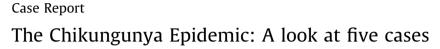
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ABSTRACT

Chikungunya is an infection caused by the Chikungunya virus and transmitted by the bite of infected mosquito. The most common symptoms of Chikungunya virus infection are fever, joint pain or rash. Chikungunya virus outbreaks had been identified in countries in Africa, Asia, Europe, and the Indian and Pacific Oceans. In late 2013, the first local transmission of Chikungunya virus in the Americas was identified in Caribbean countries and territories. Chikungunya virus disease became a nationally notifiable condition in 2015. There is a threat that Chikungunya will continue to spread to new areas in the Americas.

We describe 5 patients who presented to our hospital with Chikungunya infection, shortly after returning from endemic areas. Fever and travel history to endemic areas were documented in all of our cases. Skin rash, arthralgia and contact history were also reported by these patients. Persons with suspected Chikungunya infection should be counseled to avoid mosquito bites during illness to decrease the risk of local transmission. The transmitting mosquitos are present in the US, and limiting the viral spread is essential. In this report, we describe the clinical presentation, risk factors and laboratory tests of each patient, and attempt to ensure awareness on the risk of potential spread of the disease. © 2015 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND

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Introduction

Chikungunya, originally endemic to West Africa, is an arthropod-borne virus (arbovirus). The virus is closely related to o'nyong'nyong virus. The disease was first described by Marion Robinson and W.H.R. Lumsden in 1955, following an outbreak in 1952 on the Makonde Plateau, Tanzania. The disease Chikungunya disease manifests as acute onset of fever, muscle and joint pains, and frequently nonspecific maculopapular rash [1]. The case fatality ratio is about 1 per 1000, with most deaths occurring among newborns, the elderly, and the debilitated [1].

Since 2004, Chikungunya has spread broadly, causing massive and sustained outbreaks in Asia and Africa [2]. In 2013, Chikungunya virus infections have spread widely in the Americas [3]. As of December 2014, local transmission had been identified in 41 countries or territories in the Caribbean, Central America, South America, or North America. A total of 1,012,347 suspected and

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22,579 laboratory-confirmed Chikungunya cases had been reported from these areas [4].

The virus is transmitted by the bites of infected mosquitos *Aedes aegypti* (Yellow fever mosquito) and *Aedes albopictus* (Asian tiger mosquito), both present in the Americas. Chikungunya virus likely will continue to spread to new areas in the Americas through infected people and mosquitoes. Increasing number of cases has been identified in travelers returning from outbreak areas [5]. Therefore this case report reviews 5 cases of Chikungunya, who presented to our hospital shortly after returning from abroad, in attempt to ensure awareness on the risk of potential spread of the disease.

Case presentation

Case 1

A 36 year old female presented to the ER on October 28th, 2014 with subjective fever and generalized bone, joint and muscle pain of 8 days. The patient recently returned from El Salvador (8 days ago). She had a rash over both lower extremities which has now resolved. She gave a history of multiple sick contacts with people who had similar symptoms. Patient had a temperature of

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101.2 °F on admission. The patient was admitted for febrile illness and started with antibiotics and supportive care. She tested positive for Chikungunya ELISA test. All other investigations were negative. The patient became asymptomatic in few days and was discharged. The patient was followed in the clinic the following month, at which time she did not have any fever, joint pain or rash.

Case 2

A 50 year old male presented on July 26th, 2014 with fever of 2– 3 days after returning from Haiti. He developed rash on the feet which spread toward the trunk. The patient complained of chills, arthralgia and myalgia. On the day of admission, he developed bullous lesions on his feet. The patient had a sick contact (girlfriend) in Haiti who also had fever. The patient had maculopapular rash over all the four extremities sparing the palms and soles with intact bullous lesions on both feet. The patient was admitted for further work up, started on antibiotics and IV hydration. Basic Laboratory workup was within normal limits. The patient's symptoms improved during his stay in the hospital and he was discharged home. The patient's serology came back positive for Chikungunya antibodies.

