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DERMATOLOGICAL ATYPICAL MANIFESTATIONS OF CHIKUNGUNYA INFECTION IN TAMILNADU- 2010

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ABSTRACT

Chikungunya fever is an important arthropod-borne viral disease. The re-emergence of Chikungunya fever in 2006 has drawn global attention due to its explosive onset, rapid spread, high morbidity and myriad clinical atypical manifestations. The aim of the present work was to look for atypical manifestations following CHIKV infection in southern districts of Tamilnadu during 2010 outbreak. In this study we have isolated CHIKV from 2010 outbreak cases IgM Elisa performed and analyzed statistically for atypical manifestation. A total of 90 suspected cases were screened for Chikungunya by IgM capture ELISA, and Chi-square test was used for comparing categorical data, using Graph Pad Prism 5.0 analysis. Hyper pigmentation and thickening of nasolabial region and spreading to maxillary region, ear lobes were observed in ten of the IgM CHIKV positive cases. They also had hyper pigmentation in the arms, legs and in palms and soles. Whether these dermatological atypical manifestations are due to an unusual host response to the virus or due to mutant variants of CHIKV is unknown.

KEYWORDS: **IgM Capture ELISA, CHIKV, Atypical manifestations**

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INTRODUCTION

Chikungunya was first isolated from the blood of a febrile patient in Tanzania in 1953[1,2]. CHIKV ischaracterized by severe joint pain and rash [3]. Arthralgia is often polyarticular and symmetrical involving knees, elbows, ankles, small joints, and also sites of previous injuries [4].The rash characteristically appears on the first day of illness, it usually arises as a flush over the face and neck, which evolves to a maculopapular or macular form with pruritus. Although, similar to dengue, but significant hemorrhage is not a characteristic feature. Chikungunya infection usually causes a self-limited febrile illness [5]Including neurologic manifestations reported during the first Indian outbreak [6,7].Atypical clinical features noted in the 2005–2007 outbreak from Reunion Island [8]included neurologic manifestations in adults, fetuses and neonates,mother-to-childtransmission,meningoencephalitis,myocarditis, hepatitis, and extensive dermal lesions [9] and a number of deaths which were attributed[10]d
irectlyor indirectly, to Chikungunya. We describe the atypical clinical manifestations oflaboratory-confirmed Chikungunya cases during Chikungunya outbreak in 2010, in the southern districts of Tamilnadu.

MATERIALS AND METHODS

Sample collection and patients

Investigation of an outbreak of suspected Chikungunya in December 2010, in the southern districts of Tamilnadu was undertaken. We interviewed and examined the patients after obtaining informed consent, documented their clinical course and serum samples were collected, The study was done using ethically approved methods in outbreaks.

Clinical specimens and testing

90 Serum sample were collected from suspected patients and transported on ice to the laboratory at the King Institute of Preventive Medicine and Research, Guindy, Chennai, Tamilnadu India.

IgM Elisa

Serum samples were categorized as per the symptoms by physician and subjected Chikungunya IgM MAC Enzyme linked immunosorbant assay as per the standard protocol.

Case definitions

A suspected case of Chikungunya was defined as one who is hospitalized, or recent history of sudden onset of fever and/or joint pain. Cases without any systemic syndrome requiring maintenance therapy or monitoring of vital functions or leading to deaths were considered as classical Chikungunya. These cases had no neurologic, renal, hepatic, respiratory,cardiacorhematologic manifestations. Severe Chikungunya was defined as cases with one or more systemic syndromes, other than joint manifestations, that required maintenance or monitoring of vital function or was fatal [11,12,13.] Co morbidity was defined as a pre-existing medical disorder considered by the physician to be significant. Non-neurologic syndromes were defined as manifestations not associated with classical Chikungunya that were not neurologic. These were categorized as renal, hepatic, cardiac, respiratory, dermal and hematologic.A laboratory-confirmed case was taken as a suspected case tested positive for anti-CHIKV IgM antibodies. Patients with sera positive for both anti-CHIKV and anti-DENV IgM antibodies were considered as Chikungunya positive cases, whereas those positive only for anti-DENV IgM antibodies were considered Dengue positive and excluded [13].

Statistical analysis

The Chi-square test was used for comparing categorical data, using Graph Pad Prism 5.0 analysis. Odds ratios (OR) with 95% confidence interval (CI) were calculated.

RESULTS

A total of 90 suspected cases were screened for Chikungunya by IgM capture ELISA, of this 53 were from males and 37 samples were collected from females. IgM ELISA was positive for 73 cases (81.1%). Among the 53 males from whom samples were collected 37(70%) were positive by IgM capture ELISA. Serum samples were collected from 37 women suspected with CHIKV infection, of this 36(97%) were positive (Table 1).This difference in positivity was insignificant with p =0.2949. It was also observed that 45-55 age group was predominantly positive than the other age groups, both among the males and females, which had a P=0.9104. All the cases from whom samples were collected presented with fever and arthralgia. Eighty two (91%) of them suffered from headache and 93% had severe myalgia. Maculopapular rashes were observed in 12 (13.3%) positive patients. Hemorrhagic manifestations seen in 4 (4.4%) of cases. (Table 2) The platelet count was below 75,000 in these four cases. Dengue IgM ELISA was done in all the 90 cases, of this 4 were IgM Dengue positive. They were also IgM CHIKV positive suggesting concurrent infection of Dengue with Chikungunya. Further investigations were not done in this respect. It was also noticed that the platelet counts were normal for these patients. Hyper pigmentation and thickening of nasolabial folds as well as maxillary region and hyper pigmentation of bilateral ear lobes were observed in ten of the IgM CHIKV positive cases. They had also developed hyper pigmentation of the palms, feet and in the calf muscle region. [Fig 1] All these patients were from different but adjoining villages. Atypical manifestations were observed most in the 15-45 age group and followed by the 45-55 age group. None of the suspected patients had neural involvement. Five of the ninety patients required admission but were discharged within four days.

