

Rapidly Evolving Outbreak of a Febrile Illness in Rural Haiti: The Importance of a Field Diagnosis of Chikungunya Virus in Remote Locations

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Abstract

Although rarely fatal, chikungunya virus (CHIKV) infection can lead to chronic debilitating sequelae. We describe the outbreak of suspected CHIKV in 93 subjects who presented voluntarily over 2 months to a remote rural Haitian general medical clinic staffed by international health care providers. Diagnosis was made on clinical signs and symptoms because no serum analysis was available in this remote rural site. The subjects were 18.0 ± 16.2 (median \pm standard deviation) years of age and were of similar gender distribution. The presenting vital signs included a temperature of $102.3^\circ\text{F} \pm 0.6^\circ\text{F}$ with fever lasting for 3.0 ± 0.7 days. Symptoms mainly consisted of symmetrical polyarthralgias in 82.8%, headache in 28.0%, abdominal pain in 17.2%, cough in 8.6%, maculopapular rash in 30.0%, and extremity bullae in 12.9%. In 84.9% of subjects, symptoms persisted for 7.1 ± 8.3 days with 16.1% having ongoing disability due to persistent pain (≥ 14 days duration). There were no deaths. In Haiti, especially in remote, rural regions, the risk for CHIKV spread is high given the shortage of detection methods and treatment in this tropical climate and the lack of preventative efforts underway. Implications for global public health are likely, with outbreak expansion and spread to neighboring countries, including the United States.

Key Words: Vector borne—Epidemic—Mosquito—Chikungunya virus—Field diagnosis—Haiti.

Introduction

CHIKUNGYA VIRUS (CHIKV), from the family Toga-
viridae and genus *Alphavirus*, is a single-stranded
positive-sense RNA arbovirus with an icosahedral capsid
and lipid envelope that is spread by the *Aedes* mosquito
(Thiberville et al. 2013b). CHIKV has been an emerging
concern in the Americas since the first documented case of
autochthonous transmission in the Caribbean in December of
2013. Since then, the virus has spread to South America and
throughout the Caribbean, with more than 700,000 suspected
autochthonous cases, more than 10,000 confirmed cases, and
now 11 confirmed autochthonous cases in the United States
(Caribbean Public Health Agency 2014b). Although the virus
garnered interest in the 1960s and 1970s following its dis-
covery in Tanzania in 1952, without documented autoch-
thonous cases outside of endemic regions, interest dwindled

until the recent outbreaks beginning in 2004 (Thiberville
et al. 2013b). With a recently documented case of autoch-
thonous transmission in Florida, local spread of the virus in
the United States is likely to continue and increase public
awareness of the virus (Centers for Disease Control and
Prevention 2014, Pan American Health Organization/World
Health Organization 2014). *Aedes aegypti* and *Aedes albo-*
pictus, the known vectors for CHIKV, have been documented
in Haiti (Fernandez et al. 2012, McAllister et al. 2012). The
presence of CHIKV in Haiti further adds to the arthropod-
borne diseases already prevalent in the region.

Without definitive diagnosis of CHIKV viremia by PCR,
seroconversion, viral isolation, or antibody tests, suspected
cases are defined by a clinical syndrome of high fever
($>38.5^\circ\text{C}$) with severe arthritis or arthralgias in the absence
of other potential causative etiologies and usually appear
approximately 2–7 days after infection (Thiberville et al.

