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Case Report

Zika Virus Disease Detection - A Case Report

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Abstract

A 36-year-old white male presents to a southeastern, metropolitan clinic complaining of symptoms suspicious for Zika Virus (ZIKV). After a thorough history, physical exam and appropriate laboratory tests, the patient is diagnosed with ZIKV. The ZIKV is mainly transmitted by a bite from an infected *Aedes aegyptl* or *Aedes albopictus* mosquito. The number of cases of ZIKV may be underestimated since symptoms are often mild and self-limiting and health care is not always sought. The most frequent symptoms of ZIKV include fever, arthralgias, maculopapular rash and conjunctivitis. It is increasingly known as the disease that can cause fetal microcephaly in pregnant women infected with the virus. The history and epidemiology of the ZIKV, symptoms, diagnosis, treatment, prevention efforts, and implications for health care providers are discussed in this article.

Keywords: Microcephaly; Mosquito; Pregnancy; Rash; Zika virus infection

Introduction

A 36-year-old white male presented to a southeastern, metropolitan clinic in the late summer complaining of body aches, especially in the neck and shoulders, sweats, headache and a swollen lymph node just below the right ear lobe for 3 days. He decided to seek medical care when he awakened with a non-pruritic rash on his neck. By the time he was examined the rash had spread to the shoulders, upper chest and back. His past medical history includes hypertension and hypercholesterolemia, for which he takes triamterene/hydrochlorothiazide, 37.5 mg/25 mg and atorvastatin, 20 mg, respectively. He denied tobacco, alcohol or any illicit drug use and has no known food or medication allergies. His occupation is sales related. He returned from a church mission trip to Guatemala five days before he presented to the clinic. His symptoms began two days after his return. He denied sore throat, nasal congestion, cough, appetite loss, nausea or vomiting. He reported that he had slightly loose stools from last 12 hours.

Physical examination revealed normal vital signs (weight 292 pounds, height 74 inches, body mass index 37.5, blood pressure 120/81 mmHg, pulse 74, respirations 16, temperature 98.6), an enlarged, slightly tender right parotid node, a red, confluent maculopapular rash behind the ears radiating to the neck, shoulders, upper chest and upper back. Conjunctiva was unaffected. Heart and lung sounds were normal. Abdominal and testicular exam were normal. The only abnormality on the Complete Blood Count (CBC) was a slightly decreased white blood cell count (3.7). Complete Metabolic Profile (CMP) was unremarkable (Table 1).

Symptoms	Body aches, sweats, headache, swollen lymph node in neck below ear, non-pruritic rash, loose stools
Labs	White blood cell count 3.7 (slightly decreased) Complete metabolic profile unremarkable
Physical findings	Red, confluent, maculopapular rash on neck, shoulders, upper chest, upper back Single enlarged, slightly tender parotid lymph node on right Remainder of exam normal, including conjunctiva

Table 1: Initial physical exam.

History of Zika Virus

The Zika Virus (ZIKV) is mainly transmitted by a bite from an infected ***Aedes aegypti or Aedes albopictus*** mosquito [1]. Intrauterine, perinatal, laboratory-acquired and transfusion-associated transmission cases also have been reported [2]. Moreover, it can be transmitted via vaginal or anal sex of an infected person [3]. ZIKV RNA has been found in semen up to 6 months and in vaginal secretions for 11 days [2]. It was first detected in a Rhesus monkey in 1947 in the Zika Forest of Uganda and in a human in Uganda in 1952 [1]. It was considered benign until it caused a large outbreak of mild illness in the Pacific Islands in 2007 [1]. In 2015 the virus invaded Brazil and Latin America with serious effects including microcephaly, brain disorders and other neurological disorders such as Guillain-Barre Syndrome [1]. On February 26, 2016 ZIKV became a reportable condition in the United States by the Council of State and Territorial Epidemiologists [4]. By September 2016 there were 2,382 cases of ZIKV reported in 48 of the 50 states and the District of Columbia in the United States [5]. However, this number excluded infants with congenital ZIKV [5]. Also, the number of cases may be underestimated since the infection is often mild, self-limiting and health care is not sought [5]. In fact, ZIKV does not produce symptoms in 80% of infected individuals [6]. Four states reported half of all cases, which were New York (23%), Florida (20%), California (6%) and Texas (5%) [5]. Local transmission has occurred in Puerto Rico and within a 4.5 square mile area in Miami Beach, Florida [7]. Of the 2,382 cases that were reported, 99% were from direct travel to an

