



## Letter

## Zika virus infection as a trigger of atopic dermatitis

Zika virus (ZIKV), a single-strand RNA virus from the Flaviviridae family, has been a major worldwide public health problem primarily because of its association with congenital defects and Guillain-Barré syndrome. The ZIKV infection was first identified in Uganda in 1947. Since the description of the endemic transmission in South and Central America in 2015, travel-associated cases have been reported in every state of the United States, except for Alaska, with locally acquired cases reported in Texas and Florida.<sup>1</sup> In Puerto Rico, approximately 38,000 confirmed cases have been reported up to February 2017.<sup>2</sup> It is transmitted to humans primarily by the *Aedes aegypti* mosquito, although infection through the maternal-fetal route and sexual contact also has been described. Only 1 in 5 infected people show clinical manifestations. Symptomatology includes fever, joint pain, conjunctivitis, headache, and skin rash. The most common dermatologic finding is a nonspecific, pruritic, diffuse eruption consisting of macules and papules that appear 3 to 12 days after initial infection. It usually begins in the face and subsequently extends to the trunk and extremities. It heals with desquamation and subsides 2 to 3 days after appearing, with complete resolution seen within 1 week.<sup>3</sup> However, atopic dermatitis triggered by ZIKV has not been described among the cutaneous manifestations.

Atopic dermatitis is an inflammatory skin condition commonly seen in children. It typically presents as pruritic, erythematous macules and papules, with characteristic distribution involving extensor and flexural areas, face, and neck. Atopic dermatitis can be exacerbated by environmental allergens, food allergies, systemic infections (eg, upper respiratory viral infections), and superficial skin microbial organisms. Among the most common viruses described include herpes simplex virus, molluscum contagiosum virus, and human papilloma virus.<sup>4</sup> However, ZIKV, a flavivirus, has not been described as a trigger of this skin condition. We are presenting, to our knowledge, the first case of atopic dermatitis triggered by ZIKV.

In August 2016, a 10-year-old boy with well-controlled atopic dermatitis and allergic rhinitis presented to our clinic in Puerto Rico with a 4-day history of sore throat, generalized weakness, and an itchy rash similar to his previous atopic dermatitis exacerbations. His physical examination was consistent with obesity (body mass index > 95th percentile), gynecomastia, mild pharynx erythema, and truncal faint maculopapular rash with erythematous plaques on flexural areas of upper and lower extremities, compatible with atopic dermatitis (Fig 1A, B). No lymph node enlargement, conjunctivitis, petechial rash, nuchal rigidity, arthritis, or joint tenderness was detected. ZIKV was detected in serum by reverse transcriptase polymerase chain reaction. Nares screening reaction was negative for *Staphylococcus aureus* and

Chikungunya virus titer levels were negative for immunoglobulin (Ig) M and positive for IgG, suggesting a past infection. Prior laboratory workup done on this patient showed increased total IgE of 868 kU/L (normal < 224 kU/L) and specific IgE to *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus* of 0.5 and 0.31 kU/L, respectively (normal < 0.10 kU/L) as tested by ImmunoCAP (Phadia AB, Uppsala, Sweden). Other allergens tested by the same method, including cockroach, cat dander, and dog dander, showed negative reactions. The patient was treated with acetaminophen 325 mg orally as needed every 4 to 6 hours and bedrest. Improvement of atopic dermatitis coincided with the resolution of systemic symptoms associated with ZIKV infection within 3 days of initial evaluation, without using topical or systemic steroids (Fig 1C).

Atopic dermatitis is a common skin condition with a worldwide prevalence ranging from 1% to 20%, including children and adults.<sup>5</sup> Exacerbation of this disease commonly requires treatment with antibiotics, antihistamines, topical corticosteroids, and sometimes antiviral medications. In our patient, his skin manifestations did not require any of these treatments. His atopic dermatitis improved as his symptoms related to ZIKV infection subsided.

Information about the molecular and clinical implications of this virus continues to be discovered. Recent studies have suggested a possible mechanism that could explain the skin manifestations observed in our patient. A decrease in interferon- $\gamma$  production is a known contributory pathophysiologic mechanism for viral infection susceptibility in patients with atopic dermatitis.<sup>4</sup> A recent study observed that skin cells, including dermal fibroblasts, epidermal keratinocytes, and immature dendritic cells, were permissive for ZIKV infection. Treatment of these cells with type I and II interferons strongly inhibited ZIKV replication in a dose-dependent manner.<sup>6</sup> Furthermore, ZIKV has been found to antagonize STAT2 signal transduction, a protein involved in interferon signaling.<sup>7</sup> This mechanism most likely plays an important role in the pathogenesis of this virus and the susceptibility in patients with atopic dermatitis. This case adds new insight about the understanding of ZIKV-induced cutaneous manifestation. Furthermore, with the fast rise of ZIKV infection, this microorganism might be considered a potential trigger of atopic dermatitis in patients from endemic areas presenting with an acute exacerbation.

