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Dupilumab Therapy in a Patient with Atopic Dermatitis and Severe Atopic Keratoconjunctivitis

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Dupilumab: atopic dermatitis and keratitis

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Dear editor,

Atopic dermatitis is an inflammatory skin condition affecting 1 to 20% of the population worldwide. Ocular comorbidities like conjunctivitis, keratitis and keratoconus have been more often described in atopic patients (1). Approximately 20% need systemic therapy due to the severity of their disease (moderate to severe). Dupilumab is a human anti-interleukin-4 receptor- α antibody, approved as the first biologic treatment for atopic dermatitis (2). Cases of conjunctivitis have been reported more frequently in patients treated with dupilumab in clinical trials and in clinical practice (3-4). We describe a 45-year-old patient who has suffered from severe atopic dermatitis and conjunctivitis since childhood. Several ocular complications were observed in both eyes: repeated exacerbations of bacterial conjunctivitis, bacterial and mycotic keratitis, complicated cataract extraction, rhegmatogenous retinal detachment treated by pars plana vitrectomy, cystoid macular edema and steroid-induced glaucoma, all in the area of atopic conjunctivitis (Fig.1a,1b). He underwent his first eye surgery for steroid-induced cataract at the age of 15. In addition, three corneal transplantations were performed in each eye for corneal and graft failure, respectively (Fig.2a). The right eye is blind as a result of steroid-induced glaucoma, refractory to medical and surgical therapy. For several years he was treated with cyclosporine A for the skin lesions as well as for the ocular complications. Due to the failure and systemic side effects of cyclosporine A, we decided to switch to dupilumab on the classical dose of 600mg s.c

on baseline and then 300mg s.c every 2 weeks. The patient's initial EASI score was 38.6. After 16 weeks he achieved EASI75 (Fig.1c). Two months after starting dupilumab, the planned corneal transplantation was performed in his left eye. The ophthalmologist suggested adding azathioprine to decrease the risk of graft failure, but after 1 month azathioprine was discontinued due to leucopenia and concomitant parotitis. Dupilumab was continued. The patient has been on dupilumab for 6 months with very good results as being a EASI75 responder. No conjunctivitis/keratoconjunctivitis and/or graft rejection have been observed and he showed well postoperative healing after corneal transplantation (Fig.2b).

Patients with atopic dermatitis have an increased risk of ocular comorbidities including keratoconjunctivitis, infectious keratitis, blepharitis, tear film dysfunction, cataract, keratoconus, steroid-induced glaucoma and retinal detachment (5,6). In the clinical trials of dupilumab, conjunctivitis and keratitis have occurred more frequently in patients on dupilumab than in placebo (SOLO 1, 2% vs 7-11%; SOLO 2, 1% vs 9%) (2-3). One explanation could be that blocking IL-4Ra results probably in increased systemic bioavailability of free IL-4 and IL-13. This causes inflammatory symptoms whether by stimulating the CD40-dependent IgE production via B cells or by activating the IL-13 R alpha 2 receptor that has not been blocked by dupilumab or both (7). Treatment with dupilumab may be considered in patients with atopic conjunctivitis/keratoconjunctivitis but close follow-up is required and if eye symptoms worsen, discontinuation should be considered. The higher risk of ocular complications during dupilumab therapy is well established even though etiology is still unclear. There is a lack of data concerning treatment with dupilumab in patients with an existing eye disease, especially keratoconjunctivitis (4). We have treated our patient with severe atopic dermatitis and keratitis for more than 6 months with dupilumab and we did not observe any progression of keratitis. During treatment he had a corneal transplantation and the graft was well healed without any other immunosuppression therapy. More data are needed, but even though in clinical trials there is a higher risk of eye complications during dupilumab therapy, preexisting eye comorbidities may be finally profited as in our case, most probably by decreasing the systemic inflammation.

Acknowledgment

The patients in this manuscript have given written informed consent to publication of their case details.

References:

1. Thyssen JP, Toft PB, Halling-Overgaard AS, Gislason GH, Skov L, Egeberg A. Incidence, prevalence, and risk of selected ocular disease in adults with atopic dermatitis. *J Am Acad Dermatol* 2017; **77**:280-286.
2. Beck LA, Thaçi D, Hamilton JD, Graham NM, Bieber T, Rocklin R, Ming JE, Ren H, Kao R, Simpson E, Ardeleanu M, Weinstein SP, Pirozzi G, Guttman-Yassky E, Suárez-Fariñas M, Hager MD, Stahl N, Yancopoulos GD, Radin AR. Dupilumab treatment in adults with moderate-to-severe atopic dermatitis. *N Engl J Med* 2014; **371**:130-139
3. Simpson EL, Bieber T, Guttman-Yassky E, et al. Two phase 3 trials of dupilumab versus placebo in atopic dermatitis. *N Engl J Med* 2016; **375**:2335-2348.
4. Wang C, Kraus C, Patel K, Ganesan A, Grando S. Real-world experience of dupilumab treatment for atopic dermatitis in adults: a retrospective analysis of patients' records. *Int J Dermatol* 2019, Jul 8. doi: 10.1111/ijd.14573. [Epub ahead of print]
5. Beck KM, Seitzman GD, Yang EJ, Sanchez IM, Liao W. Ocular Co-Morbidities of Atopic Dermatitis. Part I: Associated Ocular Diseases. *Am J Clin Dermatol* 2019; **20**:797-805.