Case 3

A 65 year old Haitian female presented to the ER on July 31st, 2014 with generalized muscle aches, joint pain, and neck pain. Her symptoms had been present for few days. The patient had fever while in Haiti but this resolved before returning to the U.S. The patient denied any other complaint. Physical exam was unremarkable except for tender limb muscles and paraspinal muscles of neck. There were no meningeal signs. Viral syndrome was suspected, so supportive management was started with fluids and analgesics. Serology sent for Chikungunya was positive. The patient improved clinically while in the hospital and discharged symptoms free.

Case 4

A 14 year old female patient, previously healthy, admitted with abnormal behavior of 1 day duration on August 28th, 2014. The patient had traveled to Dominican Republic and returned to the US after staying there for 7 weeks. She developed acute behavioral changes: disorganized slow speech and abnormal thoughts. She had fever and chills. Her parents gave history of diffuse skin rash (red dots) on chest, back, abdomen, arms and legs. The patient had a history of contact with Chikungunya patients (her father and sister). On admission, she was conscious but with slow responses and disorganized speech. The remaining neurology exam was unremarkable. The patient was started on antiviral for possible viral encephalopathy. Investigations including toxicology, viral/ bacterial cultures, spinal tap, EEG and CT/MRI of brain were negative. The patient tested positive for Chikungunya and Dengue antibodies. The patient improved clinically while in the hospital and was discharged with out-patient appointment.

Case 5

A 45 year old male presented to the ER on October 3rd, 2014 complaining of fever and rash. The patient came from El Salvador 5 days ago and started experiencing fevers that persisted for 3 days after arrival. T_{max} was noted to be 102.2 °F. Three days after arrival, the patient developed rash on both upper and lower extremities, which then rapidly spread to the rest of his body. The patient also experienced arthralgia and myalgia. He reported multiple mosquito bites. On admission, patient was noted to have

diffuse maculopapular erythematous rash on the trunk and all extremities sparing palms and soles. The patient was started on supportive treatment. The patient's symptoms improved and he remained afebrile throughout his hospital course. Serum test for Chikungunya and Dengue were not sent. Based on his fever, arthralgia, rash and his recent visit to epidemic area, we strongly believe that this was a case of Chikungunya fever. The patient meets the clinical and epidemiological criteria for a probable case of Chikungunya infection [3].

Discussion

Chikungunya infection presents with abrupt febrile episodes and malaise, following an incubation period of 2–4 days [6]. All our patients presented with subjective or recorded fever, indicating that fever is the most prominent presentation of the disease. Polyarthralgia begins few days after the onset of fever, and commonly involves multiple joints symmetrically [7]. Four of our cases had associated arthralgia involving multiple joints. These resolved over time with no long term complications.

Skin involvement such as macular or maculopapular rash (starts usually 3 days after the onset of illness and lasts 3–7 days). Rash has been reported in 40–75% of patients [8]. This usually starts on the limbs and trunk, and may be patchy or diffuse. Two of the cases had history of skin rash but not noted on admission, signifying late presentation of these cases. Two of the patients had skin lesion on admission which was maculopapular rash over the extremities indicating typical presentation for Chikungunya.

Recent Chikungunya infection has been associated with neurological complications. Encephalitis is the most common neurologic complication [9]. There are no residual sequelae. One of the cases presented with altered mental status, for which work up was negative except for Chikungunya and Dengue serology. Although an atypical presentation, Chikungunya should be considered as one of the possibilities for patients presenting with altered mental status.

Chikungunya, being a viral infection, causes leucopenia or lymphopenia. Only one of our cases presented with low WBC count. The same patient also had thrombocytopenia, which is unusual for Chikungunya (Table 1). Travel history to endemic areas of the Caribbean and Latin America was documented in all of our cases. Therefore clinicians should be aware of potential Chikungunya infection in travelers returning from endemic or outbreak areas, and presenting with fever.

It is also important to consider co-infections with Dengue. One of our cases had co-infection with Chikungunya and Dengue. Both viruses are transmitted by same *Aedes* genus and both can occur in many regions due to climatic changes. The clinical presentation of both arthropod borne diseases are similar [10]. Differentiating between the two is a clinical challenge. The distinguishing feature is joint pain which is prominent in Chikungunya infection.

