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LETTER TO THE EDITOR

SERUM IL-17 AFTER ONE COURSE OF SUBLINGUAL IMMUNOTHERAPY IN ALLERGIC RHINITIS TO BIRCH

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Recently, it has been reported that IL-17 may be involved in allergic reaction. Sublingual immunotherapy (SLIT) is the unique curative treatment for allergic rhinitis. This study aims at investigating whether one course of birch SLIT could affect serum IL-17 levels. The findings provided show that some IL-17 producer patients had a reduction of serum IL-17 levels after one SLIT course. Therefore, this preliminary study shows that a single pre-seasonal SLIT course may induce a significant decreasing trend in serum IL-17 levels; further study should be carried out to define the role exerted by IL-17 in allergic rhinitis.

Allergic rhinitis (AR) is characterised by an inflammatory reaction, sustained by Th2 polarization. Peripheral blood mononuclear cells of AR patients display a predominant IL-4 production by Th2 cells compared to IFN-γ expression by Th1 cells, thus confirming the functional dichotomy between Th1 and Th2 cells. This bivalent concept has since been modified by the discovery of T-regulatory (Treg) and Th17 cells. As recently pointed out, the discovery of Th17 cells has been fundamental to our understanding of how Th1 cells can actually mediate inflammatory events by producing IFN-γ (1).

Th17 cells are characterized by the production of various cytokines, including IL-17, IL-6, TNF-α, and IL-22. IL-17 may be involved in allergic disorders as anti-IL-17 has been demonstrated to reduce neutrophil infiltration in an experimental asthma model (2), and, on the other hand, increases eosinophil infiltration. Furthermore, IL-17 induces recruitment and is a survival factor for airway macrophages (3). These facts seem to suggest a regulatory role of IL-17. It appears that Th-17-dependent neutrophil infiltration is inversely related with Th2-dependent eosinophil involvement, similar to the dichotomic Th1-Th2 balance. In addition, animal models indicate that IL-17 might play a pro-inflammatory role. Indeed IL-17 induces the expression of pro-inflammatory cytokines, including TNF-α, IL-1β, and IL-6, and some chemokines, such as CXCL1, 2, and 8, all of which are markers of acute inflammatory events (1). These chemokines induce neutrophil recruitment which may be considered the hallmark functional activity of Th17: neutrophilic inflammation. However, the

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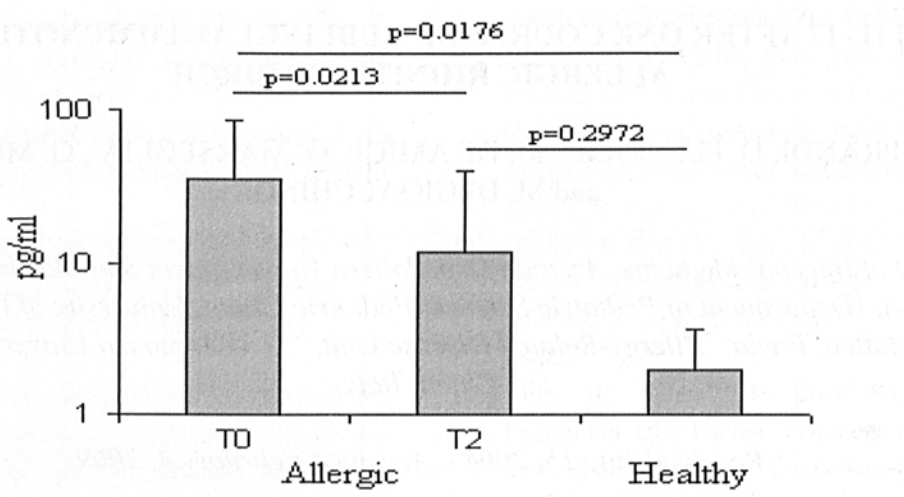

Fig. 1. *Serum IL-17 distribution in IL-17 producer allergic patients (T0= Baseline; T2= 3 months after SLIT course) and healthy subjects. Values are represented as Mean and Standard Deviation.*

role of Th17 cells in allergic inflammation is still unclear. Experimental studies seem to suggest that Th17 cells may be involved in the process of neutrophilic infiltration that occurs during the acute phase of allergic reaction. In this regard, neutrophil infiltration is also observed in acute asthma attacks as well as during the early phase following allergen-specific challenge (4).

Sublingual immunotherapy (SLIT) is the unique causal treatment for AR affecting immune response (5). However, no study has investigated the possible effect of SLIT on serum IL-17 levels. Thus, the aim of this preliminary study is to evaluate IL-17 serum levels in a group of AR patients.

Nineteen patients (11 males and 8 females, mean age: 42 years), with birch AR, were evaluated according to ARIA criteria (6). The patients' blood samples for assessing IL-17 serum levels were collected before initiating SLIT (baseline) and three months after the end of the pre-seasonal SLIT course (Anallergo, Florence, Italy). Serum samples from 8 healthy donors were also tested as controls.

The human interleukin 17 (IL-17) Immunoassay (R&D Systems) employs the quantitative sandwich enzyme immunoassay technique and was performed according to the Manufacturer's Instructions and expressed as pg/mL. Descriptive statistics were first performed and quantitative parameters were reported as mean (M), deviation standard (DS) and median (MD). The non- parametric Wilcoxon test was performed to evaluate the differences between allergic/non-allergic subjects and in allergic patients before and after 3 months of SLIT. The package "S-Plus" (MathSoft Corp.) was used for all the analyses.

In 12 of the 19 allergic patients, IL-17 levels at baseline were undetectable, these patients were therefore defined as IL-17 non-producers. In the remaining 7 patients, M levels at baseline were 35.87±49.41 SD pg/ml (MD 25.63); these patients were defined as IL-17 producers. A significant difference (p=0.0176) in serum levels was observed between baseline of IL-17 producer allergic patients (M 35.87±49.41 DS pg/ml; 25.63 MD) and healthy subjects with IL-17 detected (M 1.94±1.68 DS pg/ml; MD 1.33). In IL-17 producer allergic patients, serum levels were observed to significantly decrease (p=0.0213) 3 months after the SLIT course to M 11.59±28.59 DS pg/ml (MD 0.84 pg/ml) (Fig.1). On the contrary, serum levels were unmodified in IL-17 non-producer allergic patients after SLIT.

This preliminary study shows that a single pre-seasonal SLIT course may induce a significant decreasing trend in serum IL-17 levels; further study should be performed to define the role exerted by IL-17 in allergic rhinitis.

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