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Editorial

Chronic chikungunya, still to be fully understood

"Doctor, I will never normally work and live again; joint pain prevents me that." This was expressed by a patient in La Virginia, Colombia, three years after having been infected with chikungunya virus (CHIKV).

After more than five decades of obscurity, probably due to lack of studies, many clinical consequences of CHIKV began to be reported, particularly rheumatic ones, after the outbreaks in Réunion Island and India (Javelle et al., 2015) during the epidemic wave that crossed over the Indian Ocean in 2005–2010, and later with the emergence in the Americas since 2014. Through the first three weeks of disease, CHIKV can manifest intensely with fever, myalgia, rash and particularly polyarthralgia, polyarthritis or both. However, miscellaneous rheumatic manifestations can persist for months or even years (Javelle et al., 2015) for a variable and non-negligible part of the CHIKV-infected adults (Bouquillard et al., 2018; Dupuis-Maguiraga et al., 2012).

Over the recent era of CHIKV clinical research, studies have reported that after three months of infection - the current time criteria to define chronic disease due to CHIKV infection- the prevalence of patients with such clinical persistence is ranging from less than 15% up to more than 90% (Dupuis-Maguiraga et al., 2012; Rodriguez-Morales et al., 2015). Nevertheless, most of those studies only have followed-up patients until 32 months after infection (Bouquillard et al., 2018; Rodriguez-Morales et al., 2016). In a study having compared CHIKV-infected and uninfected adults 6 years after disease onset in Reunion island, the infected group reported higher rheumatic morbidity (joint pain, stiffness, swelling) and surprisingly, a higher prevalence of headache, fatigue, depressive mood and social disabilities, a significant impairment of the quality of life and greater health care consumption (Marimoutou et al., 2015). While the majority of the patients with post-CHIK status suffer from cumulative mechanical musculoskeletal disorders, a low percentage of people develop a *de novo* chronic inflammatory rheumatism such as rheumatoid arthritis that should be treated according to the appropriate guidelines (Javelle et al., 2015).

Most studies converge to conclude that the long-term clinical impact of CHIKV occurs in not less than 14% of the initially infected patients (Dupuis-Maguiraga et al., 2012; Rodriguez-Morales et al., 2015). However, the mechanisms and predicting factors for the development of post-CHIKV chronic disorders remain to be better identified. Studies like the one published by Murillo-Zamora et al. in the current issue of IJID should be stimulated. Such clinical scores or index that could early predict the outcome toward post-CHIKV chronic disorders (Murillo-Zamora et al., 2019) would be useful to sort out the patients and identify those who should benefit from a specific clinical management to mitigate an unfavorable evolution and its long-term burden in daily life. The score proposed by Murillo-Zamora et al. (CCAS-4) showed high sensitivity and specificity to predict the persistence of chronic chikungunya arthralgia at 12 months after acute disease. Nevertheless, retrospective validation of such scores on different cohorts and on uninfected populations are necessary to improve these tools.

Unfortunately, numerous questions remain unanswered for patients, physicians, and researchers to date. What processes induce the lasting consequences: host autoimmunity, the possible presence of the virus or its antigens at the synovial cavity promoting local inflammation, cytokines disorders? How to detect early the patients who are developing a chronic and potentially destructive inflammatory rheumatism? For how long will the post-CHIKV chronic clinical disorders persist? Would any early or very early treatment significantly benefit patients, and even avoid the progression to chronic disease? Which should be the most appropriate treatment to manage these patients specifically? How much is CHIKV emergence weighing the global burden of rheumatic diseases? Such points are still to be answered (McHugh, 2018), necessary to fully understand basic and clinical aspects of the viral pathogenesis and the chronic consequences of CHIKV. There is a real need to standardize the nosological frame of the cases and the clinical endpoints in the studies to improve the treatment strategy of these long-lasting persisting symptoms. To date, there is no magic bullet and the treatment must be personalized and based upon good clinical assessment, control of the pain and inflammation, physiotherapy and self-rehabilitation, and identification of the rare cases that should be treated specifically by disease-modifying antirheumatic drugs (Simon and Demoux, 2018). There is still a long way until all patients with a post-CHIK disorder benefit from optimal, efficient and not deleterious, evidence-based treatment.

Given the current trends of international human flows, the general practitioners, rheumatologists and specialists on infectious diseases should all be aware of the worldwide multifocal emergence of CHIKV and its related challenges in individual and public health. Still more, it is not unlikely to expect in a non-distant future, new epidemics of CHIKV in tropical and subtropical areas of the world, which again lead to acute but also chronic consequences for significant proportions of affected populations.

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Contributions

AJRM conceived the idea of the Editorial and perform a review of the literature on the topic related; all authors read the study that is being editorialized; AJRM developed the first draft of the manuscript; all authors contributed consequently with newer versions; all authors approved the final submitted version.

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