Association of ocular cicatricial pemphigoid with a history of malignancy and severe vision loss

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To the Editor:

Mucous membrane pemphigoid (MMP) is a rare autoimmune blistering disorder affecting various mucous membranes and occasionally the skin [1]. Ocular monosite MMP refers to MMP involving solely the ocular surface with the potential to compromise vision and is also known as ocular cicatricial pemphigoid (OCP), [2]. In OCP, subepithelial blisters are formed by antibodies against surface antigens at the basement membrane zone of the conjunctival epithelium [3]. Initial symptoms of OCP are usually nonspecific such as ocular burning, irritation, foreign body sensation, discomfort, and tearing [4]. Early diagnosis and treatment are essential to avoid complications.

In this study, we retrospectively reviewed 32 patient charts with a diagnosis of MMP at tertiary care centers in New Orleans, Louisiana between 2006 and 2021. Patients were diagnosed either through clinical findings or through biopsy. We determined disease severity, complications, and associated findings. Patients with OCP were placed in the OCP cohort and patients with multisite and monosite (other than ocular) MMP were placed in the MMP cohort [2]. International classification of diseases 9 and 10 codes were used to search for individual patients. All statistical analyses were conducted using the R Project for Statistical Computing, version 4.1.0.

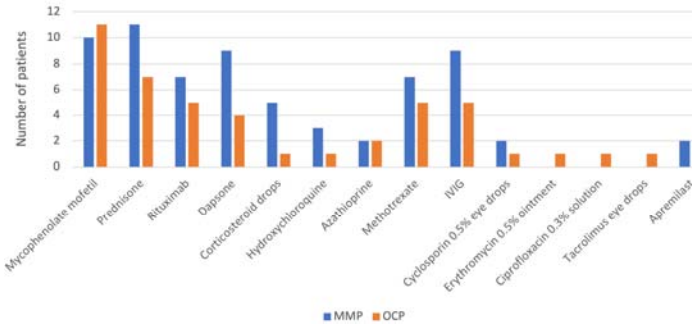

Figure 1. *Mucous membrane pemphigoid. Number of patients that received each treatment modality in ocular cicatricial pemphigoid (OCP) versus mucous membrane pemphigoid (MMP)*

In our cohort of 32 patients, there were 17 patients in the OCP group and 15 in the MMP group. **Table 1** outlines various clinical features and characteristics of OCP and MMP. Independent two-tailed t-test at 0.05 significance level was performed on patient age (P=0.72), age at presentation (P=0.54) and average number of medications per patient (P=0.03). The number of patients that received a given medication is shown in **Figure 1**. Fischer exact test was performed on gender (P=0.73) and race (P=1.00); no statistical significance was noted.

Of the 17 patients in the OCP group, 5 patients had severe vision complications (two blurry vision, three complete vision loss). Blurry vision is defined as the lack of sharpness of vision. Of the 15 patients in the MMP group, 12 patients had ocular involvement and only one patient had vision complications (blurry vision). Severe vision complications are likely associated with OCP compared to MMP, but the difference is not statistically significant (P=0.18). Patients with OCP are commonly resistant to treatment and are more likely to result in blindness

than patients with MMP restricted to oral mucosa [5]. Our study supports the association with OCP and malignancy. A history of cancer was detected in five OCP and none of the MMP cohort, and in all cases the cancer diagnosis preceded the disease occurrence. We determined there is a statistical difference that a history of malignancy precedes OCP diagnosis compared to MMP. Types of cancer included melanoma, bronchial squamous cell carcinoma, basal cell carcinoma, renal cell carcinoma, and Hodgkin lymphoma.

Ocular cicatricial pemphigoid is a devastating disease. Systemic immunotherapy can be effective, however, despite the initiation of treatment advanced stages of disease can result in significant ocular complications including vision loss. Limitations of this study include retrospective design, generalizability, a small cohort, and patients being lost to follow-up. Our data demonstrates that there is an increased risk of severe vision complications (blurry vision, vision loss) in patients with OCP and there is an association of OCP with a history of malignancy.