Table 1
Gender wise and age wise distribution of positive cases by IgM ELISA

		15-45(31)	45-55(49)	>55(10)	Total(90)
Male(53)	Positive	14	20	3	37(70%)
	Negative	7	6	3	16
Female(37)	Positive	10	22	4	36(97%)
	Negative	-	1	-	1
Total(90)		31	49	10	90

Table 2
Clinical profile among positive cases

Symptoms	Total No of cases presented with symptoms	Percentage %
Fever	90	100%
Head ache	82	91%
Arthralgia	90	100%
Heamorrhagic Manifestation/petechiae	4	4.4%
Myalgia	84	93%
Rashes	12	13.3%

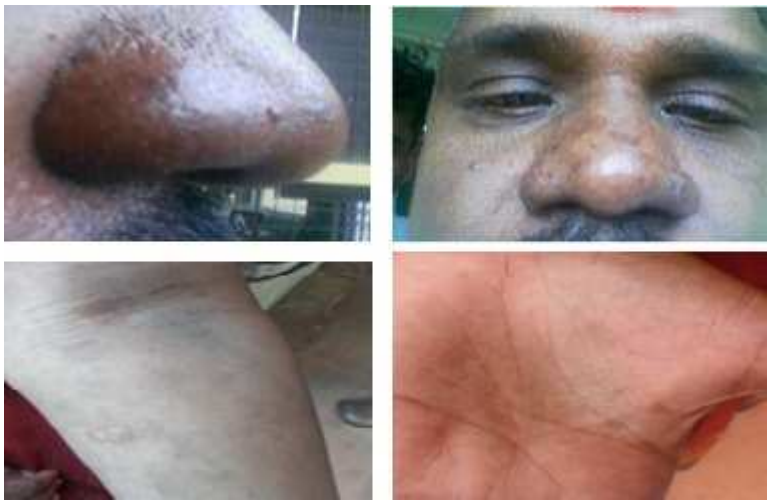

Figure 1
Hyper pigmentation and thickening of nasobial folds as well as maxillary regions and palms feet the calf muscle region

DISCUSSIONS

The most commonly documented dermatological manifestation in a 'typical' CHIKV infection is a maculopapular rash starting over the face and neck area and spreading out. We had observed maculopapular rashes in 12(13.3%) patients involving face and trunk which had settled within four to five days[14]. As mentioned in a study from India, which reported that pigmentary changes were the commonest skin manifestation, seen in 42%, followed by maculopapular eruption (33%) and intertriginous aphthous-like ulcers (21.37%). Generalized vesiculo bullous eruptions (2.75%) were rarely seen, and were found only in infants. Similar to this study hyperpigmentary changes in the nasolabial region and in maxillary region was observed in 15 (16.6%) adults. Generalized vesiculo bullous lesions nor intertriginous aphthous-like ulcers were not seen during the outbreak. In none of the cases we had attempted to identify the CHIKV virus from the skin. Mishra and Rajawat [15] reported a series of 16 males with penoscrotal ulceration during an outbreak in central India in 2008.This was again not seen during this outbreak. There are references citing the occurrence of punched out deep ulcers with surrounding skin thickening and healthy granulation tissue at base and biopsy from one patient showed a perivascular mononuclear cell infiltrate which has been reported elsewhere as a consistent finding in CHIKV induced skin manifestations [16]. In our study, the hyper pigmented lesions were not indurated and had not progressed to ulcerative bullous lesions either. We had not made attempts to identify the CHIKV virus from the skin lesions. Most of the patients had arthralgia persisting up to four and six weeks, which had settled gradually. The affected individuals were treated symptomatically. There was no mortality. We had not done a long term follow up of the positive patients to comment upon whether they had suffered from chronic arthritis or arthralgia subsequent to CHIKV infection.

Prior to the outbreak in Reunion Islands in 2005–2006, Chikungunya was not considered to be a fatal illness. During that epidemic there were many reports of severe illness and deaths attributed to Chikungunya infection and its complications[17]mortality rates are variable, but have been reported as high as 48% [18].Atypical presentations and

complications of fever include neurological, cardiac, renal, skin and ocular manifestations that can have serious consequences for the patient. Pre-existing co-morbidity appears to increase the likelihood of most of these complications. The incidence of atypical manifestations appears to be higher in patients aged 65 years and over, with patients over 40 years of age are more likely to develop severe disease.[10] It is not known whether atypical manifestations are due to an unusual host response to the virus, or due to mutant variants of CHIKV. Intrapartum viraemia in mothers increases the risk of vertical transmission that may result in severe infection in neonates. Morbidity from these complications is likely to be significant especially at times of epidemics when infection spreads rapidly. CHIKV infection can result in serious illness requiring intensive care and can cause death. Furthermore, mortality analysis during times of epidemics have shown that an excess number of deaths have occurred during such period, though not directly attributed to illness.[19] Clinicians and epidemiologists should be alert to the wide range of clinical manifestations that can occur following CHIKV infection. Early detection of these complications by the treating clinicians will doubtless improve outcome and reduce mortality in severe cases. CHIKV infection should no longer be considered a disease with a benign course.

CONCLUSION

Thus CHIKV infection can result in serious illness requiring intensive care, and can cause death. Furthermore, mortality analysis during times of epidemics have shown that an excess number of deaths have occurred during such periods, though not directly attributed to illness. In conclusion, research work can further be initiated towards aiding the clinicians and public health personnel to evolve strategic treatment and management protocols..

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