Pruritic Rash in a Recent Traveler to Central America

In December 2014, an 18-year-old male presented to Harbor-UCLA Medical Center in Los Angeles, CA with a 3-day history of pruritic, maculopapular rash, which began on the wrists and arms and rapidly spread to the rest of his body, including his palms. Four days before the rash was noted, he had a temperature of 101°F, malaise, myalgia, and polyarthralgia. The arthralgia started in his right wrist, which was swollen but not red. The pain subsequently spread to his other wrist, fingers, and knees in a migratory pattern. He also noted a mild cough, but no congestion, sore throat, conjunctivitis, vomiting, or diarrhea. He reported intermittent generalized headaches, but he denied confusion, irritability, weakness, or abnormal movements. Over the past week of symptoms, his joint pain and headache had subsided substantially, but the itchy rash persisted.

The patient’s symptoms began 2 days after he had returned from an 8-day visit to El Salvador. In El Salvador, he stayed in a rural area of the city of Santa Ana in the northwestern part of the country. While there, he swam in a nearby river and hiked, sustaining many mosquito bites on his legs without other known insect or tick bites. He did not have direct contact with animals, but there was a barn with cows across from his house. He denied consuming unpasteurized dairy products and undercooked meats. He did not receive any travel-specific vaccinations or take malaria prophylaxis. None of his family members in El Salvador were ill. The patient otherwise had no past medical history. He was born in Los Angeles and lived there all his life. His only other travel was to El Salvador 4 years ago. He had had 4 lifetime sex partners (all female) with inconsistent condom use. His routine immunizations were appropriate for age.

Physical examination revealed a well appearing and cooperative young man with vital signs as listed: temperature 36.9°C, heart rate 89 beats/minute, respiratory rate 16 breaths/minute, and blood pressure 121/79 mm Hg. A diffuse, blanching, morbilliform rash was present on his chest, abdomen, and back, most prominently seen on his upper and lower extremities, excluding the palms and soles (Figure 1). There were few petechiae on his soft palate and right shoulder. He had mild, generalized swelling of his face and lips. He had a single 1 x 1 centimeter, rubbery, tender lymph node in each inguinal region bilaterally. There was no edema, erythema, or tenderness of his joints, and he had full active and passive range of motion. The rest of his examination was unremarkable.

Initial laboratory results were as follows: total white blood cell count 5200/mm³, with a differential of 68% neutrophils, 14% lymphocytes, 10% monocytes, and 7% eosinophils; hemoglobin 16.1 g/dL; hematocrit 46.9%; platelet count 138 000/mm³; and serum electrolytes, hepatic transaminases, and coagulation studies all within normal limits. The urinalysis was normal, and a rapid human immunodeficiency virus serologic test was negative.

The Pediatric Infectious Diseases Consultants who saw this patient were asked the following questions:

- What is the differential diagnosis for fever and rash in this young man with the travel history and extensive exposures?
- What empiric therapy do you recommend?
- What diagnostic testing should be performed?
Chikungunya Virus Fever in a Recent Traveler

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Received February 6, 2015; accepted February 17, 2015; electronically published March 24, 2015.

Differential diagnosis. Given the patient’s travel history and extensive exposure to mosquitoes—and the general wisdom of Occam’s razor—infection with dengue virus or chikungunya virus (CHIKV) seemed most likely to explain the fever, rash, polyarthralgia, lymphopenia, and mild thrombocytopenia. Both viruses are prevalent in El Salvador. However, infection with either typhus or spotted fever group rickettsia (prevalent in Central America) also could have explained the headache, fever, and generalized rash. Other diagnostic possibilities consistent with some, but not all, of the clinical picture included measles, rubella, leptospirosis, infection with Epstein-Barr virus, enterovirus, or parvovirus B19, and syphilis.

Empiric therapy. The patient was admitted to the hospital and given doxycycline for empiric treatment of rickettsial infections; leptospirosis might also have benefited from this treatment.