2013b, Pan American Health Organization/World Health Organization 2014). Patients with CHIKV have a higher propensity than other arbovirus-infected patients to seek medical care due to the disabling nature of the symptomatology (Thiberville et al. 2013a, b). Following acute infection, common manifestations of CHIKV include polyarthralgias in a peripheral bilateral distribution, as well as headache, myalgias, conjunctivitis, nausea, vomiting, and maculopapular rash. There is also a high incidence of lymphopenia in presenting patients, as well as other nonspecific laboratory findings, such as thrombocytopenia, elevated C-reactive protein, and hepatic transaminases (Mirabel et al. 2007). The disease is usually self-limiting and typically shows resolution of symptoms within a week. Although rarely fatal, CHIKV infection can lead to chronic debilitating sequelae and severe manifestations, such as severe arthralgia, atypical neurologic symptoms, retinitis, hepatitis, nephritis, and/ or meningitis (Mirabel et al. 2007, Mahendradas et al. 2008, Rajapakse et al. 2010, Simon et al. 2011, Nair et al. 2012, Thiberville et al. 2013a, b). There have been 14 confirmed cases in Haiti at the time of this outbreak description; however, without the ability to diagnose CHIKV definitively, the overwhelming majority are diagnosed clinically on the basis of the suspected syndrome criteria (Caribbean Public Health Agency 2014b, Pan American Health Organization/World Health Organization 2014). There are currently no effective vaccines or definitive treatments for CHIKV; therefore, care for presumed cases is limited to supportive measures (Thiberville et al. 2013b).

The first confirmed cases of CHIKV on Hispaniola, in the Dominican Republic, were in April, 2014 (Caribbean Public Health Agency 2014a). The exact date that CHIKV spread to Haiti is confounded by the lack of testing and health statistics available for this country, as well as lack of access to health care facilities. Also known as *Kase Le Zo* in Haitian Creole (kreyòl ayisyen), or “break the bones,” CHIKV has spread rapidly and added further to the chronic disease burden that exists in Haiti. We describe the presentation of suspected cases of CHIKV infection diagnosed via patient presentation and symptom manifestation and duration at a remote outpatient rural health clinic over a 2-month period.

Materials and Methods

Study location and participants

This retrospective study was approved by the Texas A&M University Institutional Review Board. Data used were collected during a suspected outbreak of CHIKV in a remote rural Haitian general medical clinic staffed by international health care providers. Participating medical teams consisted of physicians, physician assistants, nurse practitioners, and registered nurses who received 2 h of general training in tropical medicine and local medical issues, including management of CHIKV. The evaluation and treatment of subjects took place at the LiveBeyond Medical Clinic, located in the Ouest Province in the arrondissement of Thomazeau, approximately 40 km northeast of Port-au-Prince. The surrounding rural area is a poor agrarian society with little to no access to medical care (except for this medical clinic), food, security, or clean water. This region has an approximate population of 300,000 persons, although exact census data are not available.

Subjects from the surrounding areas presented voluntarily to the clinic over a 2-month time frame. The index case was seen on May 22, 2014, and the last case seen during data collection on July 21, 2014. A standard clinical history was obtained and physical parameters were measured, including height or length, weight, and temperature. Blood pressure was measured in nonpregnant subjects over 18 years of age. The subjects were referred to our medical teams for further evaluation. Patients were followed from presentation to clinic until August 9, 2014, at 1-week intervals.

Diagnosis and treatment

A medical doctor or nurse practitioner licensed in the United States and working directly under the supervision of the clinic medical director (a medical doctor who is licensed in both the United States and Haiti and is based in Thomazeau, Haiti) examined each subject. A symptom-specific history and physical exam were performed on each patient, and a diagnosis was determined and recorded in the medical record. The patients were treated on an outpatient basis and were followed at 1-week intervals and their symptoms recorded. The charts were reviewed for completion and analyzed by the medical team.

Diagnosis of CHIKV infection was made on clinical signs and symptoms because no serum analysis is currently available in this remote rural site. Fever and polyarthralgia have been shown to be the strongest clinical indicators of CHIKV infection, with a sensitivity and specificity of 84% (95% confidence interval [CI] 79–87%) and 89% (95% CI 86–91%), respectively, during a 2006 outbreak of the East–Central–South African lineage rather than the Asian lineage responsible for the current Caribbean outbreak (Sissoko et al. 2010, Gallian et al. 2014, Leparc-Goffart 2014, Mowatt et al. 2014). There is potential for different sensitivities and specificities accounting for the different genotype and population and the potential for other endemic arboviruses to mimic CHIKV (Sissoko et al. 2010). But with the published precision of clinical diagnosis alone (Sissoko et al. 2010), barring other co-infections, field diagnosis was considered to be accurate. In remote and rural conditions, with high levels of mosquito infestation, CHIKV and dengue fever must be prominent in the differential diagnosis list.

