

Case Report

Zika virus in northern Kerala: a case report

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ABSTRACT

Being a tropical country, emerging Zika virus infection is a major concern in India. In India, the first case of confirmed Zika virus disease was reported from Gujarat. In Kerala, the first Zika Virus outbreak was reported in June 2021 in the southern district of Thiruvananthapuram. Till now there have been no documented reports in the literature about the Zika virus disease in the northern part of Kerala. Hence, we are reporting a 44-year-old lady with fever, maculopapular rash, arthralgia, retro auricular lymphadenitis, gingivitis and bleeding manifestations who on evaluation had anemia, thrombocytopenia and was later diagnosed to have Zika virus infection along with Vitamin B12 deficiency in Tellicherry in the northern part of Kerala. This case serves as a reminder of the ongoing threat of emerging infectious diseases in tropical regions and the need for early detection.

Keywords: Zika virus, Flavi virus, Northern Kerala

INTRODUCTION

Zika virus (ZIKV) is an arthropod-borne virus (Arbo-virus) within the genus *Flavivirus* and the family *Flaviviridae*. Individuals with Zika virus disease present with fever, maculopapular rashes involving the face, trunk, palms, soles, arthralgia, conjunctivitis, and headache. GBS-like presentation is also reported following Zika virus infection.¹ It is primarily transmitted to humans through the bite of infected mosquitoes, particularly *Aedes* mosquitoes, including *Aedes aegypti* and *Aedes albopictus*.² These mosquitoes are commonly found in tropical and subtropical regions. Clinical presentation is non-specific and can mimic other Arbo-viral infections like Dengue or Viral infection-induced immune thrombocytopenia with bleeding manifestations.³ Transplacental transmission is dreaded due to the chance of developing congenital malformations like microcephaly. However, majority of Zika virus disease in adults have a self-limited course without any complications.⁴ Serological testing and detection of viral RNA by RT-PCR are the most commonly employed tests

for diagnosing Zika virus infection.⁵ It was initially sporadic for about 50 years before emerging in the Pacific and Latin American regions. Though Zika virus infection was reported in Uganda in 1947, it has now spread to other African countries, Southeast Asia, Latin America, and the Caribbean.⁶ In Southeast Asia, Indonesia is the first country in which Zika virus was reported.

Other countries were the Caribbean, Thailand, and Malaysia.⁷ India reported its first case of Zika virus disease in 2016 from Gujarat.⁸ Thereafter, sporadic cases were reported from different states throughout India. However, the more notable outbreaks occurred in Southern India in Tamil Nadu and Karnataka. Later in 2021, Zika virus outbreak was reported for the first time in Kerala in the southern district of Trivandrum.⁹ During May 2021, there was an increase in the number of exanthematous fevers of unknown cause among individuals who visited the outpatient department of a private hospital in Trivandrum. This trend was also observed in the healthcare workers of the same hospital. During the third week of May, 19 healthcare workers in the hospital who developed febrile

illness with rash were selected for ease of sampling and further follow-up. Their clinical specimens (Oropharyngeal/ nasopharyngeal swabs, serum, blood, urine) were referred to ICMR, Pune for further virological investigations. All cases were screened for SARS-CoV-2, Measles, rubella, enterovirus, Parecho virus, human alpha herpes virus 1 & 2, human alpha herpes virus 3, human beta herpes virus 5, human beta herpes virus 6A & 6B & 7, human gamma herpes virus 4, human meta-adenovirus A to g and primate erythroparvovirus 1 by rRT-PCR.

Three tested positives for EBV. All 19 cases had mild disease with no complications. They were managed symptomatically with antipyretics and antihistamines on the 9th of June, 2021, Zika virus infection was detected and confirmed in a 24-year-old pregnant lady, a resident of the Trivandrum district of Kerala in the Southwest of India, who had no travel history. On further evaluation, she was found to have thrombocytopenia, and she tested positive for Zika virus RT-PCR. This prompted a retrospective evaluation for Zika virus infection in those 19 health workers. Eventually, 13 cases tested positive for Zika viral RNA and 10 individuals tested positive for anti-Zika IgM antibodies.⁹

Till now there have been no documented reports in the literature about the Zika virus disease in the northern part of Kerala. Hence, we are reporting a 48-year-old lady with fever, maculopapular rash, and bleeding manifestations associated with thrombocytopenia in Tellichery in the northern part of Kerala.

