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Chikungunya disease among infants in French West Indies during the 2014 outbreak

A. Gavotto^{a,b,*}, B. Muanza^a, F. Delion^a, J.-A. Dusacre^a, P. Amedro^b

^a Pediatric emergency, University Hospital, Pointe-à-Pitre, Guadeloupe

^b Pediatric and Congenital Cardiology Department, M3C Regional Center, University Hospital, Physiology and Experimental Biology of Heart and Muscles Laboratory - PHYMEDEXP, UMR CNRS 9214–INSERM U1046, Montpellier, France

ABSTRACT

Background: We aimed to describe the clinical and laboratory features of Chikungunya disease in infants aged from 1 month to 2 years.

Methods: This epidemiologic study was carried out at the Pointe-à-Pitre University Hospital from May to September 2014. We collected data prospectively from infants hospitalized for Chikungunya disease.

Results: A total of 154 infants were included. Hyperthermia was greater than 38.5 °C the first 48 h and during on average 2.7 days. Pain (on mobilization and/or cutaneous hyperesthesia and/or arthralgia) was present in 82% of the cases. Loss of appetite was reported for 62% of the infants. Initial maculopapular erythematous eruption occurred in 69% of the cases. A vesiculobullous eruption was secondarily observed in 7% of the cases. Edema on the feet and/or hands was present in 48% of the cases. Febrile seizure was observed in 12% of the cases. Lymphopenia was the most frequent laboratory finding, present in 94% of the infants. No cases of thrombocytopenia were observed. The reported complications were: bullous epidermolysis, state of epilepticus, and severe acute hepatitis.

Conclusion: This study highlights a suggestive clinical presentation of Chikungunya diseases combining pain, fever, tachycardia, foot and/or hand edema. Lymphopenia, monocytosis, and the absence of thrombocytopenia were relevant biological signs.

Keywords:
Chikungunya
Fever
Arbovirus
French West Indies
Pediatrics
Infant

1. Introduction

“Chikungunya” means “that which bends up” in Makonde language. The epidemic in the West Indies officially started on December 13, 2013, on Saint Martin Island, where the first two indigenous cases were observed. It then spread to Martinique where the first case was identified on December 18, 2013, and to Guadeloupe on December 24, 2013. Guadeloupe was considered in an epidemic situation on April 10, 2014 [1]. On September 18, 2014, the Antilles-Guyana Center for Disease Control estimated that the epidemic affected 40.7% of the population in Guadeloupe (403,355 inhabitants) [1].

The Chikungunya virus (CHIK-V) is an arbovirus, member of the *Alphavirus* genus [2] and *Togaviridae* family. It is transmitted to humans by two main species of mosquito of the *Aedes* genus (*A. aegypti* and *A. albopictus*) [3–6]. The *A. aegypti* mosquito was

already well known on the island for endemic transmission of dengue [7], the main differential diagnosis [8,9].

Phylogenetic analysis revealed that the strains collected in Guadeloupe and Martinique islands belonged to the Asian genotype circulating in the Caribbean, while those found on Reunion Island in 2006 belonged to the African genotype [10,11].

The disease is characterized by an incubation period lasting 2–7 days. Clinically, Chikungunya is suspected upon the association of an acute onset of high fever and severe joint pain. Symptoms may also combine myalgia, headache, nausea, vomiting, diarrhea, rash (limbs, trunk), pruritus, and gingival bleeding [6,8,12,13]. The definitive diagnosis is made through viral isolation, reverse transcriptase polymerase chain reaction (RT-PCR), or serological diagnosis [14–16].

A few observational studies have emphasized the clinical features of Chikungunya in children; however, they usually described a different clinical presentation from that observed in adults. Data from the pediatric population during the 2006 epidemic on Reunion Island reported symptoms such as high fever, joint pain, rash, and thrombocytopenia [17]. Moreover, this epidemic also pointed out several specific pediatric symptoms,

* Corresponding author. Service de cardiologie pédiatrique et congénitale, CHU Arnaud de Villeneuve, 371 avenue du doyen Gaston-Giraud, 34295 Montpellier cedex 5, France.

E-mail address: arthur.gavotto@gmail.com (A. Gavotto).

such as neurological impairment (encephalitis, febrile seizures, meningeal syndrome, acute encephalopathy) [18], cardiac lesions [17] and bullous skin lesions [19].

