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Decreased Serum Neutral Endopeptidase Activity in Children with Bronchial Asthma

Koutarou MURAKI[1], Kazuki SATOH[2], Hiroyasu OKAHATA[3], Yuko HIRAI[4], Mitoshi AKIYAMA[4] and Yoshihiro NAKATA[2]

1) Department of Pediatrics, Saiseikai Hiroshima Hospital
2) Institute of Pharmaceutical Sciences, Hiroshima University School of Medicine
3) Department of Pediatrics, Ohtake National Hospital
4) Department of Radiobiology, Radiation Effects Research Foundation

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Neutral endopeptidase (NEP) is an ectoenzyme[2] which distributes in many organs including the kidney, lymphnode, intestine, lung, brain[3], and vascular endothelium[8]. NEP is also present in the serum[6] and hydrolyses tachykinins such as substance P (SP)[7] together with that in the vascular endothelium.

In bronchial asthma (BA), symptoms such as cough, wheezing, and sputum can be deteriorated by tachykinins secreted from non-adrenergic, noncholinergic neurons in the bronchial smooth muscles[1]. It has been reported that the guinea pig with BA shows decreased NEP activity in the lung[4]. However, it is still unclear whether or not the serum NEP (sNEP) levels which affect SP concentration in the serum are altered in BA patients.

We measured sNEP activity in children with BA comparing with that of children with atopic dermatitis (AD) who were devoid of BA symptoms, and with that of allergy-free (AF) children.

MATERIALS AND METHODS

Enrolled in this experiment were 10 children clinically diagnosed as having with atopic or non-atopic BA of mild severity, 10 children with atopic dermatitis devoid of BA symptoms, and 4 children with the common cold or diarrhea who did not possess any allergic disease (AF children).

Blood samples were taken during the remission when patients did not show any respiratory symptoms in the BA group, and ad lib in other groups. The method of measurement of NEP activity has been described elsewhere[6]. Each value was expressed as a mean of triplicate measurements. Serum protein was measured by the Lowry method[5]. Lactic dehydrogenase (LDH) activity in the serum were measured in the hospital laboratory and immunoglobulin E (IgE) was measured in a commercial laboratory. The statistical analysis was conducted by the least square method and unpaired Student's t test.

RESULTS

The sNEP activity of the BA group (23.6±9.4 pmole/min/mg protein, mean±S.D., n=10) was significantly ($p<0.05$) lower than that of the AD group (31.4±6.9, n=10) (Fig. 1). The mean age of

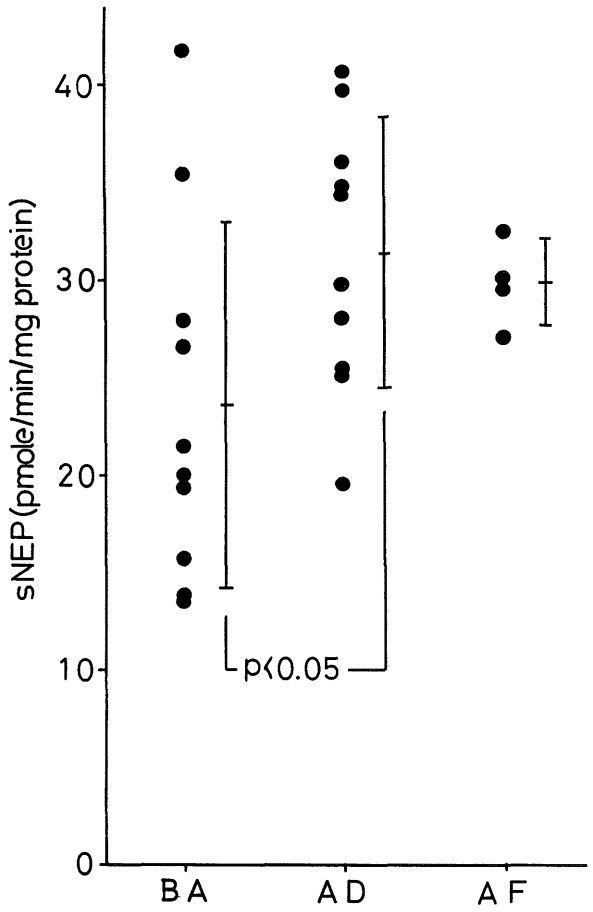

Fig. 1. BA:bronchial asthma. AD:atopic dermatitis. AF:allergy-free.

