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Disseminated life-threatening viral skin rash in a child with atopic dermatitis

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We report the case of a toddler, with a history of mild atopic dermatitis (AD) since early infancy, presented to the Giannina Gaslini, a pediatric polyclinic hospital, 14 days after measles-mumps-rubella (MMR) vaccination, for the occurrence of a disseminated vesico-pustular rash, accompanied by general malaise, fever, restlessness, and anorexia. Eczema herpeticum (EH) was diagnosed clinically and confirmed by laboratory examinations. The exact pathogenesis of EH in AD is still debated and possibly involves an inter-play between altered cell-mediated and humoral immunity, failure to up-regulate antiviral proteins, and exposure of viral binding sites through the dermatitis and an epidermal barrier failure. We hypothesize that in this particular case, MMR vaccination might have played an additional important role in the alteration of innate immune response, facilitating the manifestation of herpes simplex virus type 1 in the form of EH.

Keywords: Atopic dermatitis, Eczema, Eczema herpeticum, Exanthema, Measles-mumps-rubella vaccine

Atopic dermatitis (AD) affects almost 20% of children worldwide, making it of the top medical issues to deal with as pediatricians and pediatric dermatologists [1].

As it is well known, AD may predispose to infectious complications, requiring prompt identification and referral to an AD specialist for ultimate diagnosis and therapeutic approach [1]. Among these, eczema herpeticum (EH), mainly caused by herpes simplex virus 1 (HVS-1), represents a disseminated life-threatening infection to which AD patients are prone. However, the exact pathogenesis of EH in AD is still debated and possibly involves an interplay between epidermal barrier failure, exposure of viral binding sites, and failure to up-regulate antiviral proteins [2,3].

Herein we present the case of a 14-month-old boy, with mild AD since early infancy, presented to the pediatric polyclinic hospital Giannina Gaslini for the occurrence of a disseminated vesico-pustular rash, accompanied by general malaise, fever, restlessness, and anorexia. Disease onset was reported 2 weeks after measles-mumps-rubella (MMR) vaccination, administered according to the Italian vaccination schedule, 3 days after having played in the sand with other kids on a sunny and hot weekend.

On physical examination, the patient was agitated, with a 37.1°C temperature, 118 bpm heart rate, 31 breaths/min respiratory rate, and with cervical lymphoadenomegalia. At clinical skin examination revealed disseminated, grouped, monomorphic outcomes of vesicles in the form of oozing erosions, and coalescing sero-hematic

crusts at the erythematous base (Fig. 1). Lesions were generalized, especially evident in areas within reach of scratching, and remarkably intense in areas exposed to friction when crawling, as characteristic of atopic eczema (Fig. 2).

EH was diagnosed clinically and confirmed by laboratory examinations revealing elevated C-reactive protein (0.78 mg/dL), elevated large uncolored cells 5.5%, and by serological examinations revealing secondary herpes simplex virus type 1 (HSV-1) infection with positive immunoglobulin (Ig)G and IgM. The patient has been prescribed acyclovir 200 mg 4 times daily for 10 days and empirical antibiotic therapy with amoxicillin 500 mg in two doses for 10 days. A few days after, the mother reported clinical improvement, and at the 10th-day follow-up visit, the patient was normally active and lesions had resolved to leave hypopigmented macules.

Written informed consent was obtained for publication of the present case and of relative documentation, including photographic documentation.

AD is an immune-mediated inflammatory condition, believed to be caused by a combination of genes and external factors such as ecological influence, infections, and others, promoting the immune system to go into overdrive [1]. As a result of impaired skin barrier properties and altered cell-mediated immunity, AD patients are susceptible to severe viral infections [1].

Possibly, eczema-induced epidermal spongiosis facilitates the binding and uptake of viruses, by exposing the desmosomal protein Nectin-1, a constituent of inter-keratinocytic zonulae adherentes, that was recently identified as a relevant HSV receptor in humans [3].

Also, AD patients, show low levels of natural killer (NK)-cells and defective NK-cytotoxic activity, reducing antiviral defense [4,5]. Moreover, a recent study reported low interferon gamma (IFN-γ) and IFN-γ receptor gene expression in AD patients with EH, possibly contributing to the impaired immune response to HSV-1 [6].

We believe that in this particular case, MMR vaccination might have played an additional role in the alteration of the innate immune response, possibly demasking cutaneous binding sites for the virus, allowing the manifestation of HSV-1 in the form of EH [3].

Notably, in recent studies, MMR vaccination and measles infection have been associated with prolonged interleukin-4 (IL-4) elevation in blood plasma [7]. IL-4 is known to initiate T helper 2 cells development and allergic inflammation, as well as decreasing the expression of multiple genes associat-

Fig. 1. (A, B) Disseminated, grouped, monomorphic oozing erosions, and coalescing sero-hematic crusts, on erythematous base of shoulders, arms, and wrists. Written informed consent for the publication of this image was obtained from the patient.

Fig. 2. Coalescing crusts of the lower limbs, especially evident on areas characteristic for atopic eczema, as areas exposed to friction when crawling, such as the ankles and dorsal feet. Written informed consent for the publication of this image was obtained from the patient.

ed with innate defense in AD, including the epidermal differentiation complex gene, regulating epidermal barrier function, leading to an impairment in the protective skin barrier function in AD, thus allowing superinfections to occur [7]. Especially, in atopic patients, failure to recognize EH can result in significant morbidity, implying the need for further studies to have a more in-depth understanding of resembling situations after MMR vaccination, which was sporadically associated with fever and cutaneous rashes [8]. The authors want to highlight that AD does not represent a contraindication to the administration of preventive vaccinations, as suggested by recent recommendations, yet advise individual monitoring of AD patients after vaccine administration [9].

Conclusively, this case emphasizes the importance of careful clinical evaluation of AD patients, not to overlook possibly life-threatening complications, which need prompt diagnosis and systemic therapy to prevent disease dissemination and shorten the course of infection.

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