However, few clinical, epidemiological, and laboratory data are available for children aged less than 2 years, because they commonly do not present any typical functional symptoms.

We aimed to describe the clinical and biological presentation of Chikungunya disease among infants aged from 1 month to 2 years. We also intended to identify specific diagnosis criteria for Chikungunya disease in this young population.

2. Methods

2.1. Study design

This single-center cross-sectional epidemiological study was conducted in the pediatric units of Pointe-à-Pitre University Hospital (PAPUH), French West Indies (Guadeloupe), France. Data were prospectively collected from May 1, 2014, to September 19, 2014. Recruitment ended at the end of the generalized epidemic declared by the Antilles-Guyana Center for Disease Control [1]. The study was conducted in compliance with the Good Clinical Practices protocol and Declaration of Helsinki principles. In accordance with the Jarde law, formal approval from an ethics committee was not required for this observational study.

2.2. Population

We included all children aged from 1 month to 2 years who consulted in the PAPUH pediatric emergency room and were subsequently hospitalized for Chikungunya according to PCR testing. To exclude with certainty the existence of any maternal-fetal infection [20], children aged less than 1 month were not eligible.

2.3. Data collected

We reviewed the clinical criteria for Chikungunya disease from the literature [8,14–17]. A “Chikungunya suspected diagnosis sheet” was created to be filled out by the pediatricians for each eligible child. This document was divided into two parts: the first part described the patient’s characteristics and the first clinical examination at the emergency room; the second part concerned the infant’s progression throughout the hospitalization.

For each child, the initial biological examination included a complete blood count, platelets, blood ionogram, serum creatinine, C-reactive protein (CRP), aspartate and alanine aminotransferase (AST-ALT), urine cytobacteriology, blood cultures, and Chikungunya RT-PCR. A chest X-ray was performed when required. No systematic hemostasis assessment was performed in this study. The diagnosis of Chikungunya was based on the detection of viral RNA by RT-PCR [21].

2.4. Statistical analysis

The patients’ characteristics are presented using mean and standard deviation for continuous variables, and frequencies and proportions for qualitative variables.

3. Results

Over the 20-week study period, 154 children aged less than 2 years were hospitalized in the PAPUH center as a result of Chikungunya disease with positive RT-PCR.

3.1. Demographic criteria

The children’s mean age was 7.2 ± 5.2 months, the sex ratio was 1.4. Eating disorders (25%) and low age (22%) were the first two reasons for hospitalization. Children under the age of 3 months and children with a history of sickle-cell anemia were systematically hospitalized. The average length of the hospital stay was 2.6 ± 1.2 days. The bed occupancy rate for Chikungunya at the peak of the epidemic (weeks 27–30) was 51% [41–70%]. It is notable that 38% of the children included had been seen by a physician before their hospital admission. The number of visits to the PAPUH pediatric emergency room during this period for suspected Chikungunya accounted for 15% of the overall consultations.

3.2. Clinical presentation

Elevated fever was observed in all cases of Chikungunya disease. At day 1, the average body temperature was 39.9 ± 0.6 °C and, at day 2, 39.5 ± 0.7 °C. The fever lasted on average 2.7 ± 0.9 days.

Tachycardia was found in 88% of cases in the initial management of Chikungunya disease. In terms of pain, 82% of children had an algic syndrome (pain at mobilizing, and/or cutaneous hyperesthesia, and/or arthralgia). The hyperesthesia was more frequently found in the youngest children (< 6 months) and arthralgia was mostly reported in older children who could walk (> 12 months). When initially reported, the painful episode lasted on average 2.2 ± 0.9 days. We defined the end of this painful episode as the time when prescription of any painkillers was suspended. The majority of infants with Chikungunya disease presented feeding or digestive disorders: loss of appetite (62%), refusal of food (19%), vomiting (21%), and diarrhea (14%). An initial maculopapular erythematous eruption was present in 69% of the cases and a bullous eruption secondarily appeared in 7.3% of the cases. Edema on the feet and/or hands occurred in 25% of the cases upon hospital admission and in 48% when considering the overall progression. Febrile seizure was reported for 12% of children, but no other specific neurological sign was reported (Table 1); it mostly concerned older children (36% of the children older than 12 months). No hemorrhagic syndrome occurred in this cohort. A recent history of Chikungunya disease within the family was reported in 57% of cases.

