

Squamous cell carcinoma: an atypical presentation

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Introduction

Squamous cell or epidermal carcinoma is the most common ocular neoplasia.¹ It can arise from cornea or conjunctiva and has the capacity to spread through local dissemination or, less commonly, by metastasis. It has a wide spectrum of histological presentation that goes from displasia (mild, moderate or severe) to conjunctival intraepithelial neoplasia (NIC) and invasive squamous cell carcinoma.^{1,2,4}

These types of lesions are more frequent in males and tend to have a higher incidence in older people. The leading risk factor is ultraviolet exposure (sunlight). Other factors associated with this pathology are the presence of congenital genome repair anomaly, such as xeroderma pigmentosum, human papilloma virus (HPV) infection and any condition that produces immunodeficiency, such as HIV/AIDS. Squamous cell carcinoma has been associated with other ocular surface lesions, such as pterygium, cysts and nevi.^{2,4}

Clinically, squamous cell carcinoma may present with a wide variety of manifestations. Lesions can be nodular, diffuse or placoid. The later can be further divided into gelatinous, papilliform, velvety and leukoplakic. Lesion can be completely avascular or have plenty of vascular supply. The presence of nutritious or sentinel vessels, tortuous or cork like vessels is highly suggestive of squamous cell carcinoma. Color may vary from transparent- unpolished glass to grey or pigmented lesions. The size of the neoplasia can also be quite variable, ranging from millimeters to a few centimeters in its mayor diameter.²⁻⁴ Specifically talking about corneal disease, the lesion is usually pre-invasive and avascular, with tendency to arise from central cornea and have a centrifuge growth. Lesion is grayish- glassy and affects central vision due to pupil axis involvement.^{3,4}

Patients may complain about “chronic conjunctivitis”, fluctuating red eye, foreign body sensation, tenderness and irritation. They may also report visual acuity decrease due to affection of the visual axis by the lesion or induced refractive errors by irregular corneal curvature.^{1,2}

Treatment of ocular surface squamous cell carcinoma has many variants. Surgical excision, cryotherapy and chemotherapy are some of the options and they can be used alone or combined. Among chemotherapeutic agents interferon α 2b, mitomycin C (MMC) and 5- fluorouracil (5-FU). Success rates differ from series to series, and rates of recurrence go from 9% to 53% depending on the consulted literature.^{3,5}

Case presentation

A 77 year old male presented with a 10 month history of red eye and intermittent foreign body sensation and tenderness in the right eye. He reported diagnosis of systemic hypertension and type 2 diabetes mellitus of eight years of evolution, currently under pharmacological control. He was under topical treatment with acyclovir 3% (5 times a day) and sodium hyaluronate 0.4% (5 times a day).

His visual acuity was 20/1200 (1.9 logMAR) on the affected eye, with papillary reaction in the tarsal conjunctiva and Meibomian gland dysfunction. An epithelial defect of 7mm x 6mm was also found, with underlying stromal melting. Topical medication was modified and topical gancyclovir 1.5mg/g (q 5hrs) was initiated under the suspect of herpetic geographic ulcer (Figure 1.).