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endemic area or secondary to sexual intercourse with someone who had travelled to those areas [5]. The areas which were attributed to the most cases of ZIKV transmission are the following: Caribbean (65%), Central America (18%), South America (9%), North America (5%), Southeast Asia, the Pacific Islands and Africa (<1%) [5]. The other 1% of patients with ZIKV contracted the disease locally [8]. Twenty-six patients were bitten by infected mosquitos in Southern Florida, one acquired ZIKV from a needle stick in a laboratory setting, and it is unknown how the other patient contracted the disease [8]. However, the patient did have close personal contact with a family member with the ZIKV. This family member had a 100,000 times higher than average level of viremia and died from septic shock [8]. The most frequent symptoms of ZIKV are fever, arthralgias, maculopapular rash and conjunctivitis [2]. However, it can also cause abdominal pain, constipation or diarrhea, aphthous ulcers and itching [2]. There have been reported neurological effects such as Guillain-Barre syndrome [1]. It is increasingly known as the disease that causes microcephaly during pregnancy, but it causes many other serious problems such as deficiently developed or missing fetal brain structures, miscarriage, stillbirth, hearing and vision defects and poor growth [2].

Diagnosing ZIKV can be challenging because false positive tests can occur, and serologic testing fails to determine when the infection actually occurred [7]. Due to his recent travel to Guatemala and suspecting the patient may have ZIKV, the lab provider was contacted, who recommended obtaining ZIKV RNA QL real time RT PCR, which is only for use under the FDA's emergency use authorization. It identifies Zika viral RNA, and is usually detectable in serum during the acute phase of infection. The patient had a positive result which indicated current infection. Labs are required to report all positive results to public health authorities. The epidemiologist from the local county health department contacted the clinic and provided a Zika Virus Laboratory Testing Decision Tree for use with future patients suspected of having ZIKV (Figure 1.).

Negative test results do not rule out ZIKV and should not be used as the sole basis for patient management decisions. Clinical examination, patient history and epidemiological information should also be taken into consideration when caring for a patient suspected of having ZIKV.

Dengue fever antibody (IgM) and Chikungunya antibody (IgM) were also obtained because of the patient's symptoms and recent travel to Guatemala. Dengue fever is transmitted to humans by a mosquito bite and can cause a high fever, headache, pain behind the eyes, joint pain, muscle and/or bone pain, rash, mild bleeding of the nose or gums, petechiae, easy bruising and a low white count [7]. It can be found in the Indian subcontinent, Southeast Asia, Southern China Taiwan, the Pacific Islands, the Caribbean (except Cuba and the Cayman Islands), Mexico, Africa, and Central and parts of South America [9]. Chikungunya is also a mosquito-borne alphavirus associated with large outbreaks in Asia, Africa and the Caribbean [10]. Local transmission in the United States has been documented. Symptoms include severe arthritis pain, fever, rash and headache [10]. Both the Dengue and Chikungunya antibody titers were negative.