Dengue virus is endemic to Haiti, and its symptoms can closely mimic those of CHIKV (Halstead et al. 2001, Anderson et al. 2011, Rieth et al. 2011, World Health Organization 2014). Due to the lack of definitive diagnosis through serological testing, the possibility of co-infection with both dengue fever and CHIKV secondary to the presence of *A. aegypti*, and increased bleeding risk with dengue fever, treatment was limited to pain management, mainly with acetaminophen as well as supportive measures (Kalawat et al. 2011, Fernandez et al. 2012, McAllister et al. 2012, World Health Organization 2014). Adults were treated with 500 mg of acetaminophen as needed for pain and fever. Children were treated with 10 mg/kg acetaminophen as needed for pain and fever greater than 101.8°F. Persistent, lingering symptoms were treated similarly. Pediatric patients did not have the persistent symptoms resulting in disability that adults experienced. Patients were counseled to stay adequately hydrated and rest as much as possible; they received education on preventative measures to prevent mosquito bite exposure.

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Results

T1 ▶ An analysis was performed of 93 subjects (5.3% of total persons seen in clinic) presenting with symptomatology consistent with CHIKV infection. Descriptive data are presented in Table 1. The subjects were an average of 21.8 ± 16.2 years of age (range 0–65 years; median 18 years) and were of similar gender distribution. The presenting vitals included a temperature of $102.3^\circ\text{F} \pm 0.6^\circ\text{F}$ and body mass index (BMI; weight/height²) of 19.0 ± 4.8 . At the initial presentation, symptoms had been present for 2.0 ± 0.6 days and included moderate to severe symmetrical polyarthralgias and swollen joints (see Fig. 1) in 82.8%, headache in 28.0%, abdominal pain in 17.2%, cough in 8.6%, maculopapular rash in 30.0%, and bullae on the hands or feet in 12.9%. Interestingly, all bullae occurred on children under the age of 10 years (range 0–8 years of age). Fever lasted for 3.0 ± 0.7 days. In 84.9% of subjects, symptoms persisted for 7.1 ± 8.3 days (range 3–30 days), with 16.1% being defined as having persistent symptomatology (≥ 14 days duration). There were no deaths during the data collection period.

F1 ▶

Discussion

Demographics

Tropical infections such as CHIKV, malaria, typhoid, and dengue fever all present as febrile illnesses. We acknowledge that differentiating between the diseases may be difficult without laboratory diagnosis. However, with the recent spread of confirmed CHIKV demonstrating the globalization of infectious diseases and the lack of laboratory diagnosis in remote regions of Haiti, it is vital that practitioners be knowledgeable of the disease characteristics and treatment options, as well as the possibility of chronic disabling symptoms. CHIKV can be differentiated from other febrile illnesses, often based upon symptomatology in that the pain is more intense and concentrated in a bilateral distribution in the joints.

CHIKV affects all ages and both genders with similar distributions. Multiple outbreaks have been described in the literature, and the series presented herein is comparable. However, the location of the disease outbreak in a very impoverished nation with a marginal chance for laboratory diagnosis or future treatment is a cause for concern. The prevalence was 5.3% among the patients in this study, and all diagnoses were made by clinical means with physical exam and presenting symptoms in the absence of costly laboratory confirmation. We acknowledge the possibility of inaccuracy



FIG. 1. Painful swollen knee in a male with clinically diagnosed chikungunya infection.

of field diagnosis alone. However, without serum confirmation and with similarity of cases, prompt recognition and treatment as well as follow-up were prudent and instituted. The relatively low prevalence in this cohort may exist due to health care access barriers or perhaps is secondary to symptoms existence, making it challenging for persons to travel to our health care facility. Also concerning is the lack of preventative efforts underway in Haiti and the rapid manner in which the virus has spread throughout the region in a short time period (Caribbean Public Health Agency 2014b, Mowatt et al. 2014, Pan American Health Organization/World Health Organization 2014). Furthermore, it is difficult to know how many persons in the regions may have been symptomatic and not seen at the clinic.

