

A case of Grover disease treated with Dupilumab: Just serendipity or a future perspective?

Dear Editor

We herein present the case of a 77-year-old Caucasian male patient treated with Dupilumab for chronic rhinosinusitis with bilateral nasal polyposis (CRswNP) with concomitant Grover disease. For his chronic rhinosinusitis, he was unsuccessfully treated with oral and intranasal corticosteroid and received two endoscopic sinus surgery (ESS) followed by multiple relapses. Five years ago, he was diagnosed with Grover disease and unsuccessfully treated with topical corticosteroids and Acitretin. The severity of his CRswNP was documented by a nasal polyps score (NPS, a score attesting the degree of nasal obstruction via endoscopy) of 5, a sino-nasal outcome test (SNOT22, a 22-item health-related quality of life evaluation) of 55, the presence of severe smell impairment (VAS-hyposmia = 10), his history of relapses and the need of continuous use of intranasal corticosteroids. He was therefore eligible to be treated with Dupilumab at standard doses (600 mg the initial dose and then 300 mg every other week). Dupilumab is a human monoclonal IgG4 antibody that inhibits interleukin-4 (IL-4) and interleukin-13 (IL-13) signaling by specifically binding to the IL-4R α subunit shared by the IL-4 and IL-13 receptor complexes and it is the first biological available for the treatment of CRswNP since 2019.^{1,2} Dupilumab was used as monotherapy and was well tolerated, with no secondary adverse effects. After 14 weeks of treatment, the chronic rhinosinusitis did not improve (SNOT22 = 54, NPS = 8, VAS-Hyposmia = 9) thus requiring the administration of one cycle of oral corticosteroid, but a complete regression of the dermatological signs and pruritus was observed. Thus, even though the ETN's therapeutic failure (40 weeks after the treatment: SNOT22 = 54, NPS = 8, VAS-Hyposmia = 5, after a second cycle of oral corticosteroid), given the excellent dermatological response, the treatment with Dupilumab was not discontinued and after 44 weeks the patient remained completely clear (Figure 1).

Grover disease is a relatively common skin condition that generally affects Caucasian men older than 40 years and is characterized by an acute-to-subacute highly pruritic skin eruption of slightly flesh-colored to erythematous, edematous papules and/or papulovesicles that commonly affects the trunk. Although the pathogenic mechanism of the disease remains unknown, it has been associated with heat, sweating, renal failure, malignancy and several drugs. There is currently no standard approach: as first-line therapy topical steroids and vitamin D analogues

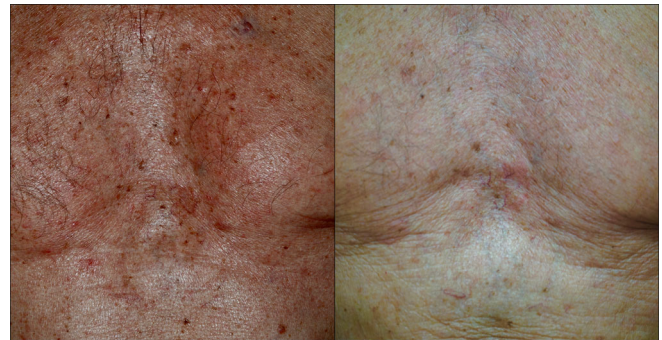


FIGURE 1 Clinical examination before treatment (on the left side) and after 40 weeks of treatment with Dupilumab at standard dose (on the left side)

are frequently used in association with adjuvant antihistamines; in severe, prolonged or refractory cases, oral retinoids and oral corticosteroids should be considered as well as phototherapy.³ Butler et al. recently described three cases of Grover disease, initially unsuccessfully treated with traditional drugs, that markedly improved with Dupilumab at standard doses in 6–8 weeks.⁴ The positive response to Dupilumab suggests that type-2 inflammation may play a role in the pathogenesis of Grover disease, as shown by previous studies. Among them, a case of Grover disease after receiving intravenous recombinant human IL4, a known Th2-inducer, and a second case induced by Ipilumab, an anti-CTLA-4 monoclonal antibody.^{5,6} In the latter report, given that the same patient did not develop the same clinical lesions under treatment with Pembrolizumab (an anti-PD1 monoclonal antibody), is consistent with preclinical data demonstrating that PD-1 inhibition induces a Th1/Th17 responses while producing less Th2 type inflammation. One knows that age-related changes of the immune system may induce a pro-inflammatory status with dysregulation in the Th1/Th2-system skewed toward a Th2-inflammation profile. The higher production of Th2 cytokines documented in elderly results, in fact, in an enhanced unspecific B cell activation and IgE antibody production.^{7–9} Since type-2-inflammation seems to contribute to the pathogenesis, the phenomenon illustrated before could explain why the incidence of Grover disease increases with age. Precisely because older patients, often dealing with

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multiple comorbidities, are the most affected from Grover disease, novel treatment options, safer and better tolerated than traditional medicines, need to be found. In the light of our case and the report of Butler et al,⁴ Dupilumab seems to provide a safe and effective treatment for patients recalcitrant to traditional medications and oral drugs. Certainly, further studies are necessary to confirm our hypothesis.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

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