

Elevated levels of soluble ICAM-1 in sera from patients with bronchial asthma

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We measured the levels of soluble intercellular adhesion molecule-1 (sICAM-1) in sera from patients with bronchial asthma. sICAM-1 levels in sera from atopic asthmatic patients in stable conditions were higher than in normal control subjects. Furthermore, the sICAM-1 levels in sera obtained during bronchial asthma attacks were higher than those in sera obtained in stable conditions. These results suggest that higher levels of sICAM-1 in sera reflect the upregulation of ICAM-1 expression in allergic inflammation.

Key words: bronchial asthma; intercellular adhesion molecule-1.

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Leukocyte–endothelial cell interaction is essential for leukocyte infiltration into inflammatory sites (5). In allergic inflammation, Wegner et al. (7) observed that administration of anti-ICAM-1 monoclonal antibodies into monkeys resulted both in reduced eosinophil infiltration into the lung and in reduced airway hyperresponsiveness, and upregulation of ICAM-1 expression was observed on the endothelium, the bronchial epithelium, and eosinophils (3–5, 7), suggesting an important role for ICAM-1 in the pathogenesis of bronchial asthma. Our group established a double-determinant immunoassay, for the first time, in order to measure the level of sICAM-1 in the serum (6). Furukawa et al. (2) reported that the level of sICAM-1 in sera from patients with Kawasaki disease was extremely high, possibly as a result of vasculitis. To our knowledge, there has been no previous report concerning sICAM-1 in patients with bronchial asthma. If the levels of sICAM-1 vary between bronchial asthma patients and normal controls, this variance would be very useful to assess the state of this disease. Therefore, we attempted to measure the levels of sICAM-1 in sera from patients with bronchial asthma.

Material and methods

The study group comprised 27 patients with bronchial asthma with a mean age of 37.2 years (range 20–60 years) and 17 normal subjects with a mean age of 34.1 years (range 26–45 years). All patients with bronchial asthma met the American Thoracic Society's definition of asthma (1). We emphasize that all asthmatic patients had a history of episodes of wheezes and dyspnea, reversible bronchoconstriction, and airway hyperresponsiveness verified by lower values of PC₂₀-methacholine. Atopic asthmatic patients had a history of a bronchoconstrictive response after allergen exposure, elevated total serum IgE levels (> 250 IU/ml), elevated specific IgE levels against house-dust mite (*Dermatophagoides farinea* – Df) (> 0.34 PRU/ml), and positive skin prick tests to Df. Nonatopic asthmatic patients generally had a history of postinfectious onset of bronchial asthma, no history of allergen-induced bronchospasm, and normal total IgE levels together with normal specific IgE levels against a standard set of allergens and negative skin prick tests. None of the asthmatic patients were taking oral corticosteroids.

The control subjects had no history of allergy and bronchial asthma, had normal total and specific IgE levels, and were not taking any medication. Serum specimens were obtained from 17 atopic asthmatics in stable conditions (asymptomatic periods). Serial serum specimens were obtained from 10 patients with bronchial asthma during asthma attacks and in stable conditions; six were atopic asthmatics and four were nonatopic asthmatics. sICAM-1 was measured by ELISA with two monoclonal antibodies which recognized different epitopes of ICAM-1. ELISA was performed as described elsewhere (6).

Results

Sera from atopic asthmatic patients in stable conditions contained more sICAM-1 ($n = 17$; range 19–57 U/ml; mean $\pm$ SD 37.0 ± 13.3) than those from normal subjects ($n = 17$; range 18–37; mean $\pm$ SD 29.1 ± 4.6 ; $P < 0.05$ by unpaired t test) (Fig. 1). Furthermore, the sICAM-1 levels in sera obtained from bronchial asthma patients during asthma attacks were higher than those in sera obtained in stable conditions ($n = 10$; range 35–61; mean $\pm$ SD 41.7 ± 7.9 , as compared with range 18.5–43.0; mean $\pm$ SD 33.6 ± 12.6 ; $P < 0.003$ by paired t test) (Fig. 2).

