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Case Report

A Case of Successful Dupilumab Treatment in Allergic Rhinitis and Atopic Dermatitis in Patient with Multiple Food Allergies, Pollen and Perennial Sensitization

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Abstract: Dupilumab is an interleukin 4 (IL-4) receptor α-antagonist that inhibits IL-4 and IL-13 signaling through blockade of the shared IL-4αR subunit. Blockade of IL-4/13 is effective in reducing Th2-oriented response including the release of proinflammatory cytokines, chemokines, and IgE. These mechanisms are known as mediators in the pathogenesis of atopic dermatitis, food allergy, allergic rhinitis with and without polyposis, and asthma. We report the clinical case of a patient in which the Th2-mediated inflammatory substrate is evident in comorbid allergic manifestations who show a good response after treatment with Dupilumab for moderate atopic dermatitis.

Keywords: dupilumab; atopic dermatitis; th2 response

1. Introduction

Dupilumab is an interleukin 4 (IL-4) receptor α-antagonist that inhibits IL-4 and IL-13 signaling through blockade of the shared IL-4αR subunit. Blockade of IL-4/13 is effective in reducing Th2-oriented response including the release of proinflammatory cytokines, chemokines, and IgE. [1-2]

Thus, Th2 inflammation is found in around 60% of patients with severe asthma. Furthermore, most patients with allergic rhinitis and chronic rhinosinusitis with nasal polyps (CRSwNP) present Th2 inflammation. Moreover, in atopic dermatitis (AD), there is an intense inflammatory reaction with marked participation of Th2 cytokines.

The Th2 signaling pathway is also recognised to be involved in food allergy. In particular, innate lymphoid cell type 2 (ILC2) have been linked to food allergy pathogenesis in mice through production of Th2-associated cytokines. [3-4]

These Th2-induced cytokines reprogrammed Tregs have diminished suppressive capacity and in fact contribute to food allergy pathogenesis by producing IL-4. [5]

Moreover in humans, mutations in the skin structural protein filaggrin, such as in AD, have been noted to confer risk for allergic diseases, including food allergy. [6-7]

In the European Countries dupilumab has been approved to treat moderate-to-severe AD and severe asthma in patients aged 12 years or over where disease is not adequately controlled by a combination of high-dose inhaled corticosteroids. Besides, Dupilumab is also the first biologic to receive a licence both in the US and Europe to treat Chronic Rhinosinusitis with Nasal Polyps(CRSwNP). [8- 9]

We report the clinical case of a patient in which the th2-mediated inflammatory substrate is evident in comorbid allergic manifestations who show a good response after treatment with Dupilumab.

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2. Case Presentation

Male patient 22 years , with a history of AD, applied to our Clinic with complaints of severe generalized intractable pruritus. On physical examination, erythematous macules with lichenification due to AD were found on the volar surfaces of arms and legs, on the back and on the hands, worsening in the last two years when started working as plumber.This clinical picture was already present in childhood and treated with topical corticosteroids.His eczema area and severity index (EASI) score was 43. Affected body surface area (BSA) was 40%.Visual analogue scale (VAS) of pruritus was 60/100 mm. Of his other allergic conditions, the patient mentioned rhinitis with seasonal exacerbations in March-June period and contact dermatitis associated with costume jewelry and belt buckle contact area. The Sino-Nasal Outcome Test-22 (SNOT-22) questionnaire was 41(0-110).No asthma related symptoms reported. No family history of allergic diseases was detected.Even considering the absence of symptoms suggestive of nasal polyposis, this manifestation was excluded by otorhinolaryngological evaluation. Also the presence of allergic asthma was excluded by spirometry with broncho-reversibility test which showed respiratory parameters within the limits.In addition, the patient showed oral allergy syndrome (OAS) with bananas, episodes of anaphylaxis like wheezing, diarrhea and vomiting eating fresh kiwi fruit. No adverse events with other foods including Rosaceae and tree nuts. During early childhood, for severe atopic dermatitis, he performed prick tests with positivity for casein, egg yolk, banana and Dermatophagoides spp. Despite these results no restriction diet was being performed. No systemic adverse events were reported by the patient eating cow milk, bovine meat and eggs. Given the complex picture of polysensitization and the inability to perform prick tests because of AD manifestations on the harm surfaces, it was requested to perform total IgE assay by electrochemiluminescent immunoassay (ECLIA) and Allergy Explorer-ALEX2® (Macroarray Diagnostics, Vienna, Austria).In the ALEX test, 300 allergens, including molecules and extracts, are spotted onto a nitrocellulose membrane in a cartridge chip, which is then incubated with 0.5 mL of a 1:5 dilution of serum, containing a CCD inhibitor under agitation. We considered positive a concentration of ≥0.3 kUA/L.The total IgE assay was >2500 U/mL. After evaluation with macroarray proteomics, the following reactivities were shown: food allergy driven by lipid transfer protein (nsLTPs) sensitization, and Act d 1 (cysteine protease) of kiwi-fruit and reactivity towards multiple pollen allergens such as cypress, olive tree, and grass pollens. Also, an important sensitization to several molecular allergens of Dermatophagoides (D.) pteronyssinus and D. farinae was detected, accounting for rhinitis symptoms.