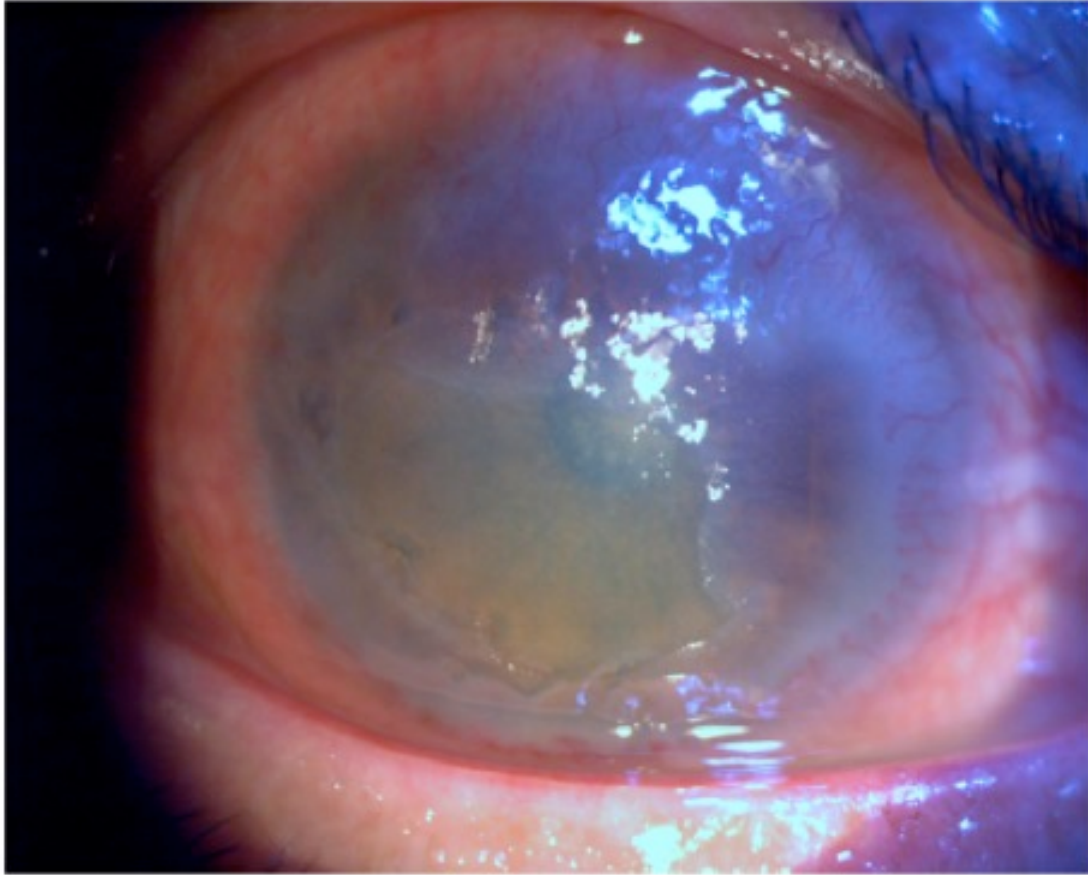


Figure 1. Corneal epithelial defect before treatment adjustment.

Even though the patient reported improvement of symptoms after 10 days of treatment, the epithelial defect increased to 8mm x 6mm. Perilimbal and stromal vascularization was found, some of them with cork appearance. Visual acuity remained stable. Due to lack of response to treatment, oral acyclovir was initiated (400mg po q4.5hrs)

One week later, patient remained with symptoms and epithelial defect persisted. At this point, diagnosis was questioned and therapeutic approach was modified. Treatment was established for a neurotrophic ulcer. Topical sodium hyaluronate 0.4% (q 2hrs) and dexpanthenol 5% qid was initiated and occlusive patch was placed.

Two months later, patient reported no symptoms. Even though there was a clinical improvement, patient remained with same visual acuity (20/1200; 1.9 logMAR), hyperemic conjunctiva, perilimbal vessels with cork appearance and an irregular corneal epithelium, with stromal edema and loss of corneal transparency (Figure 2.)

