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Short communication

Factors associated with persistence of arthralgia among chikungunya virus-infected travellers: Report of 42 French cases

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ABSTRACT

Background: In 2005–2006, a major epidemic of CHIKV infection occurred in the Islands of the south-western Indian Ocean, and longstanding manifestations seemed to be more frequent than described before.
Objectives: To describe the frequency and related factors of late clinical manifestations of CHIKV infection among imported cases living in Aquitaine area, France.
Study design: All patients recruited through the travel clinic and tropical medicine unit of the University Hospital Centre of Bordeaux with possible CHIKV infection were prospectively recorded, and confirmed cases of CHIKV infection were interviewed 2 years after infection. Factors associated with the persistence of symptoms were determined by multivariate logistic regression.
Results: Among the 29 cases followed, 17 still suffered from arthralgia 2 years after infection, and most of them had never recovered from the initial phase of the condition. The risk of persistent arthralgia tended to be higher among subjects with low educational level, subjects infected in the Reunion Island, and when initial phase lasted 30 days or more and was characterised by a severe pain.
Conclusions: Consistent with previous studies, our findings showed worsened late manifestations among patients returning from Indian Ocean area. Persistence of symptoms tended to be linked with clinical burden during the acute phase, which can be informative for early recognition and management of patients at risk for developing persistent rheumatic symptoms. Cryoglobulins failed to be identified in seronegative patients with invalidating dengue-like syndrome.

1. Background

Chikungunya virus (CHIKV) is an enveloped positive sense, single-stranded alphavirus belonging to the Togaviridae family, which may be responsible for an acute incapacitating algoeruptive dengue-like syndrome. It was first isolated in Tanzania in 1953 and has caused in 2005–2006 a major epidemic in the Islands of the south-western Indian Ocean and in India.[1] Before this epidemic, persistent rheumatic injury has been sparsely reported in infected subjects.[2,3] However, longstanding manifestations seem to be more frequent in subjects infected in the Reunion Island.[4] In this context, imported cases have been reported in mainland-France among travellers returning mainly from the Reunion or neighbouring islands.[5]

2. Objectives

The aim of this report is to describe the frequency and related factors of late clinical manifestations of CHIKV infection among imported cases living in Aquitaine area (south-western France) and recruited through the travel clinic and tropical medicine unit of the University Hospital Centre of Bordeaux.

3. Study design

From March 2005 throughout December 2007, all patients with possible CHIKV infection (recent travel or stay in endemic area and presence or history of fever, algoeruptive feature and/or arthralgia) were prospectively recorded. The inclusion criteria for confirmed cases were at least the presence of specific anti-CHIKV IgM result or a seroconversion in IgG and/or IgM, and/or positive RT-PCR of CHIKV from blood.

CHIKV serology testing was conducted using IgM-capture and IgG-sandwich enzyme-linked immunosorbent assay testing using

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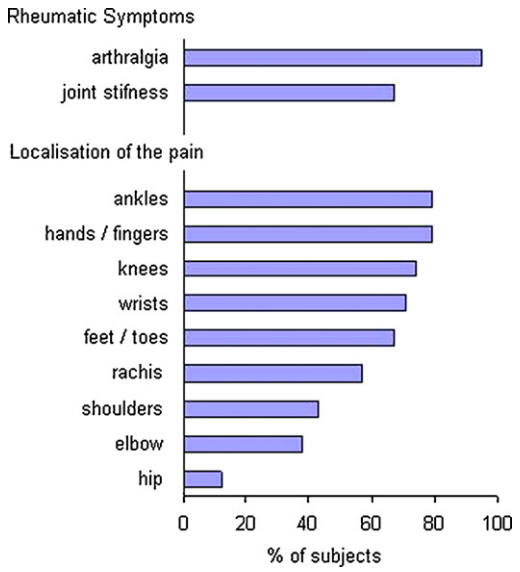

Fig. 1. Rheumatic symptoms and pain localisation during the acute phase of chikungunya infection ($n = 42$).

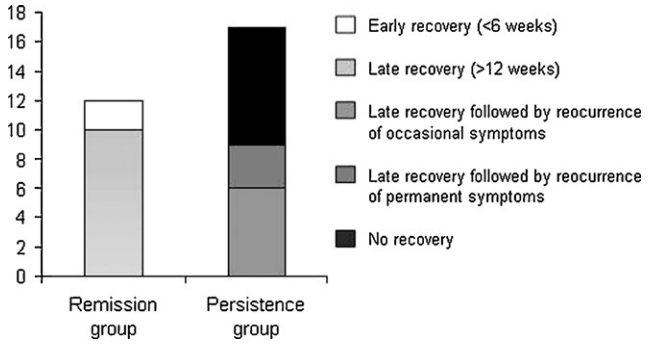

Fig. 2. Evolution of symptoms 2 years after the acute phase of chikungunya infection ($n = 29$).

an inactivated cell-culture-ground CHIKV and mouse anti-CHIKV hyperimmune ascetic fluid (Institut Pasteur, Lyon, France). Serologies were performed for all recorded patients on sera kept at 4 °C. For seronegative patients with clinical suspicion of CHIKV infection, a second analysis on pre-warmed sera kept at 37 °C was performed until new analysis to allow dissolution of putative cryoprecipitates, as to reveal trapped specific anti-CHIKV antibodies. On the latter patients, cryoglobulinemia was concurrently screened using procedures described elsewhere.[6] On acute sera, RT-PCR was per-

Table 1
Persistence of symptoms according to patients' characteristics and clinical burden of the acute phase of chikungunya infection ($n = 29$).

	N (%)	% with persistence	Univariate analysis			Multivariate analysis		
			OR[a]	[95% CI]	*p*	OR[a]	[95% CI]	*p*
Gender								
Male	15 (52)	60						
Female	14 (48)	57	0.9	[0.2–3.9]	0.88			
Age, years								
<50	12 (41)	50						
≥50	17 (59)	65	1.8	[0.4–8.3]	0.43			
Living alone								
No	16 (55)	69						
Yes	13 (45)	46	0.4	[0.1–1.8]	0.22			
Educational level								
Low	13 (45)	85						
High	16 (55)	37	0.1	[0.0–0.7]	<0.02	0.2	[0.0–1.6]	0.12
Place of contamination								
Indian Ocean	23 (79)	70						
Senegal	6 (21)	17	0.1	[0.0–0.9]	<0.05	0.2	[0.0–3.2]	0.26
Presence of a comorbidity[b]								
No	19 (66)	58						
Yes[c]	10 (34)	60	1.1	[0.2–5.2]	0.91			
Overweight[b]								
No	17 (59)	47						
Yes	12 (41)	75	3.4	[0.7–17.0]	0.14			
Impact on activities of daily living[b]								
No	13 (45)	54						
Yes	16 (55)	52	1.4	[0.3–6.3]	0.47			
Cessation of sport activities[b]								
No	7 (24)	43						
Yes	22 (76)	64	2.3	[0.4–13.2]	0.34			
Symptoms duration[b]								
<30 days	15 (52)	47						
≥30 days	14 (48)	71	2.9	[0.6–13.3]	0.18	4.7	[0.6–37.7]	0.14
Pain intensity[b]								
No, low or moderate	10 (34)	30						
Severe	19 (66)	74	6.5	[1.2–35.6]	<0.03	3.0	[0.4–23.5]	0.29

[a] Odds Ratio (OR) of having persistent arthralgia, and 95% confidence interval (95% CI).
[b] During the acute phase of the disease.
[c] Osteoarthritis or cardiovascular disease.