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A Case of Zika Virus with GBS: Manifestations, Complications and Management

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Abstract: The currently ongoing Zika virus outbreak in The Americas, Caribbean, and the Pacific have been declared by the World Health Organization (WHO) to be "spreading explosively" and its complications to be a Public Health Emergency of International Concern. Although this virus is not spread by direct contact, it is an arthropod-borne flavivirus that can also be spread sexually and through blood. In this case report, we explore the various clinical manifestations, complications, and management of Zika virus with special interest to Guillain-Barré Syndrome (GBS). This case report has explained the hospital course of a 77-year-old female to facilitate this discussion.
Keywords: Zika Virus, Elderly Female, Guillain Barre Syndrome.

INTRODUCTION

Zika virus was initially isolated in 1947 but the first human cases were detected in 1952. The first recognized outbreak of this virus occurred in Micronesia in the year 2007 and a larger outbreak in French Polynesia in 2013. The virus can be transmitted by the bite of an infected Aedes mosquito, maternal-fetal transmission, sexual contact, blood transfusion, organ transplantation or laboratory exposure. Zika virus, as most viral infections, is usually asymptomatic. But in those that do develop symptoms, approximately 20 percent of patients, it may range from an acute onset of low–grade fever, a maculopapular rash, arthralgia or conjunctivitis to debilitating complications such as Guillain-Barré Syndrome (GBS), myelitis and meningoencephalitis [1].

Complications in pregnant women are of major concern as it may cause congenital microcephaly and other developmental defects and so preventive measures are particularly important in this population. Such measures include preventing mosquito bites, abstinence from unprotected sex and screening of blood and tissue donations. Standard precautions are encouraged in healthcare settings to avert nosocomial transmission [2]. We now proceed with the case of a 77-year-old female to elaborate on a complication of Zika virus infection. She initially presented in an unconscious state but was later found to be IgM positive for Zika virus.

CASE REPORT

A 77-year-old female with significant past medical history of diabetes mellitus with associated polyneuropathy, long-standing rheumatoid arthritis with a recent travel history to Puerto Rico initially presented to the Emergency Department in an unresponsive state. She was noted to have generalized weakness and confusion prior to this arrival. She had been having significantly worsening weakness in bilateral upper and lower extremities for a month prior to this initial presentation. On imaging, she was found to have a subarachnoid hemorrhage. The patient was admitted to the Intensive Care Unit (ICU) and had required to be intubated.

The patient was then found to be septic with bacteremia with *E.coli* and *Chryseobacterium* for which she was treated appropriately with IV antibiotics after a consultation with Infectious Disease specialists. A common adverse effect with the use of antibiotics is the development of a Clostridium difficile infection. Our patient did develop this infection for which she was then treated effectively with a 14-day course of Metronidazole.

She was later extubated and downgraded from the ICU. However, she still exhibited significant weakness, pain, and edema in all four extremities. At this point, labs that were done a couple weeks prior to this admission came back positive for IgM against Zika virus. The patient reported that she had a few days of fever, rash and joint pain since her stay in Puerto Rico for which a health care provider saw her and had some labs drawn. The center for disease control was contacted to report a possible case of Zika virus. The

positive test result for IgM paved the way to suspecting Guillain Barre Syndrome (GBS), an associated complication of Zika virus, to be the cause of the patient's weakness. Aspirin was discontinued as aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) are contraindicated until a dengue infection is ruled out. Consultations with neurologists and neuromuscular specialists were attained. A nerve conduction study was done which came back positive for GBS. Confirmatory tests for Zika virus came back positive and the tests for dengue and chikungunya viruses were negative. The patient was then started on a 5-day course of intravenous immune globulin (IVIG). She then started to show remarkable improvement. During the course of the study conducted at the hospital, permission from the ethical committee was taken.

Table-1: Brighton diagnostic criteria

LEVEL 1	LEVEL 2	LEVEL 3
Bilateral flaccid weakness of the limbs	Bilateral flaccid weakness of the limbs	Bilateral and flaccid weakness of the limbs
Absent or Decreased deep tendon reflexes	Absent or Decreased deep tendon reflexes	Absent or Decreased deep tendon reflexes
Illness pattern that is monophasic ;there is an interval between onset and worsening (peak) of weakness between 12h and 28 days followed by subsequent clinical plateau	Illness pattern that is monophasic ;there is an interval between onset and worsening (peak) of weakness between 12h and 28 days followed by subsequent clinical plateau	Illness pattern that is monophasic ;there is an interval between onset and worsening (peak) of weakness between 12h and 28 days followed by subsequent clinical plateau
No alternative differential diagnosis	No alternative differential diagnosis	No alternative differential diagnosis
CSF Protien level elevation above normal value and CSF white cell count <50 cells/µl (Cytoalbuminologic dissociation) Electrophysiological findings indicative of GBS	CSF total white cell count <50 cells/µl Electrophysiological findings indicative of GBS	

DISCUSSION

While considering the possibility of a Zika virus infection, other viral causes must be ruled out especially dengue and chikungunya viruses as they are transmitted by the same mosquito vector and have similar clinical manifestations, such as arthralgias, rash, and fever as seen in this patient. Other differentials to consider would be Parvovirus, Rubella, Measles, Leptospirosis, Malaria, Rickettsial infection and *Group A Streptococcus* [3]. In our patient's case, diabetic neuropathy and rheumatoid arthritis are also significant differentials as she does have a pertinent past medical history of these.

