hydroxychoroquine, Atovaquone-proguanil, Mefloquine, Doxycycline.
  - Primaquine is added for activity against the liver hypnozoite stages of P. vivax and P. ovale.
- **For travelers to areas where P. falciparum resistant to Chloroquine, Mefloquine, and Sulfonamides:**
  - Thailand, Cambodia, Laos, Vietnam.
  - Atovaquone-proguanil, Doxycycline.

- *Key points regarding medication selection:*
  - Atovaquone-proguanil is contraindicated in pregnant women and those with creatinine-clearance <30 mL/min.
  - Mefloquine can cause strange dreams, paranoid delusions, seizures, or psychosis. It can also lead to QT interval prolongation.
  - Doxycycline is contraindicated in pregnant women and children <8 years old.
  - Primaquine can cause hemolytic anemia in those with G6PD deficiency. A G6PD level must be determined prior to beginning this medication. It is contraindicated during pregnancy and breastfeeding.
  - In Children:
    - Chloroquine and Mefloquine can be given to children of all ages. Atovaquine-proguanil can be given to children of at least 5kg. Doxycycline can be given to children >8 years old.

Malaria - Diagnosis

If there is a high level of suspicion for malarial infection, treatment should be initiated prior to definitive diagnosis. Those with acquired partial immunity due to repeated exposures may have asymptomatic parasitemia. No diagnostic test is capable of distinguishing between parasitemia causing clinical malaria, and a febrile illness due to another cause in a patient who also has asymptomatic parasitemia. Blood smear examination via light microscopy is the standard tool for diagnosis of malaria. Rapid diagnostic tests should be used if microscopy is not available.

- **Light Microscopy**
  - Allows for identification of the Plasmodium species as well as quantification of parasitemia.
  - If malaria is suspected and the initial smear is negative, smears should be repeated every 12 to 24 hours for a total of 3 sets before ruling out malaria.
  - Once a diagnosis of malaria is established, serial smears should be examined to monitor parasitological response to treatment. This should be continued to smear is negative or for a total of 7 days.
  - Parasite density correlates to severity of infection.
- **Rapid Diagnostic Tests**
  - Do not require electricity and give results within 20 minutes. Can be preformed by anyone with little training.
  - Able to determine Plasmodium species.
  - Provide a qualitative result but no quantitative information.
  - Do not have sufficient negative predictive value to justify withholding treatment
- **PCR**
  - Gold standard in efficacy studies for medications, vaccines, and evaluation of other tests
  - Rarely used in clinical settings.

Malaria - Treatment

If the infecting species is not known with certainty, treatment should include coverage for P. falciparum.

- **Uncomplicated P. falciparum with Chloroquine resistance:**
  - Artemisinin-based combination therapies (ACTs), Atovaquone-proguanil, Quinine (Plus Doxycycline or Clindamycin), Mefloquine.
  - Quinine Plus Clindamycin can be given during the 1st trimester, ACT can be given throughout pregnancy.
- **Uncomplicated P. falciparum with Chloroquine sensitivity:**
  - Chloroquine or Hydroxychloroquine (Also safe throughout pregnancy).
- **Non-falciparum malaria without Chloroquine resistance:**
  - ACT or Chloroquine (Also safe throughout pregnancy).
  - Primaquine should also be given to prevent relapse.
  - Chloroquine can be also be given as relapse prevention.
- **Non-falciparum malaria Chloroquine resistance:**
  - Quinine (Plus Doxycycline or Clindamycin), ACT.
  - Quinine Plus Clindamycin can be given during the 1st trimester, ACT can be given throughout pregnancy.
- **Severe Malaria**
  - Hemodynamic instability, pulmonary edema, severe anemia, neurologic deficits, renal failure, hepatic failure.
  - Artesunate or Quinidine (Plus Doxycycline or Clindamycin), ACT Atovaquone-proguanil, Mefloquine.

Conclusion

Obtaining a thorough travel history can provide key information in a case, as it did for this patient. Patients considering travel outside of the US should be counseled regarding mosquito avoidance and be provided with chemoprophylaxis. Diagnosis and treatment often require consultation with an infectious disease specialist, and may require transfer to a tertiary care center.

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