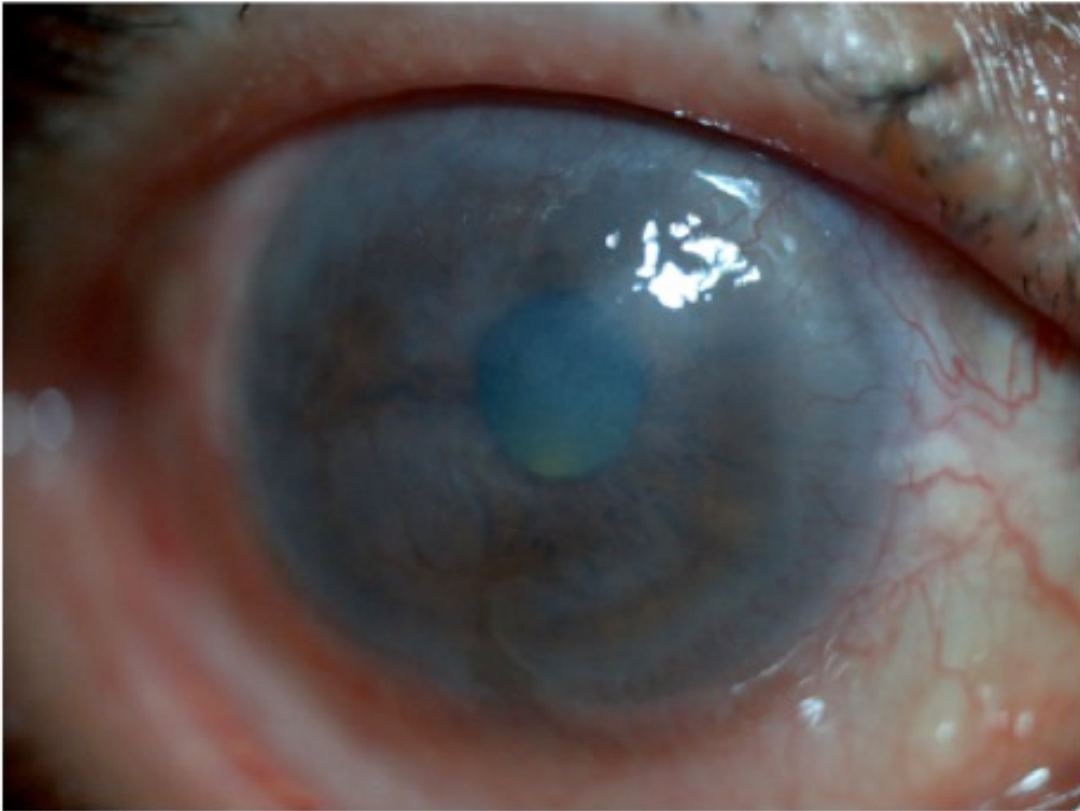


Figure 2. Persistent irregular epithelium with patchy stromal edema.

These new findings conducted to take an impression cytology of the perilimbal corneal epithelium, which reported neoplastic squamous epithelial cells, with loss of nucleus- cytoplasm relation, with big, pleomorphic nuclei and irregular cell membranes, thick granular chromatin and micronucleolus with scarce mitotic figures. Histological findings were compatible with squamous cell carcinoma with moderate differentiation (Figure 3). With this diagnosis, topical treatment was established with interferon α 2b 1 million IU/ml qid.