Treatment

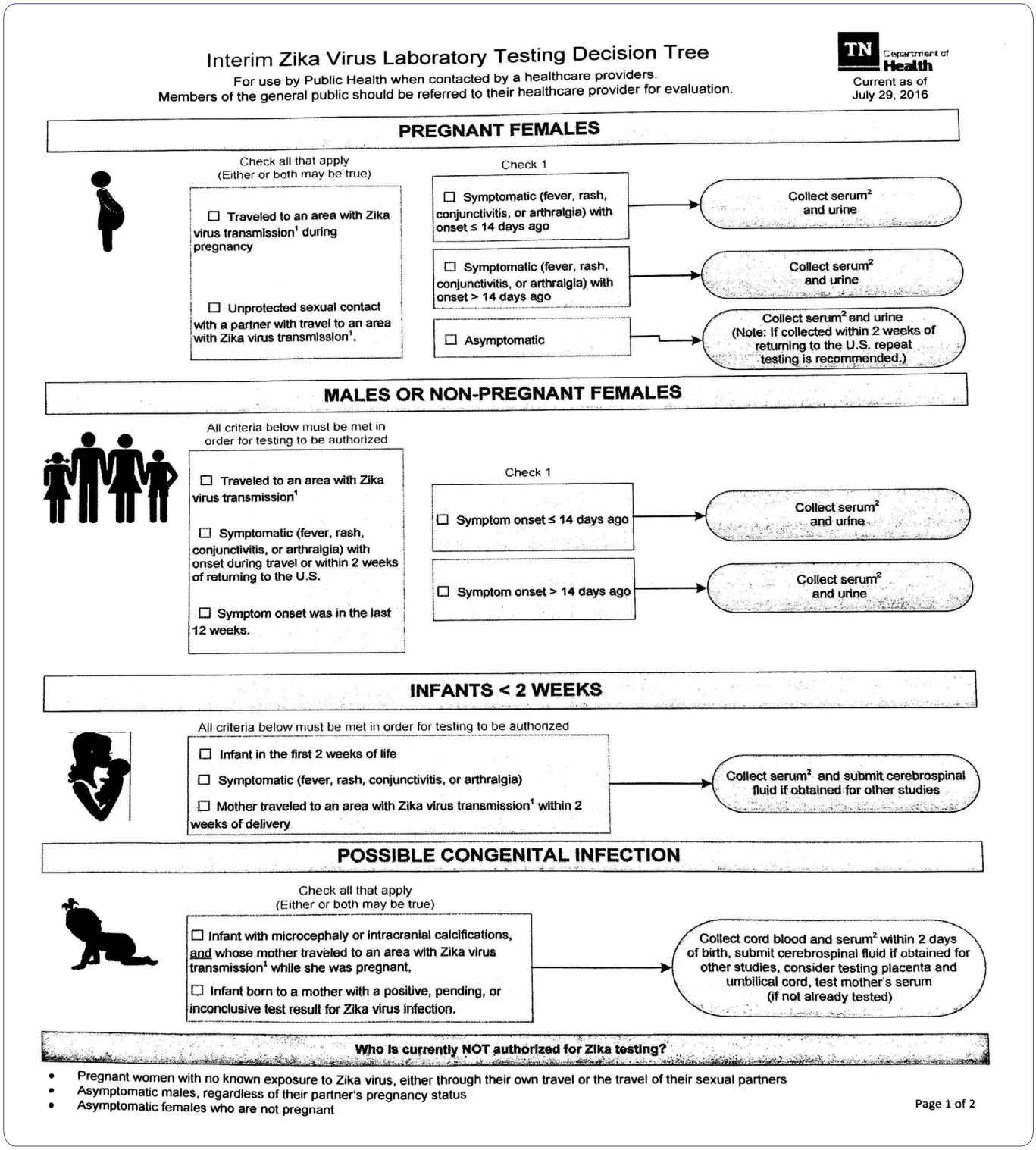
At this time treatment remains supportive [11]. Acetaminophen or NSAIDS are recommended to control fever and body aches. Adequate hydration and rest is encouraged for the acute infection. For those patients with complications due to ZIKV, such as various neurological manifestations, appropriate treatments are prescribed. Avoidance to areas where ZIKV has been detected is ideal especially for women of childbearing age, but not always realistic. If travel to ZIKV prone areas is necessary, a mosquito repellant with 20-30% concentration of DEET should be used. Light colored long sleeved clothing and long pants can help prevent mosquito bites. Also, stagnant water removal and rinsing out the container to rid mosquito eggs is recommended. In June 2016 the Food and Drug Administration (FDA) approved 2 newly developed vaccines for ZIKV phase 1 trials in human subjects [12]. The FDA predicts it will take approximately 2-3 years for vaccines to finish clinical trials and be available to be given to women of childbearing age [12]. Researchers predict there may not be enough cases of ZIKV to test the vaccine's effectiveness by the time the vaccine is available [12]. Some researchers believe the current ZIKV epidemic will be over in the next 1-3 years [12]. A live-attenuated vaccine (10-del ZIKV) is currently being evaluated. A single injection of 10-del ZIKV produced immunity in mice and prevented viremia when challenged with ZIKV [13]. Medications may soon be available to treat active ZIKV. Sofosbuvir, which is used to treat Hepatitis C virus, was discovered to decrease ZIKV levels in infected mice and prevented neuro-motor impairment by inhibiting ZIKV [14]. Ribavirin, another drug used for Hepatitis C, has been found to inhibit ZIKV replication and induce ZIKV cell death in infected mice [15]. In August 2016 the FDA produced a publication for agencies that collect blood in areas with local transmission of the ZIKV by mosquitos stating that the ZIKV was a relevant transfusion-transmitted infection [2]. Specific recommendations such as testing blood donations and screening potential donors for specific ZIKV risk factors were provided to decrease the risk of transmitting the ZIKV via transfusions [2]. For those patients, who developed symptoms of ZIKV, the virus can be spread 3-12 days before symptoms develop [6]. ZIKV can be detected in whole blood up to 58 days after symptoms have begun [2].

