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Varied Clinical Manifestations of Chikungunya in Neonates: A Case Series

Yenidoğanlarda Chikungunyanın Çeşitli Klinik Belirtileri: Bir Vaka Serisi

Santosh Kumar KAMALAKANNAN(İD)

Department of Neonatology, Saveetha University Medical College, Kancheepuram, India

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ABSTRACT

Chikungunya virus is a member of the alphavirus genus of the family Togaviridae. It is transmitted by the Aedes mosquito. It is usually a self-limiting illness. The chikungunya virus (CHIKV) infection in the neonatal period is very rare. The time of greatest risk of transmission from mother to fetus is when the mother is infected just before the delivery. The aim of this study is to describe clinical features and outcomes in neonatal chikungunya during the 2016 outbreak. Clinical, pathological, and radiological details of neonates with typical rash, later diagnosed as chikungunya, are presented. Neonates with chikungunya had varied manifestations ranging from fever, persistent cry, a generalized maculopapular rash, hyperpigmentation, severe thrombocytopenia, encephalitis, and features of multisystem involvement. It is important to consider perinatal Chikungunya in neonates who present within the first week of life with fever, encephalopathy, and perioral rashes, with or without seizures, especially if there is a history of maternal Chikungunya infection within the last week before delivery.

Key Words: *Chikunguniya; Fever; Hyper pigmentation; Thrombocytopenia; Encephalitis*

ÖZ

Yenidoğanlarda Chikungunyanın Çeşitli Klinik Belirtileri: Bir Vaka Serisi

Chikungunya virüsü, Togaviridae ailesindeki Alpha virüs cinsinin bir üyesidir. Aedes sivrisineği tarafından bulaşır. Genellikle kendini sınırlayan bir hastalıktır. Yenidoğan döneminde chikungunya virüsü (CHIKV) infeksiyonu çok nadir görülür. Anneden fetüse bulaşma riskinin en yüksek olduğu zaman, annenin doğumdan hemen önce infekte olduğu zamandır. Bu çalışmanın amacı 2016 salgını sırasında yenidoğan chikungunyadaki klinik özellikleri ve sonuçları tanımlamaktır. Daha sonra chikungunya olarak teşhis edilen tipik döküntülü yenidoğanların klinik, patolojik ve radyolojik detayları sunulmaktadır. Chikungunyalı yenidoğanlarda ateş, sürekli ağlama, genel makülopapüler döküntü, hiperpigmentasyon, şiddetli trombositopeni, ensefalit ve çoklu sistem tutulumu özellikleri arasında değişen çeşitli belirtiler vardı. Doğumdan önceki son hafta içinde ateş, ensefalopati ve nöbetli/nöbetsiz perioral döküntülerle ilk hafta içinde başvuran yenidoğanlarda perinatal chikungunya düşünülmelidir.

Anahtar Kelimeler: *Chikungunya; Ateş; Hiperpigmentasyon; Trombositopeni; Ensefalit*

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INTRODUCTION

Chikungunya infection among neonates is very rare. It is typically seen in adults and rarely among neonates being transmitted vertically from the mother. It occurs in outbreaks and during an outbreak up to 1.4 million cases have been reported among adults. Data for incidence among neonates is not available in the literature with few case reports and case series describing the manifestations of neonatal chikungunya with the largest case series comprising of 16 neonates. Densely populated areas, lack of urban planning, and multiple breeding grounds for mosquitoes are the various contributory factors to the occurrence of the disease (Figure 1).

Neonates often acquire the infection from the mother by vertical transmission, the risk of which is highest when the mother is infected just before the delivery. Vertical transmission of chikungunya infection was first reported on La Rйunion Island in 2005[1]. Neonatal chikungunya can have varying presentations ranging from fever, persistent crying, generalized maculopapular rash, hyperpigmentation, severe thrombocytopenia, and encephalitis. Early identification of the illness is important as it can present encephalitic manifestations and long-term sequelae[3]. We present a series of four neonates with classical features who presented during the outbreak of chikungunya.

