

Diagnostic challenges in chikungunya infection: Report of an atypical presentation

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Abstract

Due in part to increasing global travel, chikungunya fever has emerged as a significant public health concern. With recent outbreaks in Caribbean nations and the first report of locally acquired infection in the United States, there is concern that we may see an increasing number of cases in Canada. As chikungunya fever shares many clinical similarities to other arthropod-borne illnesses such as dengue fever, clinical diagnosis is challenging. We report an atypical presentation of acute chikungunya fever in a man returning from travel to Haiti. Microbiologic diagnosis, treatment, prognosis, and public health implications will aid clinician preparedness for this emerging pathogen.

Introduction

Chikungunya is a mosquito-borne viral disease increasingly recognized globally as an emerging pathogen. In December 2013, local transmission of chikungunya virus was reported for the first time in the Americas, leading the Public Health Agency of Canada (PHAC) to alert clinicians and public health personnel to the possibility of chikungunya in returning travellers presenting with fever and polyarthralgia (1). A recent report from the United States Centers for Disease Control and Prevention (CDC) has identified 25 Caribbean countries with reported cases of autochthonous chikungunya infection (2). In this article, we report an atypical case of chikungunya infection in a traveller returning from Haiti, to highlight clinical features shared by chikungunya and other arthropod-borne infections such as dengue, the important diagnostic tools available to clinicians, and to address concerns around global spread of chikungunya infection.

Background

Chikungunya infection is caused by an alphavirus of the *Togaviridae* family, and is transmitted primarily by *Aedes aegypti* mosquitoes, and to a lesser extent, *Aedes albopictus* (3).

Chikungunya virus was first described in Tanzania in 1953 (4) and is considered endemic to parts of West Africa. As of September 2014, there were 88 countries reporting transmission of chikungunya infection, including those in Africa, Europe, Oceania, Asia and, most recently, the Americas (5). The first autochthonous infection with chikungunya in a temperate region occurred in Italy in 2007 with a suspected index case originating in India (6). The suspected vector, *Aedes albopictus*, was thought to have acquired a genetic mutation due to ecological pressure allowing it to supplement *Aedes aegypti* as a primary vector (3). As *Aedes albopictus* is widespread in the southeastern United States, there is growing concern about local transmission in these states. In fact, the first case of locally acquired chikungunya infection in the United States was recently reported in a man from Florida (7). Transmission is not expected to occur in Canada, as the *Aedes* mosquitoes are not found in this climate region (1).

In most cases, the presenting symptom is a disabling symmetrical polyarthralgia associated with fever (8). Common joints involved include the ankles, knees, metacarpophalangeal joints, metatarsal joints, shoulders, elbows, and wrists. In approximately one third of patients, joints can be swollen, although effusive arthritis is rare

(8). Following a period of one to three days, there is often development of a diffuse maculopapular rash, usually sparing the face. Arthralgias typically resolve over weeks; however, in many cases, they can persist for months or even years, often having a significant impact on patient quality of life (9).

Clinical diagnosis is challenging as the signs and symptoms of chikungunya overlap with other illnesses, such as parvovirus B19 infection and dengue fever. Microbiologic confirmation is required, and is usually made through detection of immunoglobulin M (IgM) or immunoglobulin G (IgG) antibodies in serum via enzyme-linked immunosorbent assay (ELISA). IgM antibodies are often detected two to six days after onset of symptoms, whereas IgG antibodies usually appear during the convalescent stage of illness and can persist for years (10). Reverse transcription polymerase chain reaction (RT-PCR), performed on serum, plasma or cerebral spinal fluid (CSF), offers the greatest sensitivity and is available through investigational use by the National Microbiology Laboratory in Winnipeg, Manitoba (11). Our case will highlight some of the diagnostic uncertainty surrounding the diagnosis of chikungunya.

Treatment for chikungunya fever is generally supportive, consisting of non-steroidal anti-inflammatory agents, fluids and rest. Corticosteroids are reserved for debilitating arthritis early in the course of acute infection (3). Research into potential monoclonal antibody treatment, antiviral therapy, and vaccinations is ongoing (12, 13).

