

DR. GIULIA CALABRESE (Orcid ID : 0000-0002-2013-4802)

DR. GAETANO LICATA (Orcid ID : 0000-0002-0834-1331)

DR. EUGENIA VERONICA DI BRIZZI (Orcid ID : 0000-0002-0278-2443)

DR. GIUSEPPE ARGENZIANO (Orcid ID : 0000-0003-1413-8214)

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Dupilumab and conjunctivitis: a case-series of twenty patients.

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Authors:

Giulia Calabrese¹, Alessio Gambardella¹, Gaetano Licata¹, Eugenia Veronica Di Brizzi¹, Roberto Alfano², Giuseppe Argenziano

Name of the institutions:

¹Dermatology Unit, Department of Mental and Physical Health and Preventive Medicine, University of Campania Luigi Vanvitelli, Naples, Italy

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²Department of Anesthesiology Surgery and Emergency, University of Campania Luigi Vanvitelli, Naples, Italy.

Corresponding author:

Giulia Calabrese, MD, Dermatology Unit, Department of Mental and Physical Health and Preventive Medicine, University of Campania Luigi Vanvitelli, Via Sergio Pansini, 5, 80131 Naples, Italy; phone: 3663374397; e-mail: allergologiavanvitelli@gmail.com

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In our Dermatology Unit, from May 2018 to January 2020, we enrolled 277 patients affected by moderate-severe forms of atopic dermatitis for the treatment with dupilumab. Six patients have been treated since about 104 weeks while eighteen patients since about 78 weeks. During the first examination, all patients gave written informed consent to the publication of their case details and received the prescription of trehalose/hyaluroate tear substitute to hydrate the conjunctival mucosa. The ones with peripalpebral eczema were treated with tacrolimus 0.1% ointment. We indentified 20 cases of conjunctivitis (incidence:7,2%). Interrogating patients, 6 of them admitted not to take preventive therapy (30% of the total with conjunctivitis). Excluding these, the incidence of conjunctivitis was equal to 5%. 19 patients were affected by a non-specific keratoconjunctivitis associated with dry eye (Fig. 1A-B), 1 patient presented a follicular conjunctivitis associated with limbitis (incidence of follicular conjunctivitis:0,4%) (Fig. 2) . Considering only the 14 patients affected by conjunctivitis that performed preventive therapy, history of previous conjunctivitis was found in 6 patients (42,8% of the total). The ocular involvement was monolateral in 11 subjects and bilateral in the remaining 3. Only

two patients (0,7% of the total) interrupted therapy for non responsive conjunctivitis (pre-existing the start of the biological drug and persisting after its cessation). The mean age of patients with conjunctivitis was 35 years (minimum age : 18 ; maximum age : 83) , similar to the mean age of the total patients treated with Dupilumab (36 years ; minimum age: 18 years ; maximum age: 83 years). Speaking about gender, 11 of 14 patients with conjunctivitis were male (78,5%), while in the total cohort 203 were male and 74 female. The mean EASI score of patients affected by conjunctivitis was equal to 37 (EASI range : 26-60), higher than the mean EASI score of the total 277 patients (equal to 28) . All 14 patients had periparpebral eczema, 11 of them had seborrheic-like dermatitis and 11 facial eczema. Of 277 patients treated with dupilumab, 75 patients (27%) presented facial seborrheic-like dermatitis while 71 (26%) showed facial eczema without signs of seborrheic dermatitis. These patients were respectively treated with antifungal-corticosteroid cream, itraconazole tablets and tacrolimus 0,1% ointment. Considering the total of patients with facial eczema and peripalpebral eczema, (146 patients), the percentage of subjects who developed conjunctivitis is 9,5%. Conjunctivitis seems to be a tardive adverse effect: the mean time of onset from the start of therapy was sixth month of therapy (time lapse: 3 -14 months), two patients showed the first episode after 12 months while a patient after 14 month. All subjects showed a remarkable improvement of their AD despite the conjunctivitis. All cases of conjunctivitis were treated with cortico-antibiotic in eye drops associated with tacrolimus ointment 0.1% with complete response in all cases except two. Cyclosporine in ophthalmic drops was prescribed in the patient with follicular conjunctivitis, with regression of the disease. Thanks to the prophylactic procedures, the incidence of conjunctivitis between our patients, was equal to 5%, lower than Phase III studies (incidence equal to 8%) and the real life publications (incidence equal to 9-28%) ¹⁻¹⁰. The incidence of conjunctivitis was higher considering patients

with facial eczema (9,5%), despite specific therapy like antifungal-corticosteroid cream, tacrolimus 0,1% ointments and itraconazole tablets. A possible association between facial eczema and conjunctivitis is probable but more data are need. Probably, prophylactic therapy, based on trehalose/hyaluroate tear substitute associated with the treatment for palpebral and facial eczema, reduced dry eyes and consequently conjunctivitis.

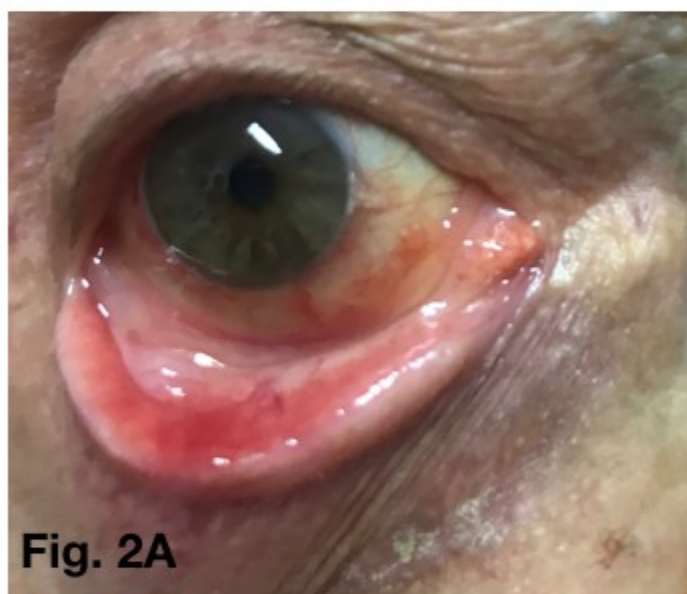
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