CASE REPORT

Case 1

An eight-day-old term neonate was admitted with a history of fever, generalized erythematous maculopapular rash, and persistent irritable crying (Figure 1). There was no vomiting, lethargy, refusal to feed, convulsions, or respiratory distress. There were no localizing signs. The baby was started on empirical antibiotics with a provisional diagnosis of late-onset sepsis. The neonate was full term at birth (40 + 2 weeks), born to a P2 L2 mother who did not have significant antenatal or intrapartum complications, and was discharged on day three from the hospital.

The septic screen revealed thrombocytopenia with a platelet count of 93.000/mm^3. The qualitative CRP test was positive, indicating the presence of inflammation. The blood culture was sterile, and radiological investigations showed no abnormalities. Additionally, both dengue and scrub typhus serology tests were negative. The renal function test and liver enzymes were normal. There was a persistence of fever with the appearance of hepatosplenomegaly and characteristic hyperpigmentation involving the perioral and nasal region by day two of admission which warranted evaluation for chikungunya which was reported as IgM positive. This was later confirmed by PCR for chikungunya for both mother and the neonate.

Figure 1. Classical hyperpigmentation involving the nose and perioral region.

The baby became afebrile on day five of admission. The repeat counts demonstrated an improvement in platelet count, and the baby was discharged on day eight of admission.

Case 2

A nine-day-old term baby was admitted for evaluation of hyperpigmentation involving the perioral region (Figure 1). The mother had a history of fever one week prior to the delivery of the baby which was managed with antipyretics. During the examination, the baby did not show any significant abnormality except for hyperpigmentation. The baby was evaluated for the cause of hyperpigmentation, the septic screen was normal, renal parameters and hepatic enzymes were normal, and the radiological workup was normal. Seventeen OHP was done to rule out congenital adrenal hyperplasia was within normal limits; methemoglobin levels were also normal. Serology for chikungunya was sent which was positive for IgM. PCR was performed to confirm the same and was reported positive.

Case 3

A 16-day-old female baby with a history of fever for three days was admitted. There was a history of maternal fever three days prior to delivery for which she was managed with antipyretics. The postpartum period was uneventful. On day 13 of life, the baby developed a fever and incessant crying for which the neonate was referred. During the examination, the neonate was irritable and had a generalized maculopapular rash (Figure 1). Another examination was significantly normal, the baby was started on antibiotics with a working diagnosis of late-onset sepsis.

The hematological workup was essentially normal. The blood culture was sterile, and CRP was negative. Chikungunya virus-specific IgM antibodies by IgM were positive. The baby was discharged on the 20^{th} day of life after an afebrile period of two days.

Case 4

An early-term (37 weeks) neonate was admitted on day four of life for poor feeding and a fever of 108.2 F. At admission, the child was excessively irritable and crying constantly. He had a generalized maculopapular rash, but his heart rate, respiratory rate, and blood pressure were normal for his age (Figure 1). He had no organomegaly, and his cardiovascular examination was normal. There was a history of fever in the mother three days before delivery. The baby was started on antibiotics and a workup for sepsis was done. He developed seizures and apnea requiring anticonvulsants and mechanical ventilation six hours after admission. There was no recurrence of seizures or apnea spells and was extubated in 48 hours. The septic workup was normal. The blood culture was sterile, and CRP was positive. CSF revealed glucose 65 mg/dL (concomitant blood glucose 80 mg/dL), protein 45 mg/dL cell count was negative for any cells and CSF culture was sterile. Serum lactate, pyruvate, and TMS were normal. Chikungunya virus-specific IgM antibodies by IgM were positive. Magnetic resonance imaging revealed a diffusion-resisting T2 hyper-intense lesion involving the bilateral frontoparietal deep white matter, corpus callosum, internal capsule, and posterior thalamus which were suggestive of chikungunya encephalitis (Figure 2). Magnetic resonanca imaging spectroscopy was normal. The baby improved dramatically and was discharged on day 19 of life. In our cases, we noticed the findings represented in Tables 1 and 2.