The case

A 74-year-old man presented to the emergency department with constipation, abdominal pain, and a new onset diffuse non-desquamating maculopapular rash over the chest, back, arms and legs, following an 11-day trip to Haiti from which he returned one day prior to presentation. His rash was non-painful and non-pruritic. A computed tomography (CT) scan was performed of the abdomen showing small bowel diverticular inflammation and possible perforation into the surrounding fatty tissue. He was admitted to hospital for supportive care, including administration of antibiotics. His perforation was presumed secondary to a previous diagnosis of small bowel diverticular disease complicated by significant constipation.

While in Haiti, he had worked as an aid worker in a local health clinic. Prior to travel, he had completed vaccination series for both hepatitis A and B and had been prescribed antimalarial prophylaxis with chloroquine, to which he had been adherent. On day nine of his travel, he awoke with severe diffuse arthralgia affecting both large and small joints in the upper and lower extremities, rigors, and subjective fever. He had no respiratory or gastrointestinal complaints. His arthralgia dramatically improved over a 48-hour period, following which he developed a truncal rash as well as significant constipation, necessitating his presentation to the emergency department.

On physical examination in the emergency department, the patient's abdomen was soft and non-tender. There were no joint swellings noted; however, a maculopapular rash was seen over the chest, and the upper and lower extremities. Cardiac, respiratory and neurologic exams were normal. Routine laboratory investigations were performed (**Table 1**). A significant lymphopenia and thrombocytopenia were noted; chest radiography was also performed on admission and was normal.

Table 1: Routine laboratory investigations upon admission to hospital¹

Investigation	Value	Reference range
Hemoglobin	143 g/L	132–170 g/L
Leukocytes	9.9 x 10 ⁹ /L	3.5–10 x 10 ⁹ /L
– Neutrophils	8.6 x 10⁹/L	2.5–7.5 x 10 ⁹ /L
– Lymphocytes	0.5 x 10⁹/L	1.0–4.0 x 10 ⁹ /L
Platelets	108 x 10⁹/L	130–400 x 10 ⁹ /L
AST	36 U/L	13–37 U/L
ALT	18 U/L	10–40 U/L
ALP	94 U/L	40–120 U/L
Bilirubin (total)	11 mmol/L	3.0–20 mmol/L
Sodium	136 mmol/L	135–145 mmol/L
Potassium	4 mmol/L	3.5–5.0 mmol/L
Bicarbonate	22 mmol/L	20–30 mmol/L
Creatinine	79 mmol/L	55–105 mmol/L

Lactate	1.0 mmol/L	0.5–2.0 mmol/L
Urine Cultures	Negative	N/A ²
Blood Cultures	Negative	N/A ²
Malaria Rapid Antigen Test ³	Negative	N/A ²

¹ Abnormal values are in bold

² N/A = Not applicable

³ Note: Microscopy of Giemsa-stained thin blood smears was also performed.

The patient received supportive care, including intravenous crystalloids, and completed a course of antibiotics in hospital. He was discharged with urgent referral to a tropical diseases clinic for evaluation of his presumed travel-related illness. Dengue virus IgG and IgM antibodies were negative by ELISA. Stool cultures were negative for *Salmonella* spp., *Escherichia coli* O157:H7, *Campylobacter* spp., and *Shigella* spp. Chikungunya IgM antibody was positive by ELISA supporting a probable diagnosis of acute chikungunya infection. Without follow-up confirmatory testing (such as by plaque reduction neutralization test), the possibility of cross-reactivity with other alphaviruses could not be definitively excluded. His abdominal pain resolved in hospital with supportive care alone, while his arthritis and rash completely resolved over a two-week period.

Discussion

We present an atypical case of acute infection with chikungunya in a man returning from Haiti, an area of known ongoing intense dengue and chikungunya transmission. Although the patient's initial symptoms included classic findings of symmetric polyarthritis and subsequent maculopapular rash, his clinical course was complicated by significant abdominal pain, constipation, as well as thrombocytopenia—features atypical of chikungunya. His dramatic improvement over 48 hours is also unusual as polyarthralgia leading to mobility and dexterity issues will frequently last for weeks to months (3). Although uncommon, other atypical manifestations of chikungunya infection have been reported in the literature. These include neurological features (including encephalitis, seizures, and Guillain-Barre syndrome), cardiovascular features (including myocarditis, heart failure, and ischemic heart disease), renal features (including acute kidney injury), ocular features (including optic neuritis), as well as atypical skin eruptions, ulcerations, and bullae (14).