3. Discussion

Atopic dermatitis is the most common chronic inflammatory skin disease. It is often the first indicator of allergic diseases, and the most of patients present allergic rhinitis and/or asthma as comorbidity [10].The blockade by dupilumab of these key drivers of Th2-mediated inflammation could help in the treatment of AD and his related diseases.Allergic rhinitis (AR) is a very common disorder that affects people of all ages.Classic symptoms include sneezing, rhinorrhea, nasal obstruction. Allergenic triggers may include airborne pollens, molds, dust mites, and pet epithelia. His management rests on symptomatic treatment with antihistamines, intranasal or orally-administered corticosteroids which are often unable to control symptoms [11].Nettis et al evaluated benefit of dupilumab after 16 weeks of treatment in perennial AR and perennial allergic asthma caused by indoor allergens in patients with severe AD. In adults with comorbid perennial AR, Dupilumab was associated with significant improvements in disease control (measured using the Rhinitis Control Scoring System) and in perennial AR quality of life [12].Moreover, a post hoc analysis of the phase 3 Liberty Asthma quest study evaluated the effects of Dupilumab in patients with comorbid perennial AR .Dupilumab reduced severe asthma exacerbations and improved forced expiratory volume in 1 second (FEV1),treatment also numerically improved the 5-item Asthma Control Questionnaire and Standardized Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ).Besides, Dupilumab treatment with 200 mg or 300 mg every 2 weeks had improved RQLQ+12 subscore in 6 of 7 domains (activities, sleep, practical problems, nasal symptoms, eye symptoms, and emotions) [13].Food allergies are characterized by Th2-driven inflammatory

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responses too.Allergen-induced IL-4 expression in peripheral mononuclear cells are associated with clinical allergy to milk and IgE-sensitization to milk and peanut [14].Moreover patients with mutations in IL-4 receptor alpha (IL-4Ra) and IL13 have an increased risk of food allergy [15]A 30-year-old patient with a history of severe AD, AR, asthma, allergic reaction to pistachio during food challenge and anaphylaxis to corn, after initiating treatment with dupilumab, has come to tolerate these foods,confirmed by oral challenge after three months of therapy.[16]Currently there are three randomized placebo-controlled phase 2 clinical trials which evaluate Dupilumab treatment in peanut allergy[17-19].

4. Conclusions

Several studies have shown an important role of type-2 immunity in the immunopathology of AD and its comorbidities like asthma and nasal polyposis, but less on allergic rhinitis and food allergy. Moreover, data of these conditions are from case reports or phase 2 studies which are ongoing. In our case, despite the short follow-up and short duration of therapy, we want to underline the good response to Dupilumab treatment in severe AD and comorbid type-2 inflammatory diseases like allergic rhinitis. Its efficacy and approval are already known for asthma and nasal polyposis but new possible indications are increasingly explored in which Th2 inflammation is involved.

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