

Correspondence

“Inflammatory skin march”: IL-1-mediated skin inflammation, atopic dermatitis, and psoriasis to cardiovascular events

To the Editor:

Recently, Silverberg and Greenland¹ declared the increased risk for cardiovascular events in adult patients with severe eczema, emphasizing the importance of more aggressive interventions for eczema. The itching affects the whole body in patients with severe atopic dermatitis (AD) and induces intensive scratching of the skin lesions. The skin damaged by scratching and eczematous inflammation releases a massive amount of the proinflammatory cytokines stored in the epidermis into the systemic circulation targeting the distant organs. Experimentally, a mouse model continually discharging IL-1s from the eczematous skin lesions represents the systemic sclerotic changes of the arteries, and these organ involvements were dramatically ameliorated by combination treatment with anti-IL-1 α - and anti-IL-1 β -neutralizing antibodies or in IL-1 α - and IL-1 β -double-knockout mice.² The inflammatory mice exhibited aberrant vascular wall remodeling from the aorta to the arteries of the limb and tail close to the human arteriosclerosis obliterans. In psoriasis, the keratinocyte-derived cytokines have been speculated as the causable factors for the “psoriatic march” resulting in myocardial infarction.³ IL-1s are major inflammatory cytokines from both AD and psoriasis skin lesions. We propose a concept of “Epidermal IL-1 march” modified from the diagram by Boehncke et al.³ (Fig 1). Patients with psoriasis persistently exposed to higher levels of IL-1s have a risk for arteriosclerosis. Interestingly, this mouse arteriosclerosis lacks the atheroma plaque that is a source of the inflammatory cytokines in arteriosclerosis. However, this model has the skin lesion as an aberrant source of IL-1s. Because of the increase in the cerebrovascular disease mortality in patients with psoriasis,⁴ we modified a part of the diagram (Fig 1). The current epidermal IL-1 march concept strongly supports the idea that overproduced IL-1s contribute to the increased risk for cardiovascular events in severe AD.

In contrast to TNF- α , IL-1s are dual targets and tough to domesticate. However, anti-IL-1s therapy provides new insights into the systemic diseases as well as severe inflammatory skin diseases.

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The Ministry of Education, Culture, Sports, Science, and Technology, Japan, provided grants for scientific research to K.Y. (grant no. 26461690) and H.M. (grant no. 24591647). K.Y. also received a grant from the Mie University Hospital Seed Grant Program 2014.

Disclosure of potential conflict of interest: K. Yamanaka has been supported by grants for scientific research from the Ministry of Education, Culture, Sports, Science and Technology of Japan; a grant from the Mie University Hospital Seed Grant program (2014); research grants from Kyowa Hakko Kirin Co Ltd, Japan, Janssen Pharmaceutical KK, Japan, MSD Pharmaceuticals, Japan, and Mitsubishi Tanabe Pharma Corporation, Japan; and has received lecture fees from Kyowa Hakko Kirin Co

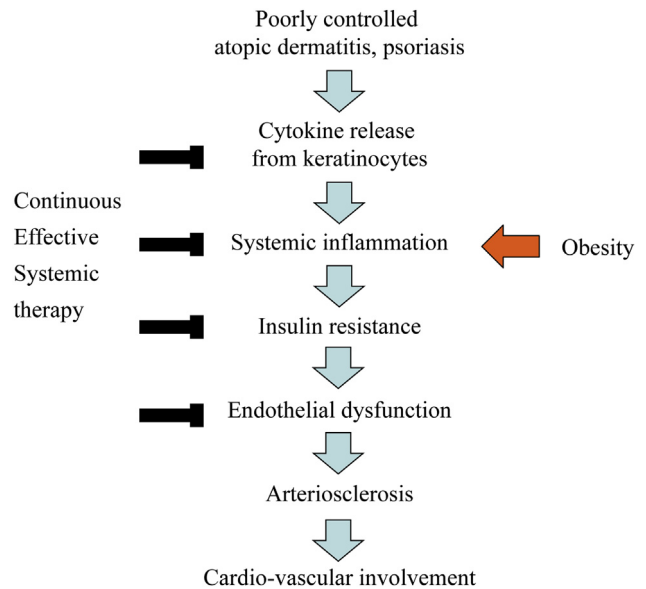


FIG 1. The concept of inflammatory skin march modified from the diagram by Boehncke et al.³ The spilled-over IL-1s from the inflamed skin including AD and psoriasis streamed into the systemic circulation, thereby causing sclerotic change, but atheroma plaques were undetected in the inflammatory model. Also, in patients with psoriasis, the risk for cerebrovascular disease mortality is increased; therefore, we modified a part of the diagram.

Ltd, Janssen Pharmaceutical KK, Mitsubishi Tanabe Pharma Corporation, Maruho Co Ltd, Japan, AbbVie Pharmaceuticals, Japan, Novartis Pharma KK, Japan, Glaxo SmithKline Pharmaceuticals, Japan, and Torii Pharmaceutical Co Ltd. H. Mizutani has been supported by grants for scientific research from the Ministry of Education, Culture, Sports, Science and Technology of Japan and a grant from the Mie University Hospital Seed Grant program (2014); is a patent coholder for caspase-1 Tg mouse with Taiho Pharmaceutical Co Ltd, Japan; and has a royalty contract for caspase-1 Tg mouse with Oriental Yeast Co Ltd, Japan; has received research support from Kyowa Hakko Kirin Co Ltd, Janssen Pharmaceutical KK, MSD Pharmaceuticals, Mitsubishi Tanabe Pharma Corporation, Eisai Co Ltd, Japan, POLA Pharma, Japan, and Kinoshokuhinkenkyusho Co Ltd; and has received lecture fees from Kyowa Hakko Kirin Co Ltd, Mitsubishi Tanabe Pharma Corporation, Janssen Pharmaceutical KK, Maruho Co Ltd, GSK, Japan, Eisai Co Ltd, Taisho Toyama Pharm, Japan, and POLA Pharma.

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<http://dx.doi.org/10.1016/j.jaci.2015.06.009>