Staphylococcal Enterotoxins sensitization and response of Omalizumab in severe atopic and non atopic asthma

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To the Editor,

About 5% to 10% of all patients with asthma suffer from severe asthma, (1) which frequently is caused by IgE-mediated hypersensitivity against perennial and/or seasonal allergens. Anti-IgE treatment is efficacious and approved for the treatment of severe allergic asthma. To be eligible for omalizumab treatment, patients must be sensitized to a perennial aeroallergen, demonstrated either by skin prick test or by serum specific IgE.

It has been suggested that Omalizumab was efficient in non atopic asthmatic patients (2). However, negative skin prick tests or specific IgE measurements to common aeroallergens may occur because the patient was sensitized to an untested allergen (3). In patients considered as non atopic, extended panel of aeroallergen found that Staphyloccocal enterotoxin (SE) sensitization was one of the most prevalent (3).

Therefore, we hypothesized that the efficacy of Omalizumab in patients considered as non atopic could be caused by a sensitization to SE.

This single-center, retrospective real life study was performed in the Chest Diseases Department of Strasbourg University Hospital, including 54 severe asthmatic patients according the 2018 GINA guidelines, treated with omalizumab. All patients underwent an evaluation by the same physician trained for severe asthma at initiation and 4 months after omalizumab treatment. The assessment was based on a clinical evaluation.

Variables of interest are reported in Table 1. Patients were defined as sensitized to common aeroallergen if they had at least one positive prick test to the following allergens: mite, cat, dog,*aspergillus, alternaria* , grass, birch, ash, ragweed and mugword pollen (ALK Lab, Varennes-en-Argonne, France). Sensitization to SE was determined by specific IgE measurement (positivity threshold > 0.1 kUA/L Thermofisher).

Out of 54 asthmatic severe patients treated with Omalizumab 32 were considered responders.

Prevalence of sensitization to SE was to 61% in all patients, to 52.2% in patients not sensitized to common aeroallergen, and to 67.7% in patients sensitized to common aeroallergens ($p = 0.273$). Chronic RhinoSinusitis with Nasal Polyps (CRSwNP) was observed more frequently in patients not sensitized to common aeroallergens but sensitized to SE (Table1). They were also more frequently treated by oral corticosteroid. Total IgE count was higher in patients sensitized to SE (Figure 1).

No difference was observed in term of response of omalizumab regarding the sensitization to SE. In multiple logistic regression no association was found between efficacy of omalizumab and sensitization to SE after adjustment with gender, body mass index, total IgE count, CRSwNP, oral corticosteroid at baseline, and the sensitization with commun aeroallergens (OR 1.47; 95% CI, 0.4-5.4; p= 0.558).

Sensitization to SE did not appear as a marker of efficacy of omalizumab in severe asthmatics not sensitized to common aeroallergens. Consequently, the efficacy of Omalizumab could not be explained by an anti-IgE effect against SE. The absence of standardized evaluation of omalizumab response, the limited population, and the retrospective design could have been limitations. However, we found similar results as larger studies. Indeed, we showed that frequency of sensitization to SE was high in severe asthmatics sensitized or non to common aeroallergens. In EGEA cohort, prevalence of SE sensitization was close to our result (62.2 and 75.6%)for moderate to severe asthma (4) . Moreover, SE sensitization appears more frequently with CRSwNP and high total IgE count. this confirms previous publications (5) (6).

Even though larger prospective studies would be needed to evaluate the association between SE sensitization and omalizumab efficacy in severe asthma, no tendency was found in our study.

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Table 1: Comparison of severe asthmatic patients in function of sensitization to aeroallergen and sensitization to SE

	Patients sensitized to common aeroallergen	**Patients not**
n	31	11
Age (years)	57.00 [51.50, 68.50]	60.00 [55.50, 6
Gender (% male)	20 (64.5)	2 (18.2)
BMI	23.00 [22.00, 27.00]	27.00 [23.00, 3
CRSwNP (%)	6 (19.4)	4 (36.4)
FEV1 (predicted %)	67.00 [54.75, 81.75]	72.50 [59.75, 8
Total IgE measurment (kU/l)	289.00 [112.50, 1115.00]	78.00 [16.50, 1
Eosinophil cells blood count (G/L)	0.25 [0.13, 0.65]	0.22 [0.06, 0.58
Oral cortisteroid at baseline (%)	6 (19.4)	6 (60.0)
Oral corticosteroid dose at baseline	0.00 [0.00, 0.00]	8.75 [0.00, 13.7
Rate of severe exacerbation the year before evaluation	1.00 [0.50, 4.00]	4.00 [1.50, 8.00
Omalizumab efficacy (%)	20 (64.5)	6 (54.5)

BMI: Body Mass Index, CRSwNP chronic rhinosinusitis with nasal polyposis, Results are presented in median [IQR] unless otherwise note, Kruskal-Wallis Rank Sum Test and Fisher's Exact Test were realized for quantitative and qualitative data respectively.

Figure 1 : Total IgE count in function of the sensitization to common aeroallergen and SE