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Is the strange case of mugwort sensitivity in ragweed-allergic subjects coming eventually to a solution?

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KEY WORDS

Cross-reactivity, ragweed, mugwort, Amb a 4, Art v 1.

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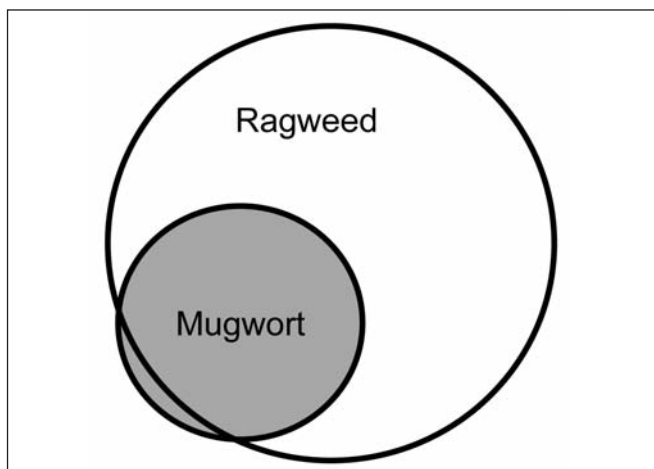
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In areas where ragweed is a relevant source of sensitization and a serious health problem as well like the surroundings of Milan, a striking phenomenon is frequently observed by clinical allergologists: the co-sensitization to ragweed and mugwort. In the '80s of the last century, before the sudden appearance of ragweed, mugwort sensitization was rarely observed; subsequently, the prevalence of mugwort sensitivity increased dramatically in parallel with the spread of ragweed. It has to be pointed out that, as a difference from Central Europe where mugwort represents a relevant source of primary sensitization and allergy, in the area of Milan IgE reactivity to mugwort is still very rare in the absence of ragweed hypersensitivity once patients sensitized to pollen pan-allergens (profilin and polcalcins) are excluded, and few subjects monosensitized to mugwort pro year are found out of > 1000 new pollen allergic subjects. In contrast, about 35% of ragweed-sensitized subjects are co-sensitized to mugwort (1). This poses a serious diagnostic problem as both plants belong to the great botanical family of Compositae and show overlapping flowering periods; in co-sensitized patients the clinician has to decide whether to prescribe one or two distinct allergen specific immunotherapies.

The described picture has suggested the existence of some sort of cross-reactivity between ragweed and mugwort pollen (other than the one linked to plant pan-allergens) ever since. Already 20 years ago studies carried out in this area found that in 50% of patients the differential diagnosis between ragweed and mugwort allergy was impossible (2,3). In-vitro studies produced contrasting results with some groups reporting the existence of cross-reacting allergens in the two pollen species (including Art v 1) (4), and other authors stating that ragweed and mugwort pollen show little or no cross-reactivity (5,6). In a more recent study including a careful in-vitro analysis it was concluded that "patients showing both ragweed- and mugwort-positive SPT and/or RAST are co-sensitized" (1), although the fact remains that in the same study 93% of mugwort-sensitized patients living in the surroundings of Milan were co-sensitized to ragweed (whereas 62% of ragweed-allergic patients were not co-sensitized to mugwort) (1). The situation observed in clinical practice is summarized in figure 1.

The recent introduction of purified recombinant and natural allergen proteins for diagnostic purposes has been an invaluable step forward in the diagnosis of allergic diseases. Analyses carried out at this allergy centre using these new powerful tools

Figure 1 - Illustration showing the distribution of ragweed and mugwort sensitivity in patients living in the area of Milan



showed that the sera from most patients showing positive SPT to both *Artemisia* and *Ambrosia* pollen extracts contain IgE specific for both Amb a 1 and Art v 1, and sera from 47/105 (45%) consecutive ragweed-allergic patients showed IgE reactivity to Art v 1 as well. Since Art v 1 has been considered as a hallmark of primary sensitization to mugwort, these data seem to confirm that patients showing positive SPT to both weeds are in effect co-sensitized (1) and should be prescribed 2 distinct allergen extracts for immunotherapy.

However, things are seemingly going to change. In a new study, Leonard and co-workers (7) have detected a homologue to Art v 1 in ragweed pollen, that has been designated as Amb a 4. Both Art v 1 and Amb a 4 are defensin-like proteins and show a molecular weight of 30 kDa and 28 kDa, respectively. In their inhibition experiments, the authors demonstrate that Art v 1 and Amb a 4 show a high degree of cross-reactivity. Further, analysing the data obtained with sera from patients of different origin, they observe that many more Austrian (which are frequently primarily allergic to mugwort) than northern Italians (which are frequently primarily sensitized to ragweed), react to Amb a 4, and that 42% of Art v 1 sensitized patients react to Amb a 4. Notably,

in that study Amb a 4 was recognized by about 30% of sera from ragweed-allergic patients, a proportion that corresponds to the percentage of ragweed allergic subjects showing co-sensitization to mugwort in previous studies (1). The clinical significance of these findings can be summarized saying that finding Art v 1 hypersensitivity in the presence of Amb a 1 hypersensitivity (which is a marker of primary ragweed sensitization) may not indicate necessarily primary mugwort sensitivity as it may be a “false positive” result. Thus, at least in some cases it is not possible to discriminate between co-sensitization and co-recognition to ragweed even using the available panel of molecular allergens. While we wait for further studies confirming these findings, as well as for other recombinant mugwort and ragweed (Amb a 4) allergens available for diagnostic purposes in order to detect subjects primarily sensitized to mugwort, it is possible to conclude that these observations have much practical relevance as they will lead to more accurate diagnosis of weed-allergic patients and to a reduced prescription of (probably) useless mugwort-specific immunotherapies to subjects that are primarily allergic to ragweed only.

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