Correspondence: Koutarou Muraki, M.D. Department of Pediatrics, Saiseikai Hiroshima Hospital, 2–3–10, Kitashinchi, Saka-cho, Aki-gun, Hiroshima 731–4301, Japan Tel: 082–884–2566, FAX: 082–884–2066

BA group (3.1±1.7 years, n=10) was not significantly different from that of the AD group (2.1±1.6, n=10). We could not find a significant difference in sNEP activity between the AD and AF group (29.9±2.2, n=4), and between the BA and AF group. This was due to the low number of AF samples. The serum LDH levels of the BA and AD groups were not significantly different. There was no significant correlation between sNEP and LDH activity in all groups. Serum IgE levels were variable in the BA and AD groups and there was no significant correlation between serum IgE and sNEP activity in these two groups.

DISCUSSION

Our result shows that the sNEP level was significantly low in mild BA patients compared to that in the AD group. This may suggest that BA patients in particular have some regulatory mechanism of sNEP activity although both AD and BA are the same allergic diseases. However, the mechanism is not clear. We could not obtain sufficient number of AF samples in this study to show whether there exists a significant difference in sNEP activity between the allergy and non-allergy group.

Since there was no significant correlation between sNEP and serum IgE levels in the BA and AD groups, we conclude that sNEP seems to be unrelated to serum IgE.

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REFERENCES

1. **Barnes, P.J.** 1986. Asthma as an axon reflex. Lancet **I:** 242–245.
2. **Kenny, A.J. and Turner, A.J.** 1987. Chapter 1. What are ectoenzymes? p.1–13. *In* A.J.Kenny and A.J.Turner (eds.), Mammalian ectoenzymes, Elsevier Science Publishers B.V. (Biomedical Division) USA.
3. **Kenny, A.J., Bowers, M.A., Gee, N.S. and Matsas, R.** 1985. Endopeptidase-24.11:a cell-surface enzyme for metabolizing regulatory peptides. Biochemical Society Transactions **13:** 293–295.
4. **Lilly, C.M., Kobzik, L., Hall, A.E. and Drazen, J.M.** 1994. Effects of Chronic Airway Inflammation on the Activity and Enzymatic Inactivation of Neuropeptides in Guinea Pig Lungs. J.Clin.Invest. **93:** 2667–2674.
5. **Lowry, O.H., Rosebrough, N.J., Farr, A.L. and Randall, R.J.** 1951. Protein Measurement with the Folin Phenol Reagent. J.Biol.Chem. **193:** 265–275.
6. **Muraki, K., Nakata, Y., Simonaka, H., Inoue, J., Hirai, Y. and Akiyama, M.** 1996. Neutral Endopeptidase Activity in Serum and Cerebrospinal Fluid. Hiroshima J.Med.Sci. **45:** 109–112.
7. **Skidgel, R.A., Engelbrecht, S., Johnson, A.R. and Erdos, E.G.** 1984. Hydrolysis of substance P and neurotensin by converting enzyme and neutral endopeptidase. Peptides **5:** 769–76.
8. **Soleilhac, J.M., Lucas, E., Beaumont, A., Turcaud, S., Michel, J.B., Ficheux, D., Fournie-Zaulski, M.C. and Roqueus, B.P.** 1992. A 94-kDa Protein, Identified as Neutral Endopeptidase-24.11, can Inactivate Atrial Natriuretic Peptide in the Vascular Endothelium. Mol.Pharmacol. **41:** 609–614.