3.3. Biological presentation

Lymphopenia ($< 4 \times 10^9/L$) was found in 94% of the cases, with a mean value of $1.86 \pm 1.14 \times 10^9/L$; it was more severe in the early stage of the disease with an average count of $1.55 \pm 0.84 \times 10^9/L$ at day 1 and of $2.3 \pm 1.28 \times 10^9/L$ at day 2. Neutrophils (normal values [$1.5\text{--}8.5 \times 10^9/L$]) were increased in 19% of cases with a mean value of $6.01 \pm 2.59 \times 10^9/L$. Secondary neutropenia ($< 1.5 \times 10^9/L$) (as of day 3) was found in 35% of the cases. Monocytosis ($> 0.11 \times 10^9/L$) was constant on the initial stage with a mean value of $0.9 \pm 0.3 \times 10^9/L$. No case of thrombocytopenia was reported, with a mean value of $287 \pm 86 \times 10^9/L$.

The CRP was positive (> 5 mg/L) in 76% of cases on day 1 (19.9 ± 20.25 mg/L) and 97% on day 2 (33.7 ± 24.5 mg/L), with a maximum value of 103.4 mg/L. Procalcitonin (PCT) was measured for 45 children (29%) and was positive (> 0.5 ng/mL) in 62% of the cases. Hepatic cytolysis was observed with increased AST values (> 33 IU/L) in 71% of cases (47.4 ± 35.3 IU/L) and increased ALT values (> 33 IU/L) in 11% (21.4 ± 14.5 IU/L).

3.4. Complications

We reported one case of epidermolysis bullosa, affecting 15% of the cutaneous surface, two cases of status epilepticus, and one case of severe acute hepatitis. The case of severe acute hepatitis was an isolated Chikungunya infection with negative dengue serology,

Table 1
Clinical and biological features of Chikungunya at hospital admission according to age.

Age	1–3 months	3–6 months	6–12 months	> 12 months	Total
Number of patients	n = 27	n = 57	n = 45	n = 25	n = 154
Male gender (n, %)	13 (48%)	38 (67%)	24 (53%)	16 (64%)	91 (59%)
Mean fever ($^{\circ}$ Celsius \pm SD)	38.7 \pm 0.7	39.2 \pm 0.7	39.3 \pm 1	39.3 \pm 0.6	39.2 \pm 0.8
Heart rate (BPM) (mean \pm SD)	198 \pm 19	190 \pm 18	181 \pm 21	165 \pm 21	185 \pm 22
Tachycardia related to the age (n, %)	24 (89%)	52 (91%)	40 (89%)	19 (76%)	135 (88%)
CRT > 3 s (n, %)	8 (30%)	24 (42%)	5 (11%)	5 (20%)	42 (27%)
Marbling (n, %)	3 (11%)	5 (9%)	1 (2%)	2 (8%)	11 (7%)
Intravenous infusion required (n, %)	7 (26%)	10 (18%)	3 (7%)	4 (16%)	24 (16%)
Pain (n, %)	24 (89%)	50 (88%)	34 (76%)	18 (72%)	126 (82%)
Hyperesthesia (n, %)	20 (74%)	32 (56%)	18 (40%)	6 (24%)	76 (49%)
Pain at mobilizing (n, %)	14 (52%)	36 (63%)	21 (47%)	11 (44%)	82 (53%)
Arthralgia (n, %)	0 (0%)	0 (0%)	6 (13%)	11 (44%)	17 (11%)
Eruption (n, %)	23 (85%)	42 (74%)	27 (60%)	14 (56%)	106 (69%)
Loss of appetite (n, %)	19 (70%)	45 (79%)	40 (89%)	22 (88%)	126 (82%)
Diarrhea (n, %)	3 (11%)	8 (14%)	9 (20%)	1 (4%)	21 (14%)
Febrile seizure (n, %)	0 (0%)	1 (2%)	8 (18%)	9 (36%)	18 (12%)
Edema (n, %)	3 (11%)	19 (33%)	13 (29%)	4 (16%)	39 (25%)
Lymphocyte count (G/L) (mean \pm SD)	1.23 \pm 0.67	1.82 \pm 1.14	2.15 \pm 1.32	2.15 \pm 0.99	1.86 \pm 1.14
Platelets (G/L) (mean \pm SD)	324 \pm 87	289 \pm 86	278 \pm 89	255 \pm 64	287 \pm 86
CRP (mg/L) (mean \pm SD)	12.5 \pm 11.6	25.3 \pm 18.5	26.7 \pm 26	28.5 \pm 28.8	23.9 \pm 22.3