Diagnostic testing. Blood cultures were negative. Serologic studies (IgG and IgM) for dengue virus, Rickettsia rickettsii, Rickettsia typhi, Rickettsia prowazekii, and Leptospira (total antibody), were obtained and returned negative. Heterophile antibodies and the rapid plasma reagin test were negative, as was a serum polymerase chain reaction (PCR) assay for parvovirus B19 DNA. A serum PCR test for CHIKV was negative, as was an assay for serum IgG antibodies against CHIKV. However, a serum CHIKV IgM antibody assay was positive at a titer of 1:160 (reference range >1:10, performed at Focus Diagnostics, San Capistrano, CA).

Chikungunya fever is a mosquito-borne illness caused by chikungunya virus (CHIKV), an alphavirus that is part of the Togaviridae family. Chikungunya virus was first isolated in 1952 in Tanzania, and it occurred in sporadic outbreaks in Africa, India, and Southeast Asia until recently. The virus re-emerged in 2004 in countries around the Indian Ocean, causing widespread disease [1–3]. Since then, it has become pandemic, with outbreaks in Asia and Europe before reaching the Americas in 2013. Multiple cases have been reported in the United States from returned travelers, with Florida being the only state with locally transmitted cases [4]. El Salvador first reported local cases in June 2014, and as of December 2014 it has had over 130,000 suspected cases [5].

The virus is spread by the Aedes aegypti and Aedes albopictus mosquito. It has been proposed that a genetic mutation leading to increased susceptibility of A albopictus to CHIKV has contributed to the rapid global spread of the disease [6]. The incubation period is usually 3 to 6 days (range 1 to 12 days). Clinical features include abrupt onset of fever, polyarthralgia, headache, and back pain. The rash is diffuse, macular or maculopapular, mostly on the trunk or extremities, and may be pruritic, as in our patient. Diarrhea, abdominal pain, and vomiting may also be present. Laboratory findings are nonspecific, but lymphopenia and hypocalcemia occur in up to 79% and 55%, respectively. Chikungunya fever is difficult to distinguish from the early stage of dengue fever. However, arthralgia is much more prominent in chikungunya fever, whereas thrombocytopenia, leukopenia, neutropenia, and shock are more commonly associated with dengue fever. Indeed, chikungunya means “to be bent over” in an east African Bantu dialect. Death is rare with chikungunya fever except for neonates exposed in the intrapartum period, individuals older than 65 years, and patients with chronic conditions such as cardiovascular disease and diabetes mellitus, with an estimated case-fatality rate of 1 of 1000 cases [1, 7, 8]. The acute illness lasts 7 to 10 days, but more than half of patients report chronic joint pain months to years afterwards, oftentimes severe enough to interfere with daily activities [8].

Diagnostic testing for CHIKV includes isolation in culture (in the first 3 days of illness), detection of RNA (first 5 days), or antibodies via enzyme-linked immunosorbent assays or immunofluorescence assay. Immunoglobulin (Ig)M typically appears by day 5 and can last for several months, whereas IgG usually appears shortly after and may persist for years [9]. Treatment for chikungunya
fever is supportive. Several compounds have been tested as antivirals in in vitro and experimental animal models with varying results; very few human data are available [2]. Mosquito avoidance is still the mainstay of disease prevention. Since its first introduction to the western hemisphere in December 2013, chikungunya fever has become established in the Americas. It should be considered in the differential diagnosis for any traveler returning from affected countries with fever, rash, and joint pain.

**Denouement and Course.** *Chikungunya virus fever, acquired in El Salvador.* After hospitalization, the patient remained afebrile, and by the next morning his myalgia and arthralgia improved substantially, as well as the facial and lip swelling. His rash was unchanged. The doxycycline was continued at discharge, because the serologic tests had not yet returned. Unfortunately, he did not return for a follow-up visit, which might have demonstrated seroconversion of CHIKV IgG antibodies.

**References**