

Serum IL-9 Levels Depend on Allergen Exposure: Preliminary Study

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Key Words

Serum interleukin 9 • Allergic rhinitis • Pollen allergy • Allergen exposure • Pollen season

Abstract

Background: Th9 is a new T cell subset characterized by interleukin 9 (IL-9) production. Serum IL-9 levels are related to symptom severity in patients with allergic rhinitis (AR). This study aimed at investigating whether IL-9 may depend on allergen exposure. **Methods:** 35 AR patients (16 males, mean age 33.2 years) with monosensitization to *Parietaria* were studied when symptomatic; 38 AR patients (22 males, mean age 30.9 years) with monosensitization to birch were recruited at the same time, but were symptom free. Serum IL-9 was assayed in all patients. **Results:** Patients with *Parietaria* allergy and exposed to allergen had higher serum IL-9 levels than patients with birch allergy and not exposed to allergen ($p < 0.05$). **Conclusions:** This preliminary study shows that serum IL-9 levels may depend on allergen exposure: symptomatic patients with pollen-induced AR, evaluated during the pollen season, have higher values than patients studied outside the pollen season and without symptoms.

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Introduction

Allergic rhinitis (AR) is sustained by an inflammatory reaction. Various populations of effector and regulatory T cells have been shown to play a crucial role in allergic inflammation [1]. Depending on the substances to which the cells are exposed simultaneously with the allergen and the status of the cells and cytokines in the milieu, CD4⁺-naïve T cells can differentiate into Th1, Th2, Th9, or Th17 effector cells [2]. Th9 cells lack a suppressive function and constitute a distinct population of effector T cells promoting tissue inflammation and mucus production [3]. In particular, interleukin 9 (IL-9) is an important stimulus for tissue infiltration by mast cells. The cell sources of IL-9 include T cells, eosinophils, neutrophils, and mast cells. A study based on nasal biopsies demonstrated that IL-9 is upregulated in the nasal mucosa during the pollen season and correlates with tissue infiltration by eosinophils [4]. More recently, it has been reported that serum IL-9 levels are correlated with symptom severity in pollen-induced AR [5]. Therefore, using the model of pollen allergy, this preliminary study aimed at investigating whether serum IL-9 levels may depend on allergen exposure.

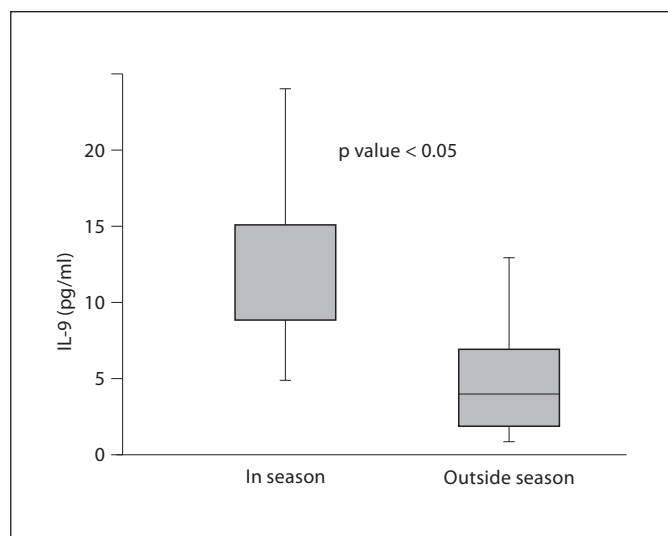


Fig. 1. Serum IL-9 levels in patients with AR evaluated in and outside the pollen season. The results are represented as medians (black middle line), quartiles (25 and 75th percentiles, black box) and p values for differences between the groups.

Materials and Methods

Thirty-five AR patients (16 males, mean age 33.2 years) with monosensitization to *Parietaria* were studied in July, i.e. at the pollen peak and so with symptoms. At the same time, 38 AR patients (22 males, mean age 30.9 years) with monosensitization to birch were recruited: all of them were symptom free as the birch pollen season ended 2 months ago.

Blood sampling for assessment of serum IL-9 was performed in all patients. AR was diagnosed according to validated criteria [6].

The study was approved by the local Ethics Committee and performed with the written informed consent of all participants.

The human IL-9 (Human IL-9 ELISA Ready-SET-Go!; eBioscience, Rome, Italy) reagent set contains the necessary reagents, buffers and diluents for performing quantitative enzyme-linked immunosorbent assays (ELISA), as previously reported [5].

The 'S-Plus' (MathSoft Corp.) package was used for all analyses.

Results

The median serum IL-9 levels in patients with *Parietaria* allergy were 12.6 pg/ml (range 5.03–24.11). The median serum IL-9 levels in patients with AR due to birch allergy were 4.83 pg/ml (range 1.97–14.01).

There was a significant difference between the two groups ($p < 0.05$), as illustrated in figure 1.

Discussion

AR is characterized by a Th2-polarized inflammation. Th2-derived cytokines, such as IL-4 and IL-13, are the main pathogenic factors able to induce, maintain and amplify allergic inflammation [7]. Recently, a new T cell subset has been identified: Th9 [3]. Allergic inflammation is strictly dependent on allergen exposure, as clearly evidenced by a natural or experimental challenge with pollens [8].

The present preliminary study was designed to investigate the effect of allergen exposure on serum IL-9 levels in AR patients.

The findings show that the serum IL-9 levels are significantly higher in pollen-induced AR during the pollen season. This phenomenon confirms the relevance of exposure to the causal allergen. In fact, the allergic reaction is closely dependent on allergen exposure. The causal pollen induces a cascade of inflammatory events that sustain symptom occurrence. In this regard, IL-9 also shows a different production level depending on exposure to the causal allergen. This preliminary study confirms a pathogenic role of IL-9 in AR, as previously reported for the relationship with symptom severity [5]. Therefore, the most important message of this paper is that allergen exposure leads to IL-9 induction, as previously reported by two studies [9, 10]. However, this study has a relevant limit as it would have been more appropriate to study IL-9 levels in and outside the pollen season in the same patients. Then changes in IL-9 would have better reflect changes in allergen exposure. Unfortunately, these patients were immediately treated with allergen-specific immunotherapy and so could not be re-evaluated. For partially obviating this bias, we evaluated a group of patients exposed to the causal pollen and so with acute inflammation and symptoms. The other group of patients was studied 2 months after the pollen season and was thus free from allergic inflammation and symptoms. Further studies should therefore be conducted to compare the same patients during and outside the pollen season.

In conclusion, this preliminary study shows that serum IL-9 levels may depend on exposure to a causal allergen.

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