The differential diagnosis of fever and non-effusive polyarthritis is broad. Common bacterial causes include Lyme disease and infective endocarditis. Frequent viral causes include parvovirus B19, hepatitis B and C, rubella, dengue and other alphaviruses, including Mayaro, O'nyong-nyong, Ross River, Barmah Forest, Sindbis, and Semliki Forest virus. Non-infectious etiologies include seronegative spondyloarthropathies, rheumatoid arthritis, crystal-induced arthropathies, and post-infectious (reactive) arthritis. Given our patient's epidemiologic risk and presenting features, the most likely infectious etiologies included dengue fever and chikungunya infection, with parvovirus B19 infection less likely. Disease characteristics, clinical features and laboratory data comparing dengue and chikungunya infection are presented in **Table 2**. Non-infectious causes were deemed unlikely based on the patient's initial fever, rash, and rapid improvement in symptoms.

Table 2: Clinical and laboratory features of chikungunya versus dengue fever

Clinical and laboratory features	Chikungunya	Dengue
Illness Characteristics (19)		
Incubation period	3–7 days (range 2–12)	4–7 days (range 3–14)
Asymptomatic: Symptomatic ratio	0.03:1–0.25:1	2:1–10:1
Clinical Features (3, 8, 9, 17, 19, 20, 21)		
Fever	Common	Common
Arthralgia	Common	Possible
Polyarthritis (without effusion)	Common	Unlikely
Myalgia	Possible	Common
Rash	Common, often day 1–4 of illness	Common, often day 3–7 of illness
Abdominal Pain	Unlikely	Possible

Retro-orbital Pain	Unlikely	Common
Chronic joint pains	Common, can last >2 years	Unlikely
Chronic fatigue	Common, can last >2 years	Common, up to 3 months
Laboratory		
Neutropenia	Possible	Common
Lymphopenia	Common	Common
Thrombocytopenia	Possible	Common

The brisk improvement in the patient's symptoms without supportive care is atypical for chikungunya infection. Although likely related to an atypical presentation of disease, the therapeutic effect of chloroquine to mitigate the symptoms of chikungunya infection has been suggested by in vitro studies (15). However, this effect has not been confirmed by randomized controlled trials in humans (16); thus, it is unclear whether his chloroquine antimalarial prophylaxis attenuated his symptoms.

Constipation leading to abdominal pain is also not a classic feature of chikungunya infection. In a comparative study performed in India, 0 of 131 (0%) patients with acute chikungunya infection reported abdominal pain compared with 22 of 104 (21%) patients with acute dengue (17). However, during an outbreak on Reunion Island, 47% of patients reported gastrointestinal symptoms, although the number with abdominal pain and/or constipation is not reported (8). Given the time course of illness, constipation appears to be associated with this patient's acute chikungunya infection in this case; however, we acknowledge that there may have been two underlying diseases contributing to his symptoms. To explain his constipation and abdominal pain, co-infection with *Salmonella* spp. enteritis remains a possibility, as this infection is frequently associated with constipation and is endemic to Haiti. Stool cultures in this case were drawn only after administration of antibiotics, which substantially decreases their yield and may have been falsely negative.

Conclusion

Chikungunya infection is becoming a global concern as countries reporting new transmissions increase. The ability for viral mutation under selective pressure along with growing worldwide travel gives chikungunya significant epidemic potential. Given the varied clinical features at presentation, clinicians need to be vigilant in considering chikungunya infection in patients returning from high-risk countries with fever and polyarthralgia, regardless of other clinical and laboratory features. Although treatment is generally supportive, patient symptoms, including a debilitating arthritis, can persist for years, stressing the importance of patient education in appropriate mosquito bite prevention techniques during travel, including use of DEET- or icaridin-based insect repellants and protective clothing (18).

Conflict of interest

None

Funding

None

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