CASE REPORT

A 44-year-old female with no known co-morbidities presented with complaints of swelling of the gum near the left upper molar tooth and retro-auricular lymphadenitis for 10 days (since 21 October 2023). She also had a history of travel to Goa on the 22nd of October 2023. She developed a generalized maculopapular rash following the consumption of seafood from Goa. She went to a local hospital with these complaints and was given antihistamines for the same.

She improved symptomatically. She came back to Kerala on 25th October and a day later, she started to have excessive bleeding PV. Two days later, she developed arthralgia involving both large and small joints which was associated with multiple ecchymotic patches over the body. She was initially evaluated in another hospital and was referred to our centers because of severe thrombocytopenia.

On reviewing her drug history, she revealed that she had been consuming biotin supplements and other multivitamin tablets for the past 3 months. On examination, she had multiple ecchymotic patches, the largest measuring 5×3 cm over her left elbow and erythematous wheal over her neck (Figure 1). Systemic examination was unremarkable. Hess's test was negative

and there was no sternal tenderness. Blood investigations showed normocytic normochromic anemia (Hb 10.6 g/dl, MCV: 87.8, MCH: 29.6, MCHC: 33.7) with severe thrombocytopenia (platelet:12000/ mm³). Her liver function, renal function, bleeding time, clotting time, PT-INR, apTT, LDH, and CRP were within normal limits. She was tested for Dengue, Leptospira, Malaria, and other common tropical infections including Salmonella, Chikungunya, and Rickettsia all of which turned out to be negative.



Figure 1: Erythematous maculopapular rash on right side of neck.

Peripheral smear examination showed normocytic normochromic anemia with marked thrombocytopenia. The Direct Coombs test was negative. Her Vitamin B12 level was low (168). ANA-IF and ANA profiles were negative. Her blood cultures were sterile and bone marrow aspiration and biopsy were done which was normal. USG Abdomen and pelvis showed Grade 1 fatty liver (Liver size: 14.8 cm and Spleen size: 8.8 cm) (Table 1).

She was initially admitted to the Medical ICU because of severe thrombocytopenia and bleeding manifestations. Multiple platelet transfusions were done. Having ruled out the common tropical infections and the possibility of autoimmune causes like SLE, chances of less common infections like Zika virus infection were considered. Zika Virus Real-time PCR was sent which eventually turned out to be positive.

She was finally diagnosed with thrombocytopenia secondary to Zika Virus infection and Vitamin B12 deficiency. She was treated with high-dose steroids (Inj. Dexamethasone 40 mg IV OD for 4 days), Folic Acid, and parenteral Vitamin B12 supplementation following which her platelet counts improved (Table 2). She became symptomatically better and was discharged after 9 days, once she fully recovered from the illness.

Table 1: Initial investigations (laboratory and radiological).

Investigation	31 October 2023
Reticulocyte count	2.4%
PT	11.4 seconds
INR	1.09
aPTT	23.8 seconds
Uric acid	2.9 md/dl
Creatinine	0.91 mg/dl
Sodium	136 meq/l
Potassium	3.5 meq/l
Total bilirubin	0.45 mg/dl
Direct bilirubin	0.08 mg/dl
AST	19 U/l
ALT	12 U/l
Total protein	6.4 g/dl
Albumin	3.7 g/dl
LDH	202 U/l
CRP	<0.1 mg/dl
hsTropI	<1.5 pg/ml
TSH	1.941 mIU/l
Vitamin B12	168 pg/ml
Ferritin	30.6 ng/ml
Fibrinogen	211 mg/dl
Dengue NS1, IgM, IgG	Negative
Malaria card test	Negative
Leptospira IgM	Negative
ANA-IF	Negative
ANA profile	Negative
Tropical fever panel-PCR (Rickettsia, Salmonella, Plasmodium, Dengue, Leptospira, Chikungunya)	Negative
Adenovirus, CMV, EBV PCR	Negative
Peripheral smear	Normocytic normochromic anemia with marked thrombocytopenia
USG abdomen and pelvis	Grade 1 fatty liver
Bone marrow aspirate and biopsy	normal
Flow cytometry gated on CD 19+ cells	Polyclonal B cells

Table 2: Improvement in blood counts with vitamin B12 supplementation and parenteral steroids.

