Significance of Histamine Metabolism in Skin Lesions of Human and Murine Lupus Erythematosus

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Key Words

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Histamine is involved in a number of immunoregulatory activities and suggested to be an important endogenous modulator of immune response. Recently, we demonstrated that impaired histamine metabolism plays a significant role in the Arthus reaction induced in guinea pig skin [1]. Based on these results, we designed the following experiments to evaluate the role of histamine metabolism in the skin lesions of human systemic lupus erythematosus (SLE) and MRL/Mp-lpr/lpr (MRL/1) mouse which is characteristic in spontaneous LE-like skin lesions [2]. Skin specimens of MRL/1 and other control mice were obtained from the back and tail. Human skin samples were taken from the fresh active lesions and uninvolved sites of 9 patients with SLE. The specific activities of histamine-degrading enzymes, histamine-N-methyltransferase (HMT) and diamine oxidase (DAO) were determined by the methods of Axelrod and Synder. Histamine concentration was assayed by a single enzymatic isotopic assay as described by Shaff and Beaven. Skin samples were also prepared for light microscopical and immunopathological studies. Some MRL mice were injected intraperitoneally 20 times 2.0 mg/kg body weight/day of betamethasone within 5 weeks.

HMT activity in MRL/1 mice at 5 months of age was significantly lower than that of control MRL/n, C57BL/6J, and BALB/c mice at the same age. Interestingly, the back skin of MRL/1 mice showed age-dependent decreases of both HMT activity and histamine concentration, whereas HMT activity of other mouse strains showed age-related increases along with a parallel increase in histamine concentration. Corticosteroid restored the HMT activity of MRL/1 mice. More significant and sensitive changes in HMT activity were observed in MRL/1 mice treated with corticosteroid, when compared with clinico-pathological changes [3]. In human SLE, HMT activity of

both fresh lesions and uninvolved perilesional sites was much lower than that of the controls. There were no positive correlations between HMT activity and the immunopathological findings. Both human and murine skins had no DAO activity.

These present results suggest that decreased activities of HMT play a particular role in the development of immune-complex-mediated skin lesions. The precise mechanisms of reduced activity of HMT in LE are not clear. However, our previous experiments showed that tissue extracts from the Arthus reaction sites induce an inhibition of HMT activity [1]. Thus, we now hypothesize that, as the result of decreased HMT activity due to inhibitory factors, the histamine released in skin lesions of LE remains effective much longer than that in the controls. This impaired histamine metabolism may be closely associated with the development of skin lesions in LE.

References

Tachibana T, Taniguchi S, Furukawa F, et al: Histamine metabolism in the Arthus reaction. *Exp Mol Pathol* 1986;44:76–82.

Furukawa F, Tanaka H, Sekita K, et al: Dermatopathological studies on skin lesions of MRL mice. *Arch Dermatol Res* 1984;276:186–194.

Furukawa F

Taniguchi S

Tachibana T

et al: Pathogenesis of lupus dermatoses in autoimmune mice. X. Evaluation of histamine-N-methyltransferase activity in the skin of autoimmune. *Microbiol Immunol* 1988;32:83–96.