The incubation period between the mosquito bite and onset of clinical manifestations of Zika virus is usually 2-14 days with mild symptoms such as an acute onset of low-grade fever, maculopapular rash, arthralgia and non-purulent conjunctivitis. It typically resolves within two to seven days. Severe cases that require hospitalization are relatively rare with low case-fatality rates [4]. Severe cases may include manifestations of GBS that include features of abrupt onset of rapidly ascending weakness or paralysis of all four extremities which can progress to involve respiratory, facial and bulbar muscles. Brighton's Diagnostic Criteria (Table 1) is a useful tool to assess GBS.

A case-control study conducted on GBS in correlation with Zika was conducted in French Polynesia during the 2014 worldwide outbreak. Cases included 42 patients diagnosed with GBS; 98 patients with non-febrile illness and a second control group of 70 patients with Zika without any neurological complications. IgM was positive in 93 percent of GBS cases, however anti-glycolipid IgG antibodies were detected in fewer than 50 percent of GBS cases which may indicate direct viral neurotoxicity. Symptoms of GBS occurred in 88 percent of the Zika infections, and the onset of symptoms was around 6 days between viral onset and neurological symptoms. All GBS cases received intravenous immune globulin (IVIG), 38 percent required intensive care and 29 percent needed respiratory care; all survived. Results of nerve conduction studies were consistent with an acute motor axonal type of GBS that showed clinical improvement

during follow-up suggesting reversible conduction failure. The incidence of GBS during the outbreak was estimated to be around 2.4 cases per 10,000 Zika virus infections [5-7].

Clinical manifestations

Clinical manifestations occur in only about 20 percent of those infected with Zika virus. Signs and symptoms of Zika virus include an acute onset of low-grade fever, maculopapular rash, arthralgia and non-purulent conjunctivitis. The presence of two or more of these manifestations are consistent with a Zika virus disease[8].

Other commonly reported signs and symptoms include myalgia, headache, retro-orbital pain and asthenia. Less commonly reported are abdominal pain, nausea, diarrhea, mucous membrane ulcerations, thrombocytopenia, palatal petechiae, and uveitis. Children have a similar presentation to adults. Although arthralgia may be difficult to detect in infants and young children, it may be observed as irritability, walking with a limp, difficulty moving, refusing to move an extremity, pain on palpation or pain on active or passive movement of the affected joint[9].

In-utero Zika virus infection can result in congenital microcephaly, fetal losses and ocular abnormalities such as pigmentary and hemorrhagic retinopathy, circumscribed chorioretinal atrophy, abnormal vascular development, torpedo maculopathy, optic nerve abnormalities, microcornea, microphthalmia, falciform folds, cataracts, retinal dysplasia, and nystagmus. Other central nervous system abnormalities include ventriculomegaly, of the corpus callosum and cerebellum, intracranial calcifications, global hypogyria, and hydranencephaly. It may also result in hydrops fetalis, impaired prenatal and postnatal growth and hearing loss [10].

Complications

Complications of Zika virus can also include Guillain-Barré Syndrome (GBS). GBS is an inflammatory demyelinating polyneuropathy that primarily affects motor nerves. It is usually preceded by viral or bacterial infections such as Mycoplasma, Campylobacter jejuni, CMV, hepatitis, and HIV but may also occur in Hodgkin disease, lupus, after surgery, or after HIV seroconversion. Clinical features include abrupt onset of rapidly ascending weakness or paralysis of all four extremities and can progress to involve respiratory, facial and bulbar muscles [11]. Brighton's Diagnostic Criteria (Table 1) is a useful tool to assess GBS.

Other neurologic complications of Zika virus may include brain ischemia, myelitis, and meningoencephalitis.

Management

As most viral infections, there is no specific treatment for Zika virus infection but management includes rest, symptomatic treatment, fluids to prevent dehydration and acetaminophen for fever and pain. Aspirin and other NSAIDs are contraindicated until a dengue infection is ruled out to reduce the risk of hemorrhage. IVIG can be administered for the treatment of GBS[12]. Development of a vaccine is currently under trials.

CONCLUSION

As with most viral infections, there is no specific treatment for Zika virus infection. But complications of Zika virus do arise, which may include Guillain-Barré Syndrome (GBS). GBS is usually preceded by viral or bacterial infections, hepatitis, HIV, Hodgkin disease, lupus or surgery. IVIG can be administered to treat the symptoms of GBS while aspirin and other NSAIDs are contraindicated until a dengue infection is ruled out to reduce the risk of hemorrhage. Though this patient was negative for Campylobacter jejuni or the various common etiologies for GBS, a patient with a significant travel history should always be screened for or at least suspected of a Zika virus infection while also keeping in mind to rule out any other common etiologies such as dengue infection. This patient also had early-onset symptoms such as arthralgias, fever, and rash which were consistent with Zika or dengue infection. There should also be an emphasis on the importance of the awareness of the Brighton's Diagnostic Criteria (Table 1) and we hope this report will raise awareness for it.

Abbreviations

World Health Organization (WHO); Guillain-BarréSyndrome (GBS); Intensive Care Unit (ICU); Non-Steroidal Anti-Inflammatory Drugs (NSAIDs); Intravenous Immune Globulin (IVIG)

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