Potential conflicts of interest

Dr. Andrea Murina is a speaker for Abbvie, Amgen, Eli Lilly and Company, Janssen, Ortho-Dermatologics. She has served as a consultant for Janssen, Novartis and UCB.

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Table 1. *Patient demographics and disease characteristics.*

Patient	Age	Gender	Race	Age at present	Autoimm disease	Ocular history	Past medical history	Complications
MMP								
1	59	M	C	55	No	Dry eyes	HTN	None
2	73	F	C	66	SS, HypoTH	Dry eyes, cataract	HTN, HCL	MSSA conjunctivitis of R eye, corneal scarring, trichiasis
3	77	F	C	74	No	Dry eyes	HCL, asthma	Conjunctival injection, blepharitis
4	71	F	C	66	HypoTH	No	DM, thrombocytopenia	None
5	80	M	C	80	No	No	Dyslipidemia	None
6	72	M	C	68	No	Dry eyes	HTN, HCL	conjunctival abrasion
7	74	M	C	71	Graves	Cataracts	Asthma, Barrett, HSV	None
8	71	F	C	62	No	Glaucoma	DM, HTN, HCL	trichiasis, dermatochalasis, symblepharon
9	33	F	AA	23	Bechet	No	Atrophic rhinitis	entropion, trichiasis
10	37	M	C	32	Bechet	No	No	cicatricial conjunctivitis
11	81	F	C	71	No	Dry eyes	No	none
12	87	F	Other	77	No	Cataracts	HTN, DM, HSV	corneal abscess
13	66	F	C	47	No	Cataracts	HTN	symblepharon
14	77	F	C	72	No	No	No	trichiasis
15	74	F	C	73	Psoriasis	No	HTN, DM	none
OCP								
1	89	F	C	80	HypoTH	Dry eyes	HTN	corneal ulceration
2	83	F	C	73	SS	Cataract	Dyslipidemia, GERD	cornea abrasion & clouding, entropion
3	67	M	C	59	No	No	HTN	None
4	78	M	C	75	No	No	Dyslipidemia	trichiasis
5	70	M	C	70	No	Dry eyes	Anemia, HTN	None
6	50	F	C	50	HypoTH	Dry eyes	No	trichiasis, symblepharon, R eye vision loss
7	63	M	AA	53	No	No	DM, HTN, HCL	trichiasis, symblepharon, cicatricial entropion
8	44	F	C	39	No	No	No	None
9	66	F	C	62	No	No	No	Corneal ulcer, blurry vision, trichiasis
10	72	M	C	68	HypoTH, RA, UC	No	HTN, seizure, HCL, angina	Complete vision loss R eye, partial in L eye
11	92	M	C	88	No	No	No	None
12	49	F	C	46	No	No	No	trichiasis, symblepharon, R eye vision loss
13	65	F	C	59	No	No	HTN, DM	conjunctival fibrosis, mild trichiasis
14	86	F	AA	85	HypoTH	Glaucoma, cataract	HTN, DM, hyperlipidemia	trichiasis, symblepharon, cicatricial entropion
15	84	M	C	79	No	Glaucoma, FESD	No	corneal ulceration, blurry vision
16	75	F	C	69	No	No	No	None
17	69	F	C	64	RA	No	No	symblepharon, trichiasis

AA, African American; C, Caucasian; DM, diabetes mellitus; FECD, Fuchs endothelial corneal dystrophy; HCL, hypercholesterolemia; HSV, herpes simplex virus; HTN, hypertension; HypoTH, hypothyroidism; L, left; MMP, mucous membrane pemphigoid; MSSA, methicillin-sensitive staphylococcus aureus; N/A, not available; OCP, ocular cicatricial pemphigoid; R, right; RA, rheumatoid arthritis; SS, Sjogren syndrome; UC, ulcerative colitis.