Conclusion

The patient tested positive for ZIKV RNA. The remainder of his illness was uneventful and he did not suffer any complications from contracting the virus. He returned to work a week and a half later. The physician from the local health department called the patient and suggested to use a condom to prevent possible ZIKV exposure to the patient's wife, stay indoors, empty any standing water outside around his home, and avoid parks and use insect repellent if he had to go outdoors. Health department workers sprayed his neighborhood and set bait around his house for mosquitos. Incidentally, the patient reported upon follow-up that a female in her 60's on the same mission trip to Guatemala tested positive for ZIKV. She lived in another town and was reportedly much sicker.

Healthcare providers should educate their patients regarding tips to avoid ZIKV. This includes avoidance of areas where mosquito-borne transmission occurs, using insect repellent with at least 20-30% concentration of DEET, wearing long sleeved shirts and long pants, and emptying any containers with standing water. Healthcare providers should also educate their patients regarding the signs and symptoms of ZIKV, which include acute onset of fever, a maculopapular rash, arthralgias, and/or purulent conjunctivitis, and to seek medical attention immediately if symptoms develop and have positive risk factors for contracting the ZIKV [5]. Pregnant patients and women of childbearing age should be educated to avoid travel to affected areas due

to the risk of fetal loss, microcephaly, vision or hearing complications or other serious abnormalities of the brain. Also, all patients who are pregnant should be questioned regarding the potential of having been exposed to ZIKV, such as travelling to an area known to have ZIKV or having sex without a condom. Pregnant women with symptoms and possible exposure should be tested for ZIKV [7]. Testing is no longer routinely recommended to pregnant women without ZIKV symptoms who have had a recent ZIKV exposure, but is recommended to pregnant women who have ongoing ZIKV exposure [7]. Patients who have travelled to or live in an area with ZIKV transmission or who have had unprotected sex with an individual who visited those areas or has ZIKV should be tested for ZIKV.



Interim Zika Virus Laboratory Testing Decision Tree

For use by Public Health when contacted by a healthcare providers.
Members of the general public should be referred to their healthcare provider for evaluation.

TN Department of Health
Current as of July 29, 2016

PREGNANT FEMALES

Check all that apply (Either or both may be true)

- ☐ Traveled to an area with Zika virus transmission[1] during pregnancy
- ☐ Unprotected sexual contact with a partner with travel to an area with Zika virus transmission[1].

Check 1

- ☐ Symptomatic (fever, rash, conjunctivitis, or arthralgia) with onset ≤ 14 days ago → Collect serum[2] and urine
- ☐ Symptomatic (fever, rash, conjunctivitis, or arthralgia) with onset > 14 days ago → Collect serum[2] and urine
- ☐ Asymptomatic → Collect serum[2] and urine (Note: If collected within 2 weeks of returning to the U.S. repeat testing is recommended.)

MALES OR NON-PREGNANT FEMALES

All criteria below must be met in order for testing to be authorized

- ☐ Traveled to an area with Zika virus transmission[1]
- ☐ Symptomatic (fever, rash, conjunctivitis, or arthralgia) with onset during travel or within 2 weeks of returning to the U.S.
- ☐ Symptom onset was in the last 12 weeks.

Check 1

- ☐ Symptom onset ≤ 14 days ago → Collect serum[2] and urine
- ☐ Symptom onset > 14 days ago → Collect serum[2] and urine

INFANTS < 2 WEEKS

All criteria below must be met in order for testing to be authorized

- ☐ Infant in the first 2 weeks of life
- ☐ Symptomatic (fever, rash, conjunctivitis, or arthralgia)
- ☐ Mother traveled to an area with Zika virus transmission[1] within 2 weeks of delivery

→ Collect serum[2] and submit cerebrospinal fluid if obtained for other studies

POSSIBLE CONGENITAL INFECTION

Check all that apply (Either or both may be true)

- ☐ Infant with microcephaly or intracranial calcifications, and whose mother traveled to an area with Zika virus transmission[1] while she was pregnant,
- ☐ Infant born to a mother with a positive, pending, or inconclusive test result for Zika virus infection.

