Research letter

Spectrum of severe ocular complications following dupilumab exposure: A perspective from the ophthalmology clinic

To the Editor: Dupilumab has been associated with ocular side effects in 30% to 50% of patients, mostly including mild dryness and redness that respond to over-the-counter topical lubricants.[1-4] However, most studies have not systematically included formal ophthalmologic examinations that may identify more comprehensive ocular pathologies.[5] Herein, we report a 5-year retrospective review of patients treated with dupilumab evaluated at an academic ophthalmology center.

Between 2016 and 2021, 49 patients being treated with dupilumab predominantly for the treatment of atopic dermatitis were evaluated in the ophthalmology clinic (Fig 1). Of the 49 patients, 57% were asymptomatic and evaluated for preexisting ocular disease while 43% were referred for ocular complications occurring at a mean time of 1 month after initiation of dupilumab. Although there were no statistically significant differences in the characteristics of the patients who demonstrated ocular symptoms, we observed a small yet notable number of patients with ophthalmological reactions considerably more severe than ocular surface conditions that have been most widely reported. These diagnoses included cataracts (10%), corneal scarring (14%), and elevated intraocular pressure (10%). The majority of patients who experienced ophthalmic complications demonstrated improvement after discontinuing dupilumab (Table I). Many patients (47%) had ophthalmic diagnoses before dupilumab initiation, consistent with the patient population seen in ophthalmology clinics. Approximately 35% of the patients had undergone prior ocular surgeries.

There were several examples of severe reactions in patients who had preexisting ophthalmic diagnoses and prior ocular surgeries, and who often required further ophthalmic intervention after dupilumab exposure to address these reactions. For example, those with preexisting dry eyes generally demonstrated exacerbation of symptoms with dupilumab use, including a patient who was found to have 30% to 60% meibomian gland loss and required eyelid thermal pulsation treatment to continue using dupilumab. In a patient with prior corneal

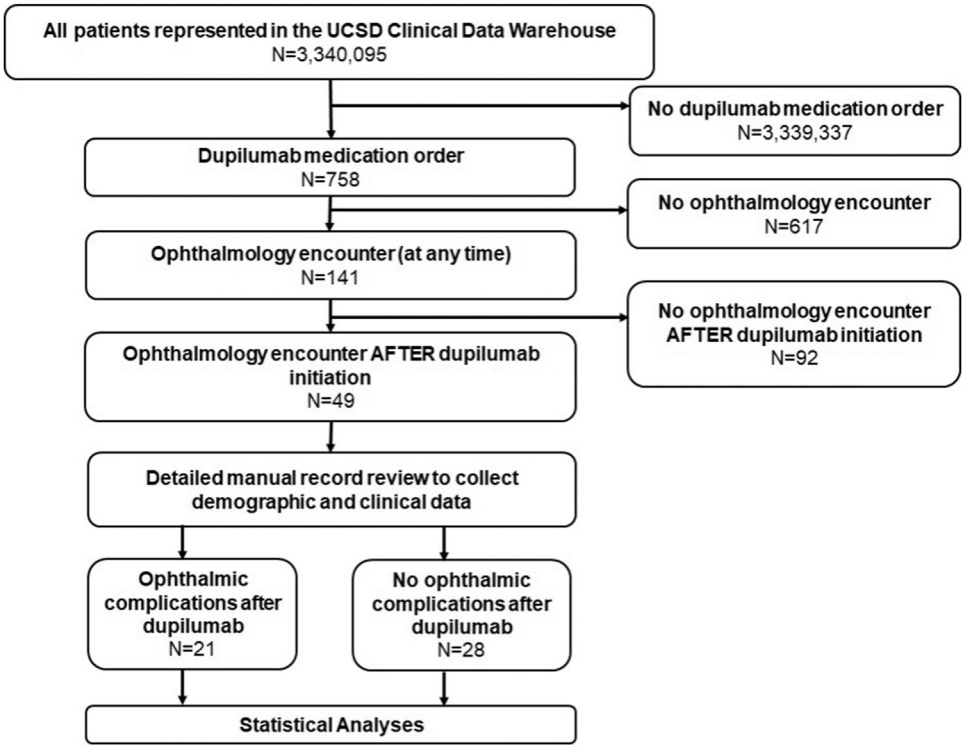

Fig 1. STROBE diagram depicting the study cohort definition and identification of adult patients who were prescribed dupilumab and underwent ophthalmological evaluation at the University of California San Diego from January 1, 2016 to June 11, 2021.