6. Chen JJ, Applebaum DS, Sun GS, Pflugfelder SC. Atopic keratoconjunctivitis: A review. *J Am Acad Dermatol* 2014; **70**:569-75.
7. Wohlrab J, Werfel T, Wollenberg A. Pathomechanism of dupilumab-associated inflammatory eye symptoms. *J Eur Acad Dermatol Venereol* 2019; **33**:e435-e436.

Figure legends:

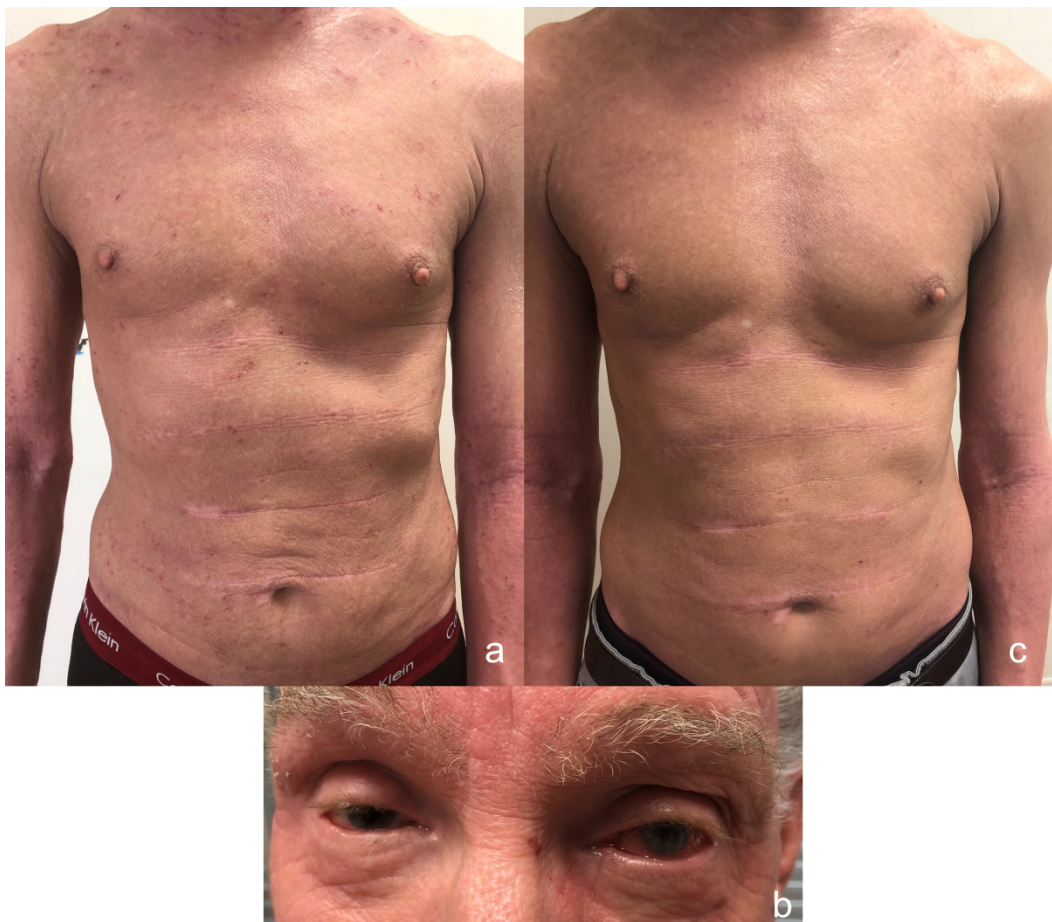
Fig.1a: Severe form of atopic dermatitis with erythematous lesion, excoriations, papulation and lichenification

Fig.1b: Severe atopic keratoconjunctivitis

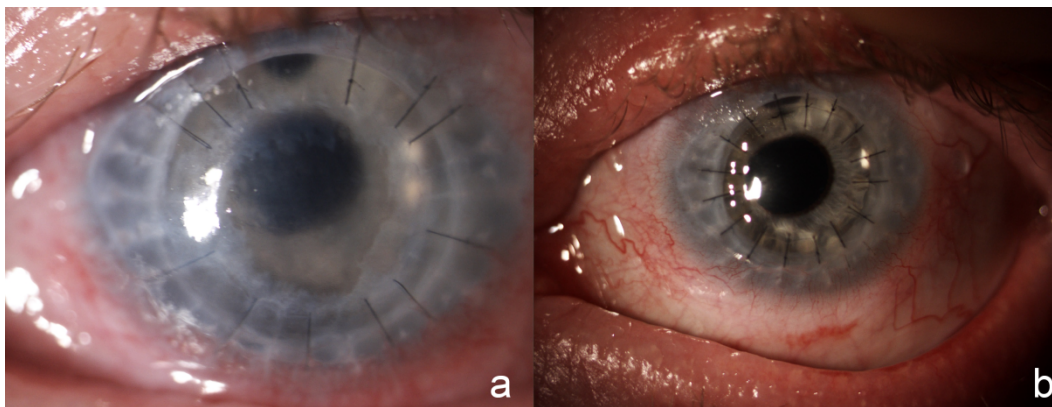
Fig.1c: Achieving EASI75 after 16weeks on dupilumab therapy

Fig.2a Atopic keratoconjunctivitis and graft failure 3 years after transplantation

Fig.2b Clear corneal graft 90 days after repeat transplantation



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