Investigation	31 Oct 23	1 Nov 23	2 Nov 23	3 Nov 23	4 Nov 23	5 Nov 23	6 Nov 23	8 Nov 23
Hb (G/DL)	10.6	10.3	11.7	10.4	10.4	10.7	11.5	11
Total WBC (Cells/MCL)	6800	6900	8600	22800	23400	18800	20800	12100
DC (%)	N55L33		N84L13	N91L6.6				
Platelet (Cells/MCL)	12,000	40,000	58,000	1,45,000	1,69,000	2,85,000	3,81,000	3,89,000

DISCUSSION

Zika virus disease is a major public health concern. Many major and minor outbreaks have been reported worldwide.³ Due to the advancements in air travel and international trade, the Zika virus is easily spread to regions where the virus was previously not endemic. India, being a tropical country, is an easy breeding ground for mosquitoes and hence Arbo viral infections like Dengue,

Chikungunya, West Nile virus, Japanese encephalitis, etc have been fairly common since time immemorial. However, the Zika virus was not heard of in India until recently. It was in 2016 that the first case of Zika virus was reported from India in the state of Gujarat. Later major outbreaks occurred in Southern India in the states of Tamil Nadu and Kerala. The clinical profiles of patients identified to be infected with the Zika virus in Kerala were similar, with all cases having a mild self-limited illness

with no major complications.⁸ The patient had no comorbid conditions but had a travel history to Goa on 22 October 2023. After consumption of seafood, she had a generalized maculopapular rash which was relieved with antihistamines indicating an allergic etiology. After returning to Tellichery, she developed bleeding per vaginum followed by polyarthralgia with cutaneous bleeding manifestations due to severe thrombocytopenia (Platelet count: 12000/ mm³).

Her presentation with fever, arthralgia, and cervical lymphadenopathy was similar to that observed in the cases reported from Trivandrum. However, she also had gingivitis near the left upper molar tooth, and retro-auricular lymphadenitis almost simultaneous with the generalized rash, features which were not observed in the cases reported from Trivandrum or other states of India. The degree of thrombocytopenia was also more severe when compared to that seen in cases in Trivandrum where almost all had normal or near normal platelet count. Vitamin B12 deficiency in our patient could have played a role in this. Contrary to the cases reported in Trivandrum, all of which had a self-limited illness, our patient required ICU admission and platelet transfusions given the severe thrombocytopenia and excessive bleeding per vaginum. Considering the mechanism of virus-induced immune-mediated thrombocytopenia, she was treated with high-dose steroids (Inj. Dexamethasone 40 mg IV OD for 4 days) along with Vitamin B12 and Folic acid supplementation. Following this, her platelet counts showed an improving trend. She was discharged once she fully recovered from the illness.

CONCLUSION

With expanding global outbreaks, Zika infection is emerging as a significant threat to public health. The major outbreaks in Brazil and India have proved their potential for rapid spread. The pathogenesis of Zika virus infection is not fully understood yet. The investigation of the association between Zika virus infection and neurological sequelae, including potential neuro-pathophysiologic mechanisms is still underway. As observed in our case, individuals with risk factors that predispose to thrombocytopenia like vitamin B12 deficiency, when infected with Zika virus illness may follow a more severe course with frank bleeding manifestations unlike those commonly reported in the literature.

The use of high-dose steroids for treating Zika virus-induced thrombocytopenia may be justified given the immune-mediated mechanisms. Its ability to cause such severe disease in predisposed individuals and congenital malformations via transplacental transmission in pregnant

women makes it a necessity to distinguish it from other common Arbo viral infections like Dengue and chikungunya. It also raises the need to curtail its transmission via stringent surveillance, rapid diagnosis, and vector control measures. The advent of new antivirals and vaccines along with strict vector control measures may help in controlling the transmission of the Zika virus in the coming years.

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