Serum interleukin 5 concentrations in atopic and non-atopic patients with glucocorticoid-dependent chronic severe asthma

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Abstract

Background – Interleukin (IL)-5 is thought to play a part in asthmatic bronchial mucosal inflammation and is a potential therapeutic target. Detectable serum IL-5 concentrations have been found previously in a proportion of patients with acute severe asthma, but not in the same patients following oral glucocorticoid therapy or in normal controls. A study was undertaken to investigate whether or not IL-5 is detectable in the serum of patients with glucocorticoid-dependent chronic severe asthma.

Methods – Serum concentrations of IL-5 were measured in 29 patients with stable oral glucocorticoid-dependent chronic severe asthma (mean PEFR 59.7% predicted) and seven normal controls using a specific enzyme-linked immunoassay calibrated with recombinant human IL-5 standards (lower limit of sensitivity 40 pg/ml).

Results – Interleukin 5 was detectable in the serum of 15 of the 29 patients at a median concentration of 150 pg/ml (range 40–690), but was undetectable in the serum of all the control subjects. The patients with detectable serum IL-5 concentrations did not differ from those with undetectable concentrations in terms of atopic status, disease severity (percentage predicted PEFR or FEV₁), prednisolone dosage, serum IgE concentrations, or peripheral eosinophil count.

Conclusions – Interleukin 5 is detectable in the serum of a proportion of both atopic and non-atopic patients with chronic severe asthma, and concentrations in these patients were higher than in normal controls. These observations are compatible with the hypothesis that IL-5 release occurs in these patients during a period of stable asthma despite systemic glucocorticoid therapy.

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There is increasing evidence that the eosinophil-rich bronchial inflammation characteristic of asthma is orchestrated, at least partly, by cytokine products of activated CD4 T lymphocytes. Of these, interleukin (IL)-5 is particularly implicated because, together with IL-3 and granulocyte/macrophage colony stim-

ulating factor, it promotes the differentiation, priming, and survival of eosinophils in vitro.¹ Interleukin 5 has also been clearly implicated in the pathogenesis of asthma from in vivo studies. Increased IL-5 mRNA expression was observed in bronchial mucosa² and in bronchoalveolar lavage fluid cells³ from mild atopic asthmatics compared with controls. The degree of expression correlated with disease severity and symptomatology.

We have previously shown that peripheral blood CD4 T lymphocyte activation is accompanied by raised serum concentrations of IL-5 in a proportion of both atopic and non-atopic patients with acute severe asthma, but that IL-5 was not detectable in the same patients following oral glucocorticoid therapy, or in normal controls.⁴ Others have reported raised plasma concentrations of soluble IL-2 receptor in oral glucocorticoid-dependent asthmatics compared with patients controlled without oral glucocorticoids, suggesting that ongoing T lymphocyte activation is associated with severe chronic disease despite maintenance prednisolone.⁵ The aim of this study was to investigate whether IL-5 may be implicated in the pathogenesis of oral glucocorticoid-dependent chronic severe asthma.

Methods

Documented chronic asthmatic subjects aged 18–65 years with FEV₁ and/or PEFR below 75% of the predicted value and >20% reversibility to β_2 agonist were considered for the study if they required long term maintenance treatment with 5–20 mg oral prednisolone daily, in addition to maximal tolerated and effective other therapy including high dose inhaled glucocorticoids. Written informed consent was obtained from each patient and the study was approved by the ethics committee of the Royal Brompton National Heart and Lung Hospitals.

A total of 11 men and 18 women aged 21–62 (mean 49) years who had had asthma for 5–54 (mean 29) years and had received continuous treatment with oral prednisolone for 0.5–26 (mean 9.7) years were enrolled. Mean (SE) daily dosage of prednisolone was 8.6 (0.8) mg and of inhaled glucocorticoid was 1630 (99) μ g; median (range) total serum IgE concentration was 76 (6–1250) IU/ml and peripheral blood eosinophil count 0.2 (0–1.2) $\times 10^9/l$. Twenty of the patients studied were atopic (as defined by one or more positive skin prick tests to

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concentrations lower than 40 pg/ml, variable clearance from the circulation as well as variable release, the range of prednisolone dosage, and the unknown effects of circulating soluble IL-5 receptors. The presence of IL-5 within the bronchial mucosa, which might be more relevant to the pathogenesis of asthma, may therefore not be closely reflected by its presence in peripheral blood. This, in addition to the relatively small patient numbers, may explain why – in contrast to the findings in mild asthma in which the degree of IL-5 mRNA expression in bronchial mucosa and bronchoalveolar lavage fluid correlated with disease severity – no relation was seen between serum concentrations of IL-5 and disease severity in either the acute or chronic severe patients.

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