→ Collect cord blood and serum[2] within 2 days of birth, submit cerebrospinal fluid if obtained for other studies, consider testing placenta and umbilical cord, test mother's serum (if not already tested)

Who is currently NOT authorized for Zika testing?

- Pregnant women with no known exposure to Zika virus, either through their own travel or the travel of their sexual partners
- Asymptomatic males, regardless of their partner's pregnancy status
- Asymptomatic females who are not pregnant

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Current as of July 26, 2016

RECORD THE FOLLOWING INFO FOR ALL PATIENTS FOR WHOM TESTING IS AUTHORIZED, REGARDLESS OF PREGNANCY STATUS

Patient Information

Patient Name: _____
Med. Record #: _____
Date of Birth: _____/_____/_____
Sex: □ Male □ Female
Pregnancy Status □ Yes □ No □ UNK
Due Date: _____/_____/_____

Address: _____
City: _____ State: _____ ZIP: _____
County: _____
Patient Phone Number: _____

If infant patient:
Mother's Name: _____
Mother's Zika Test Result: □ Positive □ Inconclusive □ Negative □ UNK
Mother's Test Date: _____/_____/_____ □ UNK

Provider Information

Provider Name: _____
Provider Phone Number: _____

Epidemiological Information

Countries Visited: (If Infant, Mother's Travel)

_____
_____
_____
Date of Return to US: _____/_____/_____

Patient Symptom Onset Date(s):

Fever	n/a	_____/_____/_____
Rash	n/a	_____/_____/_____
Arthralgia	n/a	_____/_____/_____
Conjunctivitis	n/a	_____/_____/_____

Specimen Information

Expected date of specimen collection: _____/_____/_____
Specimen(s) submitted (use page 1 for guidance, check all that apply) □ Serum □ Urine □ CSF □ Placenta □ Umbilical cord

Public Health Information

Date of PH Authorization: _____/_____/_____ Authorizer: _____
Public Health Region: _____ Provided Mosquito □ & Sex □ Transmission Education

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Email both pages to SHOC.Operations@tn.gov & Jim.Gibson@tn.gov. CC: Michael.McWilliams@tn.gov if the specimen is sent to the Knoxville lab. C
Stephen.Gooch@tn.gov if the specimen is sent to the Memphis lab. Password protect the file if sending from a non-tn.gov email address.

Share with Provider or Patient as Appropriate:
Guidelines for Specimen Collection and Submission[2] | Mosquito Avoidance messages[3] | Sexual Transmission messages[4]
Updated: Guidance for Health Care Providers:
1) Caring for Women of Reproductive Age with Possible Zika Virus Exposure http://www.cdc.gov/mmwr/volumes/65/wr/pdfs/mm6529e1.pdf
2) Caring for Infants and Children with Possible Zika Virus Infection Healthcare http://www.cdc.gov/mmwr/volumes/65/wr/pdfs/mm6507e1.pdf

1. For a current list of countries with ongoing Zika virus transmission, please see list and map here: http://www.cdc.gov/zika/geo/americas.html

2. Collect 2.0 mL of serum or plasma. Tube should be centrifuged and serum/plasma decanted prior to shipment to avoid hemolysis. Ship serum/plasma specimen in a sterile plastic tube with a tightly-sealing screw cap (if unavailable a red-top vacutainer can be used). The specimen should be kept cold. The sample may be placed in an insulated container with ice packs. Additional blue ice packs should be used in the summer to ensure specimen integrity in hot weather. If symptomatic within last 14 days, also collect 10.0 mL of urine

3. Prevention messages regarding mosquito avoidance: http://www.cdc.gov/zika/pdfs/control_mosquitoes_chikv_denv_zika.pdf and http://www.cdc.gov/chikungunya/pdfs/fs_mosquito_bite_prevention_us.pdf)

4. Interim Guidelines for Prevention of Sexual Transmission of Zika Virus — United States, 2016 (03/25/16): http://www.cdc.gov/mmwr/volumes/65/wr/pdfs/mm6529e2.pdf

Figure 1: Zika virus decision tree.

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