Notes from the Field

Splenomegaly of Unknown Etiology in Congolese Refugees Applying for Resettlement to the United States — Uganda, 2015

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Approximately 70,000–90,000 refugees are resettled to the United States each year, and during the next 5 years, 50,000 Congolese refugees are expected to arrive in the United States. The International Organization for Migration (IOM) performs refugee medical examinations overseas for the U.S. Refugee Resettlement Program. In 2014, IOM reported that a large number of U.S.-bound Congolese refugees from Uganda had spleens that were enlarged on examination. During two evaluations of refugee populations in western Uganda in March and July 2015, refugees with splenomegaly on physical examination were offered additional assessment and treatment, including abdominal ultrasonography and laboratory testing. Among 987 persons screened, 145 (14.7%) had splenomegaly and received further testing. Among the 145 patients with splenomegaly, 63.4% were aged 5–17 years (median = 14.8 years). There was some evidence of family clustering, with 33 (22.7%) of the 145 cases occurring in families.

Overall, 144 of the 145 patients had abdominal ultrasonography, 122 (84.7%) of whom had massive splenomegaly (defined as >4 standard deviations above the local mean for splenic size, adjusted for height, based on the World Health Organization ultrasonography protocol) (*1*); 135 (93%) patients had normal liver architecture; and eight (5.5%) had hepatic nodules or masses. Specimens from 39 (26.9%) patients tested positive for malaria using rapid diagnostic testing; thin blood smear tests performed for all 145 cases were negative (thick films were not performed). Specimens from 134 (92.4%) patients were positive for *Plasmodium falciparum* merozoite surface protein 1 immunoglobulin G, indicating past exposure to *P. falciparum*. Specimens from three persons (2.1%) were positive for *Schistosoma mansoni* ova by stool wet preparation; no *Schistosoma* ova were detected in urine specimens. Enzyme-linked immunosorbent assay (rK39 ELISA) tests for infection by *Leishmania* were negative for all patients; however, one (0.7%) patient was positive by serology. Specimens from five (3.5%) patients were positive for hepatitis B surface antigen, and 10 (6.9%) had detectable hepatitis C virus antibodies.

Fewer than 33% of refugees had evidence of an active infection known to cause splenomegaly at the time of assessment (via positive malaria antigen, hepatitis B antigen, or *Schistosoma* ova). Low rates of serologic evidence of past or current leishmaniasis and hepatitis C eliminated these diseases as a common etiology. Although a definitive underlying etiology could not be determined, malaria-associated splenomegaly is one consideration: among potential infectious agents, malaria was the most prevalent, although active infection was found in less than one third of persons with splenomegaly. Malaria-associated splenomegaly is a diagnosis of exclusion and occurs following repeated malaria infections. The condition persists despite the absence of active parasitemia and usually resolves within 6 months after antimalarial treatment if subsequent malaria exposure can be prevented (*2*). Because no alternative diagnosis was identified, and because of the risk for severe sequelae of untreated malaria and the low risk for adverse effects of malaria medications, all refugees with splenomegaly were empirically treated for malaria with artemether-lumefantrine at the time of diagnosis, and were provided with bed nets for further prevention. In addition, all refugees received predeparture artemether-lumefantrine, as routinely administered during IOM predeparture examinations, per CDC recommendations; thus, persons with detectable splenomegaly received two treatment courses for blood-stage malaria infection before departure (*3*). CDC has recommended further laboratory and radiology testing for all refugees with splenomegaly after relocation to the United States, including repeat malaria testing in symptomatic patients (using one or more of the following: thick/thin blood smears, rapid diagnostic test, or malaria polymerase chain reaction testing) and empiric treatment with primaquine (after assuring normal glucose-6-dehydrogenase levels). Testing for additional etiologies of splenomegaly in this population and clinical support to receiving states and providers is ongoing. Because the interval between diagnosis of splenomegaly and departure to the United States was short, only a limited diagnostic and treatment protocol was developed. However, splenomegaly is a challenging clinical entity that appears to be an emerging, highly prevalent condition in Congolese refugees. Further investigation into its etiology and directed management is needed.

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References

1. Akpata R, Neumayr A, Holtfreter MC, et al. The WHO ultrasonography protocol for assessing morbidity due to *Schistosomiasis haematobium*. Acceptance and evolution over 14 years. Systematic review. Parasitol Res 2015;114:1279–89. http://dx.doi.org/10.1007/s00436-015-4389-z
2. Leoni S, Buonfrate D, Angheben A, Gobbi F, Bisoffi Z. The hyper-reactive malarial splenomegaly: a systematic review of the literature. Malar J 2015;14:185. http://dx.doi.org/10.1186/s12936-015-0694-3
3. CDC. Immigrant and refugee health: treatment schedules for presumptive parasite infections. Atlanta, GA: US Department of Health and Human Services, CDC; 2015. http://www.cdc.gov/immigrantrefugeehealth/guidelines/overseas/interventions/interventions.html