Table I. Demographic and clinical characteristics of patients undergoing ophthalmological evaluations after initiating dupilumab at the University of California San Diego, 2016-2021

Characteristic	Total cohort (N = 49)	Dupilumab patients with ophthalmic complications (N = 21)	Dupilumab patients without ophthalmic complications (N = 28)	*P* value
Age				.28
Mean (SD)	53.2 (20)	49.7 (22)	56 (18)	
Sex				.06
Female	24 (49%)	7 (30%)	17 (18%)	
Male	25 (51%)	14 (70%)	11 (56%)	
Race/ethnicity				.28
Caucasian	26 (51%)	8 (38%)	18 (35%)	
Asian	12 (24%)	8 (38%)	4 (8%)	
Black or African American	3 (6%)	1 (5%)	2 (4%)	
Hispanic	1 (2%)	1 (5%)	0	
Other/mixed	4 (8%)	2 (10%)	2 (4%)	
American Indian or Alaskan Native	1 (2%)	1 (5%)	0	
Middle Eastern	1 (2%)	0	1 (2%)	
Not reported	1 (2%)	0	1 (2%)	
Indication for dupilumab				.43
Atopic dermatitis	43 (88%)	19 (90%)	23 (88%)	
Spongiotic dermatitis	1 (2%)	0	1 (2%)	
Severe persistent asthma	2 (4%)	0	2 (4%)	
Bullous pemphigoid	1 (2%)	0	1 (2%)	
Recurrent sinusitis	3 (6%)	2 (10%)	1 (2%)	
Dupilumab dosing				.09
600 mg/300 mg every 2 weeks	36 (73%)	15 (71%)	21 (43%)	
300 mg every 2 weeks	11 (22%)	5 (24%)	6 (12%)	
400 mg/200 mg every 2 weeks	2 (4%)	1 (5%)	1 (2%)	
Ophthalmic history				
Prior ophthalmic diagnosis	23 (47%)	11 (52%)	12 (43%)	.54
Prior ophthalmic surgery	17 (35%)	9 (43%)	8 (29%)	.31
Ophthalmological reaction				
Dryness, irritation		13 (62%)	N/A	N/A
Conjunctivitis		11 (52%)	N/A	N/A
Vision abnormality		8 (38%)	N/A	N/A
Eyelid pathology (ectropion, entropion, lagophthalmos)		7 (33%)	N/A	N/A
Blepharitis (meibomian gland dysfunction)		6 (29%)	N/A	N/A
Corneal scarring		3 (14%)	N/A	N/A
Cataracts		2 (10%)	N/A	N/A
Intraocular sequelae (anterior uveitis, elevated pressure)		2 (10%)	N/A	N/A
Need for dupilumab discontinuation due to ophthalmic reaction				
Discontinued dupilumab*		9/21 (43%)	N/A	N/A
Symptom resolution after discontinuation†		5/9 (56%)	N/A	N/A

Percentages do not add up to 100% due to patients having multiple simultaneous reactions.
*Discontinuation specifically due to adverse ophthalmologic reaction.
†Improved symptoms within 6 months of dupilumab discontinuation.

transplantation, dupilumab use was associated with evidence of corneal transplant rejection consisting of edema, corneal haze, and neovascularization. Steroid and antihistamine treatment was initiated, but unfortunately, the patient was lost to follow-up. Finally, as an illustration of the extent of ocular surface irritation that can be associated with dupilumab use, one patient with a history of retinal tear, ocular hypertension, and intraocular lens instability developed severe refractory conjunctivitis after dupilumab initiation that provoked eye rubbing aggressive enough to cause complete lens implant dislocation. This required surgical intraocular lens repositioning and iris fixation.

Currently, no official guideline exists regarding ophthalmic screening examinations for dupilumab.

The perspective from our ophthalmology clinic demonstrates the broad range and severity of ocular complications possible with dupilumab treatment. Pathophysiological mechanisms of ophthalmic complications remain an area of ongoing investigation, as it is unclear whether adverse effects are secondary to interleukin (IL) 4/IL-13 effects or reflect altered underlying immune milieus such as type 1 T helper shift in the conjunctiva, particularly in atopic dermatitis and eosinophilia.[5] We recommend specific ocular history and review-of-systems for patients considering dupilumab therapy. Ophthalmic evaluation should be considered in patients with a history of preexisting ocular diagnoses or surgeries.

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Conflicts of interest

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