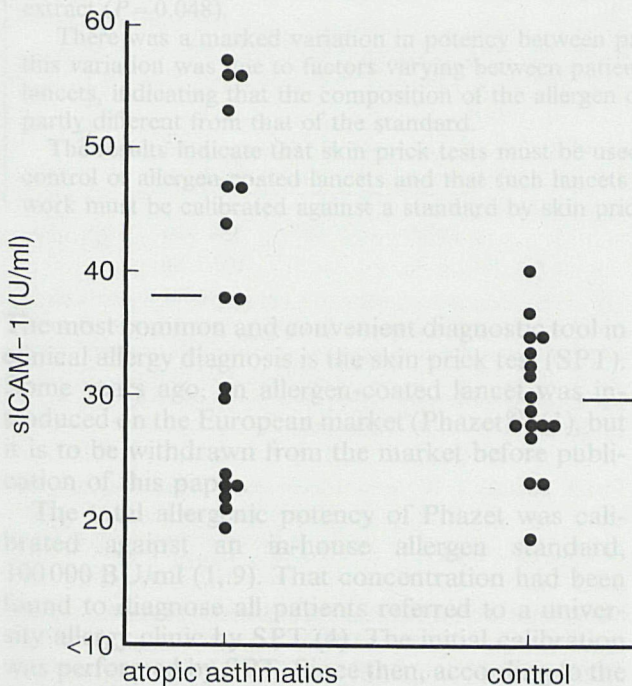


Fig. 1. Serum sICAM-1 levels in atopic asthmatic patients. Horizontal short lines represent mean of each group. One unit of sICAM-1 corresponds to 2 ng/ml of sICAM-1.

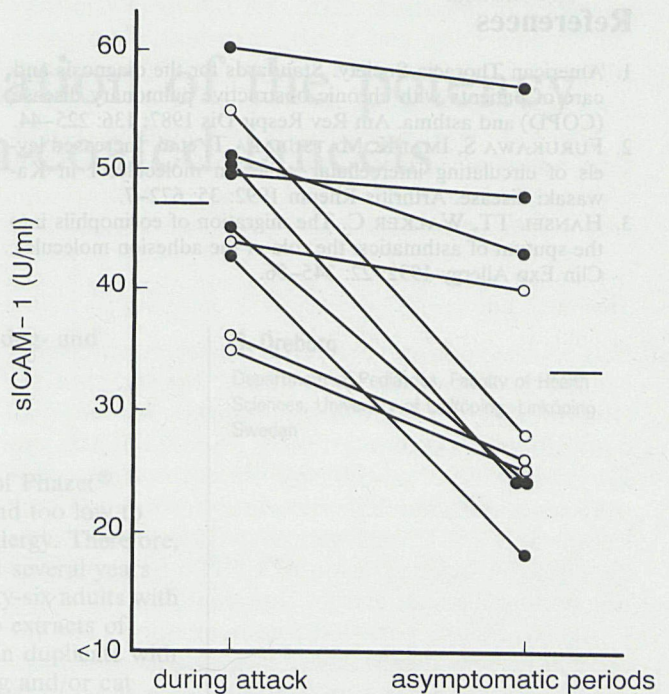


Fig. 2. Serum sICAM-1 levels in patients with bronchial asthma during asthma attacks and in stable conditions. Serum sICAM-1 levels in atopic asthmatics (●) and nonatopic asthmatics (○) during asthma attacks and in stable conditions were measured. Horizontal short lines represent mean of each group.

Discussion

Our results show that the sICAM-1 levels in sera obtained from atopic asthmatic patients were higher than those from normal control subjects; furthermore, the sICAM-1 levels in sera obtained from bronchial asthma during asthma attacks were higher than those in sera obtained in stable conditions. The last-named findings were observed regardless of atopic status.

ICAM-1 can be induced on various cell types by inflammatory stimuli (5). In allergic inflammation, cell surface ICAM-1 expression has been shown to be upregulated on the endothelium, the bronchial epithelium, and eosinophils (3–5, 7). The present results suggest that higher levels of sICAM-1 in sera from bronchial asthmatic patients reflect the upregulation of cell surface ICAM-1 expression in allergic inflammation. It would be interesting to know whether sICAM-1 can modulate the allergic inflammatory reaction. We postulate that sICAM-1 can attenuate eosinophil adherence to the endothelium and subsequent infiltration into allergic inflammatory sites and can modulate eosinophil functions by binding of sICAM-1 to CD11a/CD18 on eosinophils. Further studies should be done to clarify the regulatory mechanism in expression and shedding of ICAM-1 and the precise function of sICAM-1 in allergic inflammation.

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