Wilfredo Cosme-Blanco, MD, PhD

Erving Arroyo-Flores, MD

Sylvette Nazario, MD

Department of Allergy and Immunology

University of Puerto Rico

Medical Sciences Campus

San Juan, Puerto Rico

w.cosme@gmail.com

**Disclosures:** Authors have nothing to disclose.

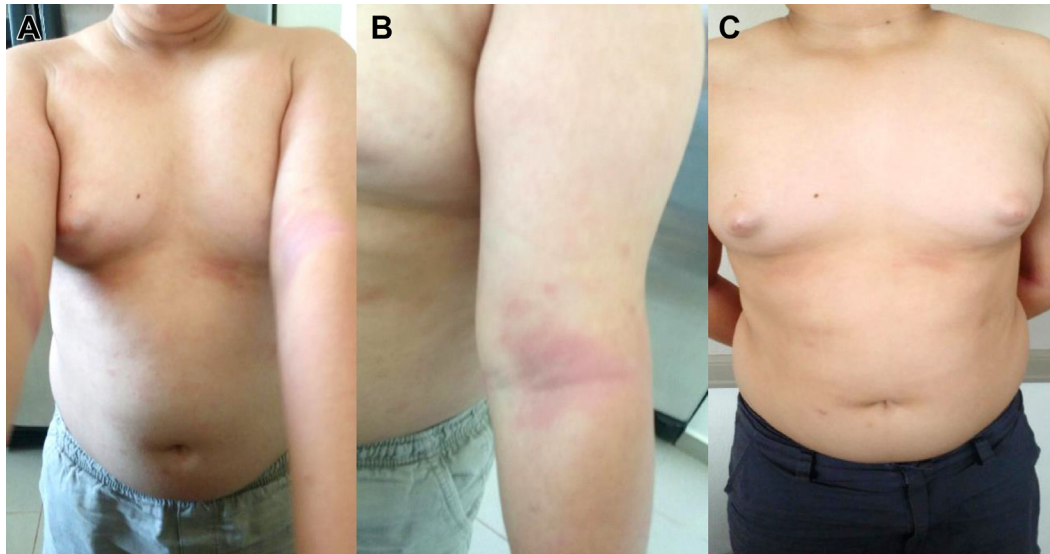


**Figure 1.** Atopic dermatitis triggered by Zika virus infection. (A, B) Maculopapular rash with accentuation of erythematous plaques on flexural areas of upper extremities and inframammary area. (C) Improvement of atopic dermatitis within 3 days of initial examination coinciding with resolution of systemic symptoms.

## References

- [1] Center for Disease Control and Prevention. *Maps of Zika in the United States*, <https://www.cdc.gov/zika/intheus/maps-zika-us.html#zika-cases-us>. Accessed February 14, 2017.
- [2] Puerto Rico Health Department. *Vigilancia de Zika*, <http://www.salud.gov.pr/Estadisticas-Registros-y-Publicaciones/Pages/VigilanciadeZika.aspx>. Accessed February 14, 2017.
- [3] Nawas ZY, Tong Y, Kollipara R, et al. Emerging infectious diseases with cutaneous manifestations: viral and bacterial infections. *J Am Acad Dermatol*. 2016;75:1–16.
- [4] Boguniewicz MaLD, Leung YM, Donald YM. Atopic dermatitis. In: Adkinson NF, Bochner BS, Burks AW, et al, eds. *Middleton's Allergy: Principles and Practice*. 8th ed. Philadelphia, PA: Elsevier; 2014:540–564.
- [5] DaVeiga SP. Epidemiology of atopic dermatitis: a review. *Allergy Asthma Proc*. 2012;33:227–234.
- [6] Hamel R, Dejarnac O, Wichit S, et al. Biology of Zika virus infection in human skin cells. *J Virol*. 2015;89:8880–8896.
- [7] Grant A, Ponia SS, Tripathi S, et al. Zika virus targets human STAT2 to inhibit type I interferon signaling. *Cell Host Microbe*. 2016;19:882–890.