DISCUSSION

Chikungunya is a viral disease transmitted by the bite of infected mosquitoes. Chikungunya virus was first isolated in 1953, in Tanzania. Among adults, it can cause fever, headache, fatigue, nausea, vomiting, muscle pain, rash, and joint pain[1-3]. Unlike dengue, hemorrhagic manifestations are relatively rare, and shock is a rare clinical presentation of chikungunya infection. The incubation period (time from infection to illness) is 2 to 14 days and "silent" infections (infections without illness) are common[4,5].

Among neonates, the common clinical presentations are fever, excessive crying, maculopapular rash, nasal blotchy erythema, freckle-like pigmentation over the centrofacial area, and vesicular bullous lesions. Conditions that present with fever and rash in neonates must be considered during the differential diagnosis.

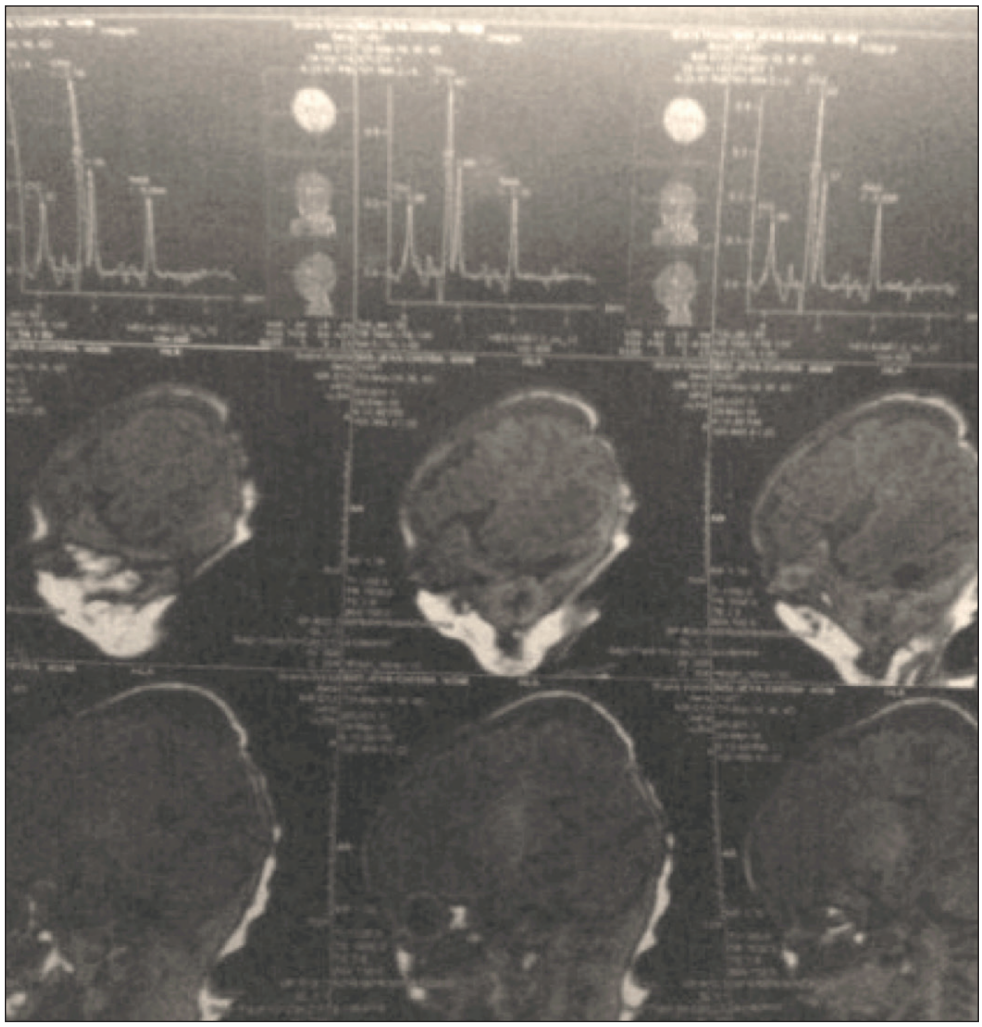

Figure 2. Magnetic resonance imaging revealing T2 intense images from the bilateral frontoparietal deep white matter, corpus callosum, internal capsule, and posterior thalamus suggestive of chikungunya encephalitis.