Values are means \pm standard deviation (SD) and n (%). BPM, beats per minute; CRT: capillary refill time; CRP: C-reactive protein; G/L: 10^9 per liter; mg/L: milligram per liter.

hepatitis A, B, and C negative serology, and no suspicious drug intake. The disease regressed spontaneously. No death was reported.

4. Discussion

This large cohort of 154 infants provided original data on Chikungunya disease in a young population of children aged less than 2 years old.

In comparison with the 2006 epidemic study on Reunion Island [17], we found similar results in terms of occurrence of hyperthermia, rash, digestive disorders, febrile seizure, and lymphopenia. Nevertheless, this study highlighted the relevant occurrence of pain among infants, as well as the high frequency of foot or hand edema.

Moreover, as in the 2006 epidemic study, we found no hemorrhagic syndrome and no thrombocytopenia. The occurrence of a severe bullous skin eruption was less frequent in the present study [17,19]. The 2006 epidemic study reported two deaths (meningoencephalitis, multiple organ failure), while none occurred in our cohort. However, this study did not include neonates, who usually have severe presentations. A similar study, conducted over the same period in the PAPUH adult department, reported 12 deaths [22].

The present study provided useful data on the clinical presentation of Chikungunya disease in infants aged less than 2 years: pain, fever $>$ 38.5 $^{\circ}$ C, maculopapular erythematous eruption, foot and/or hand edema, tachycardia, and nonspecific digestive symptoms, and a few cases of bullous eruption secondarily. These results are in line with the recent study carried out in French Guiana by Elenga et al. in infants aged less than 3 months old with Chikungunya disease [23]. The biological presentation included lymphopenia, monocytosis, and the absence of thrombocytopenia.

Our study highlighted the frequency of pain at clinical presentation of Chikungunya disease in infants. The regular and systematic evaluation of the pain by an appropriate pediatric scale is therefore necessary in this condition [24]. The management of the pain mainly consisted in level 1 analgesics (paracetamol) and sometimes in level 2 analgesics (nalbuphine) during the first 24 h of hospitalization.

This study presented some limitations. The results are related to a population of hospitalized infants, which may increase the

severity of the symptoms. We did not investigate the cardiac involvement of the disease among infants, whereas pericarditis, heart dyskinesia, and coronary artery disease have been reported previously [17,25].

We purposely did not include neonates in this study because maternal–fetal Chikungunya infections have specific and severe clinical features [26].

5. Conclusion

In 2014, the Chikungunya epidemic affected 40% of the Guadeloupe population in just a few months. Pediatricians had to diagnose issues among the youngest population, especially infants. From a cohort of 154 infants, this study highlighted a suggestive clinical presentation of Chikungunya diseases combining pain, fever, tachycardia, and edema of the feet or hands. Lymphopenia, monocytosis, and the absence of thrombocytopenia were relevant biological signs.

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Disclosure of interest

The authors declare that they have no competing interest.

References

- invs.sante.fr. Situation épidémiologique du chikungunya dans les Antilles. Point-au-20-novembre-2014. <http://invs.santepubliquefrance.fr/fr./Publications-et-outils/Points-epidemiologiques/Tous-les-numeros/Antilles-Guyane/2014/Situation-epidemiologique-du-chikungunya-dans-les-Antilles>.
- Stapleford KA, Coffey LL, Lay S, Borderia AV, et al. Emergence and transmission of arbovirus evolutionary intermediates with epidemic potential. *Cell Host Microbe* 2014;15:706–16.
- Staples JE, Fischer M. Chikungunya virus in the Americas—what a vectorborne pathogen can do. *N Engl J Med* 2014;371:887–9.
- Lahariya C, Pradhan SK. Emergence of chikungunya virus in Indian subcontinent after 32 years: a review. *J Vector Borne Dis* 2006;43:151–60.
- Burt FJ, Rolph MS, Rulli NE, et al. Chikungunya: a re-emerging virus. *Lancet* 2012;379:662–71.
- Weaver SC, Lecuit M. Chikungunya virus and the global spread of a mosquito-borne disease. *N Engl J Med* 2015;372:1231–9.
- Pialoux G. Infection à virus Chikungunya : revue générale par temps d'épidémie. *Med Mal Infect* 2006;253–63.