Serology is the primary diagnostic tool. Immunoglobulin M (IgM) anti-Chikungunya virus antibiodies can be detected starting about 5 days following the onset of symptoms. IgM usually persists for several weeks to 3 months, whereas Immunoglobulin G (IgG) antibodies begin to appear about 2 weeks following the onset of symptoms and can persist for years [13]. Four cases tested positive to both Chikungunya antibodies IgM and IgG with higher titer for IgM indicating a recent infection.

Treatment is mainly supportive. Anti-inflammatory and analgesic agents are used to relieve symptoms. There are no studies confirming the efficacy of antiviral agents in human infection, although ribavirin and interferon-alpha appear to have some in vitro activity against viral replication [14]. Our patients were started empirically on antibiotics for possible infections but the

Table 1

Characteristics of 5 cases based on clinical presentation and risk factors.

Characteristics	Case 1	Case 2	Case 3	Case 4	Case 5
Fever	+	+	+	+	+
Joint pain	+	+	+	_	+
Skin rash	+	+	_	+	+
Travel history to endemic area	El Salvador	Haiti	Haiti	Dominican Republic	El Salvador
Contact history	+	+	_	+	_
White blood cells (cells/mm ³)	3800	6630	6630	13,720	6730
Platelet (cells/mm ³) Chikungunya antibodies (titers)	(N: 73%, L: 10%) 91,000 IgM (1:1280) IgG (1:640)	(N:84% L:11%) 192,000 IgM (1:640) IgG (1:640)	(N: 55%, L: 37%) 319,000 IgM (1:1280) IgG (1:320)	(N: 78%, L: 15%) 345,000 IgM (1:640) IgG (1:1280)	(N: 79%, L:9%) 300,000 unavailable
Co infection with Chikungunya and Dengue	_	_	unknown	+	unknown

This table illustrates the similarity and difference among the cases, based on different characteristics. These characteristics were extracted from the WHO proposed case definition of Chikungunya including the different criteria for diagnosis.

(+) indicates that the specific character is present. (-) indicates that the specific character is absent. (unknown) indicates that there is no evidence available to document as either.

N: neutrophils (in percent) and L: lymphocytes (in percent).

ELISA test for Chikungunya antibodies detected IgM (Immunoglobulin M) and IgG (Immunoglobulin G). Reference range is negative for IgM and IgG. In the table, the antibodies are reported in titers.

Case 2 and 3 were screened for Malaria and results were negative.

antibiotics were de-escalated as the earliest. All received supportive treatment to which they responded. This experience highlights the need for more awareness about the disease and avoiding unnecessary interventions.

Some risk exists that Chikungunya might be introduced into previously non-endemic areas by travelers with viremia, leading to local transmission of the virus, especially in tropical or subtropical areas of the United States [11]. Persons with suspected Chikungunya infection should be counseled to avoid mosquito bites during the first week of illness to decrease the risk of local transmission [5]. We would like to emphasize on the potentials of local transmission, as the mosquito (*A. albopictus*) is reported to be found in central and eastern regions of the U.S., including New York [12]. The likely danger of spreading the mosquitoes from endemic area by means of aircraft should also be investigated, as this was a recognized mechanism for "airport malaria" cases [15].

Chikungunya fever is a mosquito-borne infection for which no licensed vaccine is currently available [16]. Therefore, prevention recommendations for travelers to endemic areas should emphasize on mosquito repellent and avoidance measures like mosquito nets, long pants and sleeves. It is important for providers to give preventive information to their patients traveling to endemic areas.

Conclusion

Chikungunya disease should be considered as one of the differential diagnoses when a traveler returns from an endemic area with fever, rash, arthralgia, or a combination of these symptoms. The increased frequency of individuals traveling around the world, increased incidence of the disease and the presence of mosquitos in the Americas is a major concern for possible outbreaks in the western hemisphere. Clinicians and public health officials should be cautious of the possibility of local transmission of Chikungunya virus. The importance of educating the public and bringing awareness to the health care providers should be emphasized.

Conflict of interests

The authors declare that there is no conflict of interests regarding the publication of this article.

Consent

Written consent was not obtained from the patients but no identifying information or images were used in this case report.

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