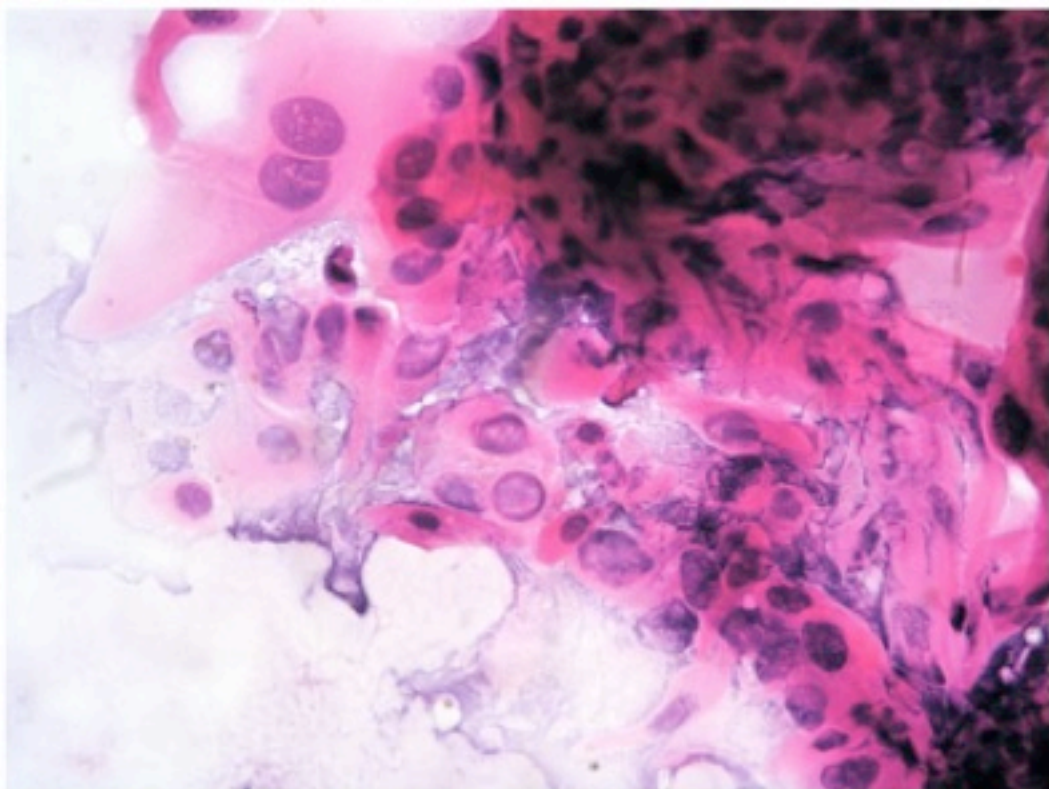
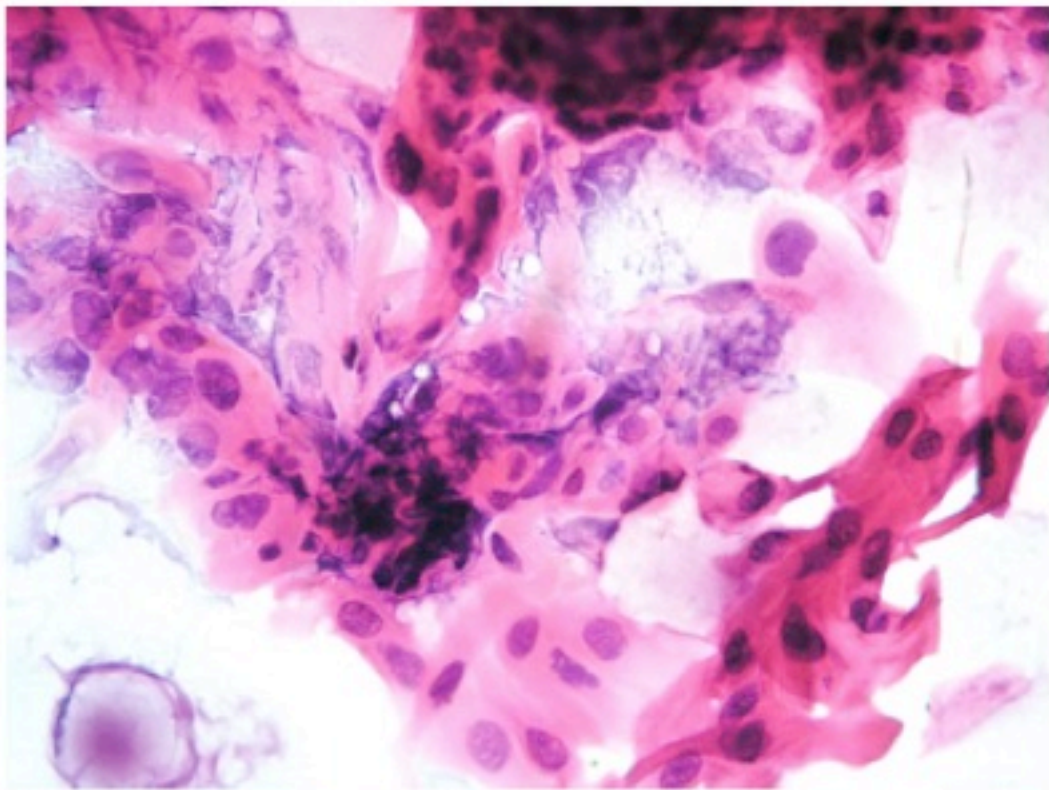


Figure 3. Squamous cell carcinoma with moderate differentiation

After two months of treatment, corneal transparency was recovered, corneal epithelium showed uniformity and perilimbal vessels showed discrete involution. Visual acuity after treatment was 20/80 (0.6 logMAR).

Discussion

Squamous cell carcinoma is an uncommon diagnosis, even though is the most common ocular surface neoplasia. For a proper diagnosis, clinician has to have a high level of suspicion based on the characteristic findings of this pathology.

Most of the literature reports classic presentation of this kind of diseases (dysplasia, intraepithelial neoplasia and invasive carcinoma), but it may have an atypical presentation like the case of our patient, which presented a persistent epithelial defect. On first instance, it was managed as a herpetic ulcer, then as a neurotrophic ulcer and finally as a squamous cell carcinoma. Initial therapeutic approach was based on clinical findings and epidemiologic probability.