- [8] Laoprasopwattana K, Kaewjungwad L, Jarumanokul R, et al. Differential diagnosis of Chikungunya, dengue viral infection and other acute febrile illnesses in children. *Pediatr Infect Dis J* 2012;31:459–63.
- [9] Calvo EP, Coronel-Ruiz C, Velazco S, et al. Dengue and Chikungunya differential diagnosis in pediatric patients. *Biomed Rev Inst Nac Salud* 2015;36:35–43.
- [10] Stapleford KA, Moratorio G, Henningson R, et al. Whole-genome sequencing analysis from the Chikungunya virus Caribbean outbreak reveals novel evolutionary genomic elements. *PLoS Negl Trop Dis* 2016;10:e0004402.
- [11] Weaver SC. Arrival of Chikungunya Virus in the New World: prospects for spread and impact on public health. *PLoS Negl Trop Dis* 2014;8:e2921.
- [12] Jupp P, McIntosh B. Chikungunya virus disease. In: Monah T, editor. *The arboviruses: epidemiology and ecology*. Boca Raton, FL: CRC Press; 1988. p. 137–57.
- [13] Laoprasopwattana K, Suntharasaj T, Petmanee P, et al. Chikungunya and dengue virus infections during pregnancy: seroprevalence, seroincidence and maternal-fetal transmission, southern Thailand, 2009–2010. *Epidemiol Infect* 2016;144:381–8.
- [14] Weaver SC, Lecuit M. Chikungunya virus infections. *N Engl J Med* 2015;373:94–5.
- [15] Cabié A, Ledrans M, Abel S. Chikungunya virus infections. *N Engl J Med* 2015;373:94.
- [16] Simon F, Javelle E, Gasque P. Chikungunya virus infections. *N Engl J Med* 2015;373:93–4.
- [17] Ernould S, Walters H, Alessandri JL, et al. Aspects pédiatriques de l'épidémie de Chikungunya à l'île de la Réunion. *Arch Pédiatr* 2008;15:253–62.
- [18] Robin S, Ramful D, Le Seach' F, et al. Neurologic manifestations of pediatric chikungunya infection. *J Child Neurol* 2008;23:1028–35.
- [19] Robin S, Ramful D, Zettor J, et al. Severe bullous skin lesions associated with Chikungunya virus infection in small infants. *Eur J Pediatr* 2010;169:67–72.
- [20] Haas H, Robin S, Ramful D, et al. Infections à virus Chikungunya chez l'enfant. *Arch Pédiatr* 2009;16(Suppl. 2):S72–9.
- [21] Pfeffer M, Linssen B, Parke MD, Kinney RM. Specific detection of chikungunya virus using a RT-PCR/nested PCR combination. *J Vet Med B Infect Dis Vet Public Health* 2002;49:49–54.
- [22] Rollé A, Schepers K, Cassadou S, et al. Severe sepsis and septic shock associated with chikungunya virus infection, Guadeloupe, 2014. *Emerg Infect Dis* 2016;22:891–4.
- [23] Elenga N, Folin M, Vandamme YM, et al. Chikungunya infection in hospitalized febrile infants younger than 3 months of age. *Pediatr Infect Dis J* 2017;36:736–40.
- [24] Fournier-Charrière E, Tourniaire B, Carbajal R, et al. EVENDOL, a new behavioral pain scale for children ages 0 to 7 years in the emergency department: design and validation. *Pain* 2012;153:1573–82.
- [25] Pellot AS, Alessandri JL, Robin S, et al. Infections graves a virus chikungunya en réanimation pédiatrique à l'île de La Reunion. *Med Trop* 2012;72 Spec No:88–93.
- [26] Gérardin P, Barau G, Michault A, et al. Multidisciplinary prospective study of mother-to-child chikungunya virus infections on the island of La Réunion. *PLoS Med* 2008;5:e60.