Development of atopic dermatitis-like scratching model in hairless mice and analyses of its pathophysiologic mechanisms

○Masanori Fujii, Takeshi Nabe and Shigekatsu Kohno
(Kyoto Pharm. Univ.)

To elucidate pathophysiologic mechanisms of itching in atopic dermatitis (AD), we have developed an animal model showing AD-like skin inflammation accompanied with itch-related scratching, and analyzed mechanisms of the symptoms. HR-1 hairless mice fed with a special diet, HR-AD, showed barrier disruption in the skin, and scratching with prolonged duration on and after the day 28 from the start of feeding. In contrast, such changes were not seen in mice fed a normal diet at all. In addition, inflammatory changes, including increased number of skin cellular infiltrates and elevated levels of serum immunoglobulin E, were characteristically observed in HR-AD-fed mice. However, these inflammatory changes followed the development of prolonged scratching. The prolonged scratching was ameliorated by treatment with petrolatum ointment, depending on the recovery of skin barrier function. Additionally, extension of nerve fibers into the epidermis was detected in HR-AD-fed mice. These results thus suggest that hypersensitivity to exogenous irritants caused by skin barrier dysfunction and/or nerve fiber extension is involved in the itch-related scratching in this model. Next, to clarify mechanisms underlying the skin barrier dysfunction, effects of supplementing nutrients to HR-AD were investigated. Consequently, deficiency of linoleic acid in HR-AD is responsible for the skin barrier dysfunction. On the other hand, we recently demonstrated that ethanol intake markedly aggravated the scratching response in HR-AD-fed mice, while its mechanism remains to be elucidated. Taken together, this animal model could be used to elucidate pathophysiologic mechanisms of itching in human AD and to develop appropriate drug therapies.