Table 1. Clinical presentation

Symptoms	No of cases n (%)
Hyper pigmentation	4 (100%)
Fever	3 (75%)
Lethargy	2 (50%)
Convulsions	1 (25%)
Persistent crying	3 (75%)
Maculopapular rash	3 (75%)

Table 2. Laboratory parameters

Lab parameters	No of cases n (%)
Thrombocytopenia	3 (75%)
Hypoglycemia	1 (25%)
Hyperbilirubinemia	2 (50%)
Elevated CRP	2 (50%)
Electrolyte imbalance	0
Elevated liver enzymes	1 (25%)
Serum IgM positivity in both mother and baby	4 (100%)
RNA PCR positive in both mother and baby	2 (50%)

Conditions such as neonatal dengue, herpes infection, TORCH infections, and generalized sepsis can present similarly. Other manifestations among neonates include apnea and circulatory shock in rare situations[6-9].

Neurological complications such as meningoencephalitis have also been reported in patients during the first Indian outbreak as well as in the recent French Rйunion Island outbreaks[3-6].

In our case series, we have observed and documented most of the clinical presentations that have been reported in the literature. The vertical transmission of the chikungunya virus has been previously documented in the literature, particularly from Rйunion island[7,8]. Robillard PY et al.[9] also reported that transplacental transmission of chikungunya can also occur before 16 weeks and suggest the virus played a direct role in fetal deaths. When vertical transmission occurs it usually leads to encephalitis in the affected neonate[3,9].

The CHIMERE cohort study provides neurocognitive functions of infants infected by the maternal-fetal transmission of CHIKV at birth. This study demonstrated that infected children exhibit poorer neurocognitive skills. CHIKV encephalopathy gives the poorest neurocognitive outcome. Gérardin P concluded that the neurocognitive outcome of children exposed to perinatal mother-to-child CHIKV infection is poor[10]. Hence, these infected neonates need to be followed up for neurocognitive defects when they grow up.

Diagnosis is typically established by reverse transcription polymerase chain reaction (RT-PCR) test or serology. Anti-CHIKV IgM antibodies are detectable after an average of 2 days (1-12 days) by enzyme-linked immunosorbent assay (ELISA) and remain positive for several weeks to three months. IgG antibodies can be detected in the convalescent samples a few weeks later and persist for years. CHIKV infection seems to provide long-lasting protective immunity[10].

Our study confirmed previously reported findings, including the presence of hyperpigmentation, fever, and maculopapular rash, which are commonly observed in neonates with this condition.

Our study reinforces the importance of considering Chikungunya as a potential diagnosis in neonates presenting with high-grade fever and erythematous rash. Additionally, our findings highlight the frequent poor neurocognitive outcome in children exposed to perinatal mother-to-child CHIKV infection, emphasizing the need for long-term follow-up of neonates diagnosed with Chikungunya.

CONCLUSION

Tropical fever epidemics are common in the Indian subcontinent. Early recognition and appropriate supportive care form the mainstay of management in case of viral fevers like dengue and chikungunya. This report aims to emphasize the diverse clinical manifestations of chikungunya in neonates and underscore the importance of closely monitoring neonates infected with chikungunya due to their elevated risk of experiencing neurodevelopmental delays.

ETHICS COMMITTEE APPROVAL

This study was approved by the Saveetha Medical College and Hospital Institutional Ethics Committee (Decision no: SMC/IEC/2021/03/091, Date: 25.03.2021).

CONFLICT of INTEREST

No conflict of interest declared.

AUTHORSHIP CONTRIBUTIONS

Concept and Design: SKK

Analysis/Interpretation:SKK

Data Collection or Processing: SKK

Writing: SKK

Review and Correction: SKK

Final Approval: SKK

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Address for Correspondence/Yazışma Adresi

Dr. Santosh Kumar KAMALAKANNAN

Department of Neonatology,
Saveetha University Medical College,
Kancheepuram, India
E-mail: drsantoshmddm@gmail.com