

Letters

RESEARCH LETTER

Main Characteristics of Zika Virus Exanthema in Guadeloupe

Zika virus (ZIKV) has recently started to spread in the Americas leading to successive outbreaks from Brazil to the French West Indies.¹ The virus was declared a public health emergency by the World Health Organization because of its unpredictable associated morbidity (eg, fatal outcomes and severe neurologic complications).¹ However, the clinical characteristics of this emerging arbovirolosis are not completely known, and, to our knowledge, exanthema, the major symptom of ZIKV infection, has not been fully described.

Methods | This prospective study was conducted between February 1, 2016, and April 29, 2016, during a time of active ZIKV circulation preceding the outbreak on Guadeloupe, a French overseas territory in the West Indies. Our aims were to assess clinical characteristics of ZIKV exanthema at the time of ZIKV emergence and to familiarize physicians with its cutaneous features prior to the epidemic. All private-practice dermatologists, pediatricians, general practitioners, and hospital physicians in Guadeloupe were invited to record every case of exanthema possibly associated with ZIKV infection as defined by the World Health Organization (ie, erythematous eruption with or without fever and ≥ 1 of the following symptoms: arthralgia, arthritis, or nonpurulent conjunctivitis).¹ Suspected cases confirmed by reverse transcription-polymerase chain reaction with concomitant negative results for endemic Dengue virus were included. (Dengue is nonpruritic macular exanthema located on the trunk and limbs, including the palms and/or soles, with frequent hemorrhagic signs [ie, petechiae and purpura] associated with high-grade fever and flulike symptoms.²) Clinical patterns of ZIKV exanthema were described and compared between adults and children using appropriate statistical tests. The study was approved by the Ethics Committee for Non-interventional Research of Rouen University Hospital in Rouen, France.

Results | Ten of the 25 invited physicians collected 87 consecutive medical records of ZIKV exanthema. Of the 87 records, 60 were laboratory confirmed by reverse transcription-polymerase chain reaction.

Among the 60 confirmed cases, 31 were adults (mean [SD] age, 39 [12] years) and 29 were children (mean [SD] age, 7 [5] years), with a male to female ratio of 25 to 35 (0.71) and the following ethnic distribution: Afro-Caribbean (n = 30), white (n = 27), and Asian (n = 3) (Table). The exanthema's median body surface area was 45% (interquartile range [IQR], 25%-80%) with the following frequent sites: face (56 of 59 cases [95%]), upper limbs (57 of 60 [95%]), trunk (55 of 59 [93%]), abdomen (52 of 58 [90%]), lower limbs (50 of 58

Table. Clinical Characteristics of Zika Virus Exanthema in Adults and Children

Characteristic	No. (%)		P Value
	Adults (n = 31)	Children (n = 29)	
Type of exanthema ^a			.06
Micropapular (small tiny papules)	23 (77)	28 (97)	
Dengue "like" (confluent macules)	7 (23)	1 (3)	
Dynamism of the exanthema ^b			.81
Descending	19 (73)	19 (76)	
Ascending	7 (27)	6 (24)	
Body surface area with exanthema, median (IQR), %	50 (30-80)	40 (30-90)	.47
Location of the exanthema ^c			
Face	28 (90)	28 (100)	.27
Upper limbs	28 (90)	29 (100)	.26
Trunk	30 (97)	25 (89)	.53
Abdomen	27 (90)	25 (89)	>.99
Lower limbs	25 (83)	25 (89)	.78
Palms	8 (26)	10 (34)	.46
Soles	6 (19)	2 (7)	.30
Pruritus	25 (81)	24 (83)	.83
Moderate	12 (39)	13 (45)	.63
Intense	12 (39)	9 (31)	.53
With insomnia	8 (26)	2 (7)	.11
Acral edema	16 (52)	4 (14)	.002
Conjunctival hyperemia ^d	14 (48)	18 (64)	.22
Dysesthesia	19 (61)	12 (41)	.12
Autonomic symptoms ^e			
Dry mouth	12 (39)	9 (35)	.75
Lack of tolerance to heat	10 (32)	5 (17)	.18
Sweating troubles	7 (23)	4 (14)	.35
Dry eyes	5 (16)	3 (12)	.91
Bladder incontinence	2 (7)	4 (14)	.61
Associated low-grade fever ^c	16 (53)	17 (59)	.68

Abbreviation: IQR, interquartile range.

^a Data were missing for 1 adult.

^b Data were missing for 3 adults and 3 children. Patients (2 adults, 1 child) with ascending and descending exanthema were not taken into account.

^c Data were missing for 1 child.

^d Data were missing for 4 patients (2 adults, 1 child).

^e Data were missing for 4 patients (1 adult, 3 children).

[86%]), but rarely palms (18 of 60 [30%]) or soles (8 of 60 [13%]). In adults and children, the exanthema was mostly micropapular (51 of 59 cases [86%]), descending (38 of 54 [70%]), and pruritic (49 of 60 [82%]). Itching was the most common reason of medical consultation because of its high intensity (21 of 49 cases [43%]), with insomnia reported in 10

Figure. Zika Virus Exanthema in an Adult Woman



This case shows typical converging tiny red papules of the cheek associated with a conjunctival hyperemia.

of 49 cases (20%). A low-grade fever was present in 33 of 59 patients (56%). Associated mucous lesions mostly consisted of conjunctival hyperemia (32 of 57 cases [56%]). The acral edema classically reported in the literature was rarely observed in children (4 of 28 [14%]) in contrast to cases in adults (16 of 31 [52%]; $P = .002$).