Currently there is no vaccine to prevent possible CHIKV infection. Chronic recurring arthralgia or musculoskeletal pains may occur with a corresponding decrease in quality of life and thus limit a parent or guardian's ability to provide for the family. Preventative measures include removing sources of standing water, using insect repellent, and using window and door screens to prevent mosquito entry (Gibney et al. 2011, Powers 2015). However, these measures have not been found to be widely implemented in the Thomazeau region.

Most patients presented soon after fever onset, and none were referred to a distant hospital. Studies have documented the acute onset ranging from 2 to 7 days after the infective mosquito bite (Pan American Health Organization/World Health Organization 2014, Thiberville et al. 2013a, b). Also described has been a group of persons who have

TABLE 1. DEMOGRAPHICS OF PATIENT COHORT

	(n = 93)
Mean age (years)	18.0 ± 16.2
Temperature ($^\circ\text{F}$)	102.3 ± 0.6
Body mass index	19.0 ± 4.8
Number of days with symptoms	7.1 ± 8.3
Polyarthralgias	82.8%
Headache	28.0%
Abdominal pain	17.2%
Maculopapular rash	30.0%
Bullae on hands and feet	12.9%

Median \pm standard deviation or percent.

asymptomatic disease, ranging from 5% to 10% of those with serum documentation. Unfortunately, this region in Haiti has no way of knowing the actual numbers of those with possible CHIKV infection, symptomatic or asymptomatic, due to lack of reporting standards, centralized data collection, or serum analysis. High fever and symmetric musculoskeletal symptoms that are progressive, indicative of probable CHIKV infection, were common in this cohort. Peripheral joints are usually swollen with pain occurring with both passive and active range of motion. Inflammatory joint effusions have also been described. Attention should also be given to bullae that appear on the extremities, particularly in young children. The diagnosis of CHIKV should be considered. No current treatment exists beyond pain medication and nonsteroidal anti-inflammatory agents. This clinic chose to give acetaminophen to affected individuals to avoid any potential bleeding risk, which could occur with aspirin.

Impact

The most common presentations in this cohort were febrile polyarthralgia or very high fever alone. The risk of a chronic debilitating arthralgia could potentially pose a further economic burden on an already impoverished Haitian economy. Infectious diseases in the developing world are predominant factors for poor health status and poverty. The recent CHIKV epidemic most likely has negatively impacted the working population, and therefore it is imperative to continue efforts aimed at diagnosing, controlling, and educating the general public on febrile illnesses, including CHIKV. Education of the surrounding population on signs and symptoms as well preventative measures will be imperative. Furthermore, the CHIKV epidemic has not been limited to Haiti. Autochthonous cases have been documented in the United States as well as imported cases from tourists, missionaries, and aid workers.

There are several limitations to this study. First, this is a retrospective chart review with its inherent limitations, particularly with the language and education barrier. Second, the lack of definitive serological testing adds a large potential for confirmation bias and misidentification, especially with other endemic illnesses having similar presentation (*e.g.*, dengue fever). Third, there is a limitation in evaluating chronic sequelae in the relatively short follow-up times for the patients that presented near the end of the data collection period.

Conclusions

This cohort highlights the importance of clinical diagnosis of CHIKV infection in remote field conditions. The clinical features described herein of polyarthralgia, especially when combined with fever, are reasonable for a field diagnosis of CHIKV in the absence of serological testing. Patients with a presumptive diagnosis should be followed for development of chronic recurring and disabling arthralgias. Persistent disabling symptoms may lead to devastating economic impact in an impoverished society. Developing countries with lacking health care infrastructure have difficulties coping with high caseloads, which highlights the need for surveillance, vector control, laboratory confirmation, and communication, none of which have been readily available. International health care providers need to heed preventative measures to avoid international importation of CHIKV.

Author Disclosure Statement

No competing financial interests exist.

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AU1: —do you mean “dissemination” rather than “importation”?