Possible Interaction of Histamine and Serotonin in the Arthus Reaction Induced in Guinea Pig Skin

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Key Words

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Histamine is nominated for a primary chemical mediator of inflammation by its intense effects on vasodilation and vasopermeability. As histamine is released from mast cells or basophils by such complement fragments as C3a and C5a which are synthesized in type III allergic inflammation, it is supposed that this amine has some particular role in the injury of the tissue in the reaction sites.

We have already demonstrated that the activities of histamine-degrading enzymes are impaired in the Arthus reaction sites induced in guinea pig skin [1]. We have also suggested a possible occurrence of some inhibitory factor(s) in the reaction sites [1]. In order to clarify the mechanisms, we have succeeded in purifying histamine-N-methyltransferase (HMT), a major histamine-degrading enzyme in cutaneous tissues, from guinea pig skin about 150-fold, and investigated regulatory mechanism(s) of the enzyme activity by biogenic amines. Consequently, it is concluded that the enzyme activity is inhibited by such compounds in which a certain chemical structure, CH₂-CH₂-NH₂ neighboring the hydrophobic group, is contained [2].

The concentrations of such biogenic amines as serotonin, tryptamine, dopamine and tyramine, which inhibit HMT activity in vitro, were quantitatively analyzed in the Arthus reaction sites induced in guinea pig skin [3], since some biogenic amines might be involved in vivo by inhibiting the enzyme activity. Only one of them, serotonin, was increased about 200% of the control levels 24 h after the initiation, though others were rather decreased in the reaction sites. Moreover, the increase of serotonin and concomitant decrease of HMT activity in the Arthus reaction sites produced an apparent mirror image, suggesting that serotonin not only exhibited its proper effect as a chemical mediator but also inhibited the enzyme activity in the reaction sites. However, as the net decrease of other amines was so far greater than the increase of serotonin, the decrease of HMT activity was not stoichiometrically elucidated from the increase of serotonin.

Although it is generally considered that the concentration of tissue serotonin depends on the number of mast cells, no significant increase in mast cell number was observed in the Arthus reaction sites. Platelets, which are rich in serotonin, are considered to be another convenient source of the amine. We have recently obtained some evidence suggesting that the increase of serotonin in the Arthus reaction sites is produced by the accumulation of platelets in the reaction sites [4],

We have also investigated the localization of HMT in the guinea pig skin using an immunofluorescent technique, and found that the enzyme localizes in the epidermis (basal cell layer) and the perivascular area in the upper dermis. Taken together, in such a microenvironmental situation as the perivascular area in the Arthus reaction sites, increased serotonin due to the accumulation of platelets may reduce the activity of HMT. This information may provide a new finding about the mediator interaction in type III allergic cutaneous inflammation.

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