Interestingly, most patients (19 adults and 12 children; 31 of 60 [52%]) complained of dysesthesia, which was possibly associated with these autonomic symptoms: dry mouth (21 of 57 cases [37%]), lack of tolerance to heat (15 of 60 [25%]), sweating disorder (11 of 59 [19%]), dry eyes (8 of 57 [14%]), and bladder incontinence (6 of 60 [10%]).

Discussion | Although not comparative in design, this study focused on ZIKV dermatological signs, which—compared with other endemic arboviruses in the Americas—included several original patterns (ie, itchy, micropapular exanthema rarely located on palms and soles with frequent conjunctival hyperemia [Figure]; high prevalence of dysesthesia; and possibly associated autonomic symptoms). These discriminating clinical features might be useful in cases of concurrent outbreaks of arboviruses given that systemic complications are not similar between Zika and Dengue or Chikungunya viral infections. (Chikungunya is nonpruritic, generalized maculopapular exanthema associated with high-grade fever and acute incapacitating arthralgia.³) Moreover, the association of pruritus with dysesthesia and autonomic symptoms strongly suggests a small-fiber neuropathy resulting from ZIKV, for which neurological tropism has now been clearly demonstrated.^{4,5} Similar to that of West Nile virus, another neurotropic RNA (ribonucleic acid) flavivirus, ZIKV axonal

transport from cutaneous small fibers to peripheral nerves might mediate Guillain-Barré syndrome, which has shown a high prevalence in the course of Zika infection but for reasons that remain unclear.⁶

Nadège Cordel, MD
 Xavier Birembaux, MD
 Hugo Chaumont, MD
 Frédérique Delion, MD
 Olivier Chosidow, MD, PhD
 Benoit Tressières, MD
 Cécile Herrmann Storck, MD

Author Affiliations: Dermatology and Internal Medicine Unit, Guadeloupe University Hospital, Pointe-à-Pitre, Guadeloupe (Cordel); EA 4546, Antilles University, Pointe-à-Pitre, Guadeloupe (Cordel); Office of Paediatrics, Basseterre, Guadeloupe (Birembaux); Department of Neurology, Guadeloupe University Hospital, Pointe-à-Pitre, Guadeloupe (Chaumont); Department of Pediatrics, Guadeloupe University Hospital, Pointe-à-Pitre, Guadeloupe (Delion); Department of Dermatology, AP-HP, Hôpital Henri Mondor, Créteil, France (Chosidow); Centre d'Investigation Clinique Antilles Guyane, Inserm CIC 1424, Paris, France (Tressières); Microbiology Laboratory, Guadeloupe University Hospital, Pointe-à-Pitre, Guadeloupe (Herrmann Storck).

Corresponding Author: Nadège Cordel, MD, Dermatology and Internal Medicine Unit, Guadeloupe University Hospital, BP 465, 97159 Pointe-à-Pitre CEDEX, France (nadege.cordel@chu-guadeloupe.fr).

Accepted for Publication: November 16, 2016.

Published Online: February 22, 2017. doi:10.1001/jamadermatol.2016.5442

Author Contributions: Dr Cordel and Mr Tressières had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Cordel.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Cordel, Chosidow.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Tressières.

Administrative, technical, or material support: Cordel, Herrmann Storck.

Study supervision: Cordel.

Conflict of Interest Disclosures: None reported.

Additional Contributions: We are indebted to the following Guadeloupean physicians for their help in recording patients' data: Annick Samyn-Winter, MD, Guadeloupean Society of Dermatology; Julie Ballandras, MD, general practice office; Lydie Cuhe, MD, general practice office; Audrey Cesaïre, MD, Guadeloupe University Hospital; Stéphane Pelczar, MD, Regional Hospital of Basse-Terre; and Stéphanie Guyomard, MD, Institut Pasteur de Guadeloupe. We thank Richard Medeiros, Medical Editing International, for editing various versions of the manuscript. We thank the patient depicted in the Figure for granting permission to publish this information. These individuals were not compensated for their contributions.

- Garcia E, Yactayo S, Nishino K, Millot V, Perea W, Briand S. Zika virus infection: global update on epidemiology and potential associated clinical manifestations. *WHO Wkly Epidemiol Rec.* 2016;91:73-88.
- World Health Organization. Dengue vaccine: WHO position paper—July 2016. *WHO Wkly Epidemiol Rec.* 2016;91(30):349-364.
- World Health Organization. Zika virus infection: global update on epidemiology and potentially associated clinical manifestations. *WHO Wkly Epidemiol Rec.* 2016;91(7):73-88.
- Misery L, Bodere C, Genestet S, Zagnoli F, Marcorelles P. Small-fibre neuropathies and skin: news and perspectives for dermatologists. *Eur J Dermatol.* 2014;24(2):147-153.
- Cao-Lormeau VM, Blake A, Mons S, et al. Guillain-Barré Syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study. *Lancet.* 2016;387(10027):1531-1539.
- Samuel MA, Wang H, Siddharthan V, Morrey JD, Diamond MS. Axonal transport mediates West Nile virus entry into the central nervous system and induces acute flaccid paralysis. *Proc Natl Acad Sci U S A.* 2007;104(43):17140-17145.