

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Centers for Disease Control and Prevention

Addendum

Splenomegaly in Congolese Refugees from Uganda; clinical guidance on initial management September 10th, 2015

Dear Refugee Clinical Provider,

As noted in the accompanying letter to the State Refugee Health Coordinator, approximately 16% of Congolese refugees originating in Hoima, Uganda have been noted to have splenomegaly. This condition is occurring in all ages. Splenomegaly can result from many different causes. In this case, the etiology has not been determined. Testing is being conducted for other possible etiologies such as schistosomiasis, visceral leishmaniasis and viral hepatitis. However, the most common cause in this setting, and current presumed etiology, is repeated malaria infection. Patients with malaria-associated splenomegaly may not have any other signs or symptoms of malaria, or detectable parasites or antigen in their blood. Symptoms can be variable but most commonly the person experiences abdominal fullness and vague discomfort (particularly with physical activity such as running).Malaria-associated splenomegaly is often self-resolving after malaria treatment and the individual leaves a malaria endemic area. A more severe form of this, termed "hyper-reactive malarial splenomegaly syndrome" (HMS) may occur in some individuals and is believed to be due to an exaggerated immune response associated with recurrent malaria infections, which causes massive splenic enlargement. Complications of HMS may include secondary bacterial infection and hematological abnormalities (e.g. anemia [low red blood cell counts], thrombocytopenia [low platelet counts]). In addition, patients are at risk for splenic rupture especially following abdominal trauma (even minor trauma such as playing soccer). HMS is considered a "diagnosis of exclusion".

Overseas Screening and Testing

Refugees are examined approximately 2-6 months prior to departure ("initial medical exam"). Those who are noted to have an enlarged spleen during this initial examination will be offered additional testing, including malaria testing, and an abdominal ultrasound if they agree to consent (written informed consent will be obtained). At the initial examination, all refugees with splenomegaly who test positive for malaria will be treated for acute malaria per the Uganda guidelines.

 Laboratory tests will be offered—as available will be recorded on the DS 3026 form:

 AST, ALT, Bilirubin, Alkaline phosphatase

 Malaria Microscopy - Thick and Thin Blood Smear microscopy

 Malaria rapid antigen test

 Stool Ova & Parasite (by wet prep, x 3 samples total)

 Urine Ova & Parasite

 Rk39 for Leishmaniasis

 Hepatitis C antibody

 HIV Screening Test

 CBC with differential and platelets

 Virinalysis

 Sickle cell screen

 Malaria IgM serologic testing (will not be complete prior to departure)

Overseas Monitoring Prior to Departure

All persons with splenomegaly detected on initial examination who have no other etiology identified will be considered to have suspect HMS. Refugees with splenomegaly with be monitored prior to departure and will have repeated malaria testing if they have signs or symptoms of malaria infection. Any refugee with a positive malaria test at any point prior to departure will be treated for acute malaria per the Ugandan guidelines (note that this may mean multiple treatments prior to departure). In addition, all Congolese refugees (including those with splenomegaly) will continue to receive pre-departure antimalarial treatment with arthemeter-lumafantrine immediately prior to departure for the U.S. per current guidelines.

Documentation

Available results at the time of departure will be recorded DS 3026 Form (under "other/remarks" section of the Medical History and Physical Examination form). In addition to test results an attempt to include splenic measurements (length, depth, width) and splenic and liver architecture, and still ultrasound photos with measurements, will be included on the DS form (for comparison following arrival).

Domestic follow-up

Although the relapse rate for HMS is high in areas endemic for malaria following treatment, the natural history of the condition in someone who leaves an endemic setting is unknown. It is recommended that all refugees with suspect HMS be offered further diagnostic testing, treatment and ongoing follow-up after arrival in the United States. Recommended initial clinical approach to Congolese refugees with suspect HMS arriving from Uganda are below.

Initial testing and management may include:

- 1. Blood
 - a. Total malaria IgM (these generally decline over time with successful treatment of malaria HMS)
 - b. Repeat hematology (complete CBC with differential) and repeat other testing if abnormal prior to departure (e.g. liver function tests)
 - c. Testing for glucose-6-phosphatase (G6PD) deficiency
- 2. Abdominal ultrasound with a focus on the spleen. Can be used for comparison with pre-departure ultrasound when available (on DS form), and also for ongoing monitoring. With successful treatment this condition generally slowly resolves.

Initial post-arrival treatment:

- 1. Additional malaria treatment.
 - a. A 14-day course of the antimalarial primaquine. Primaquine is used for the dormant phases of malaria that can persist in the liver for months to years, eventually causing relapse. This medication is currently unavailable in Uganda so should be administered following arrival in the U.S.
 - i. PRIOR to primaquine use, a glucose-6-phosphatase (G6PD) level must be checked since primaquine is an oxidizing agent and may trigger a hemolytic anemia in someone with G6PD deficiency. If the G6PD level is normal, and the refugee is not pregnant, the refugee should be treated with a 2-week course of primaquine. CDC recommends a primaquine phosphate dose of 30 mg (base) by mouth daily for 14 days. If the refugee has low G6PD level, or the refugee is pregnant, treatment with primaquine should be withheld until expert consultation is obtained. Additional information on treatment with

primaquine can be found at: <u>http://www.cdc.gov/malaria/diagnosis_treatment/clinicians2.html</u>.

Monitoring and counseling:

Patients should be monitored with routine follow-up every 1-3 months for the first year. Those with signs or symptoms of recurrent malaria, with ongoing splenomegaly, with ongoing complications of splenomegaly (e.g. hematologic abnormalities) should be referred to a specialist. Persons with a large spleen should be reminded not to participate in physical activities that can cause trauma (e.g. soccer)—most individuals in this community know this already.

A representative from the CDC may contact the State/provider requesting follow-up clinical data on specific patients. Technical clinical guidance and questions can be directed to Dr. William Stauffer (<u>stauf005@umn.edu</u>).

Additional recommendations for the monitoring and/or treatment of refugees with malaria-associated splenomegaly *may* follow; if so, states/providers will be notified. Other routine post-arrival guidance for patients without a history of malaria-associated splenomegaly remains unchanged.

Sincerely,

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