A key element to the proper diagnosis was the presence of abnormal vessels in the corneal periphery, which, according to the consulted bibliography, should always rise the suspicion of a malignant underlying process, especially if they have uncommon appearance, such as cork vessels. A second key element was the partial response to an adequate treatment to the original diagnosis, which forced to reanalyze the case and its evolution.

Although one of the first treatment lines for this disease is the surgical excision, topical treatment was elected due to lack of a defined lesion borders and the integrity of corneal structure. Fortunately, clinical response to chemotherapy was optimal, based on the described regimens for interferon α 2b.

Of the available chemotherapeutics described to treat squamous cell carcinoma, interferon α 2b has not been associated with limbal stem cell damage and has demonstrated efficacy as a single- agent treatment. It is a cytokine with antineoplastic and immune functions which action mechanism is thought to be the modulation of enzymatic intracellular response, cell proliferation and increased cytotoxic response of leukocytes.^{8,9}

Interferon α 2b is usually prepared to 1 million IU/ml for topical use as eye drops and is recommended 4 to 6 times a day until clinical resolution of lesion is noted, which in average takes 8 to 10 weeks according to consulted literature. Some authors recommend continuation of treatment up to one month after resolution. Interferon α 2b has also been described for subconjunctival use.^{8,9}

Conclusion

The main lesson from this case is to always keep in mind that diseases may have erratic behavior. This case report should serve as a guide to those whose practice is centered on eye surface diseases, since there may be underdiagnosis of squamous cell carcinoma due to atypical presentations.

Unlike nodular, diffuse or plaque lesion (classic presentation), this patient's main findings were a persistent epithelial defect with stromal edema and abnormal perilimbal vessels. Once other more common causes of these findings are ruled out, complementary tests should be done if there is no conclusive diagnosis. When ocular surface squamous cell carcinoma is to be tested, impression cytology is a good alternative, since it is a noninvasive technique that can be easily done at practitioner's office.

The location of this type of neoplasia offers the possibility of different types of treatment. Besides surgery, topical treatment with antineoplastic medications has offered good results, being Interferon α 2b a very good option with clinical response over few weeks of treatment in most cases.

References

1. Yousef, Y, Finger, P. Squamous Carcinoma and Dysplasia of the Conjunctiva and Cornea. An analysis of 101 cases. *Ophthalmology* 2012; 119: 233-240.
2. Chauhan, S, Sen, S, Sharma, A *et al.* American Joint Committee on Cancer Staging and Clinicopathological High- Risk Predictors of Ocular Surface Squamous Neoplasia. *Arch Pathol Lab Med* Vol 138, November 2014.
3. Krishnaraj, J, Surya, S, Exhil, K. Ocular surface squamous neoplasia. Review Article. *International Journal of Ocular Oncology and Oculoplasty*, January- March 2016; 2(1): 19-30.
4. Honovar, S, Manjandavida, F. Tumors of the ocular surface: A review. *Indian Journal of Ophthalmology* Vol. 63, No. 3: 187-203.
5. Zarei- Ghanavati, S, Alizadeh, R, Deng, Sophie. Topical Interferon Alpha-2b for Treatment of Noninvasive Ocular Surface Squamous Neoplasia with 360° Limbal Involvement. *J Ophthalmic Vis Res* 2014; 9(4): 423-426
6. Padma, P, Padma, M. Ocular Surface Squamous Neoplasia (OSSN): A Retrospective Study. *Journal of Clinical and Diagnostic Research*. 2015 Nov, Vol 9 (11); NC10-NC13
7. Nguena, M, can den Tweel, J, Makupa, W *et al.* Diagnosing Ocular Surface Squamous Neoplasia in East Africa. *Ophthalmology* 2014; 121:484-491.
8. Ramberg, I, Heegard, S, Sjo, N. Squamous cell dysplasia and carcinoma of the conjunctiva. A nationwide, retrospective, epidemiological study of the Danish patients. *Acta Ophthalmol* 2015: 93 663-666
9. Huerva, V, Manges, I. Treatment of conjunctival squamous neoplasia with interferon alpha 2b. *Journal Français d' Ophthalmologie* 2008: Vol 31 No3; 317-325

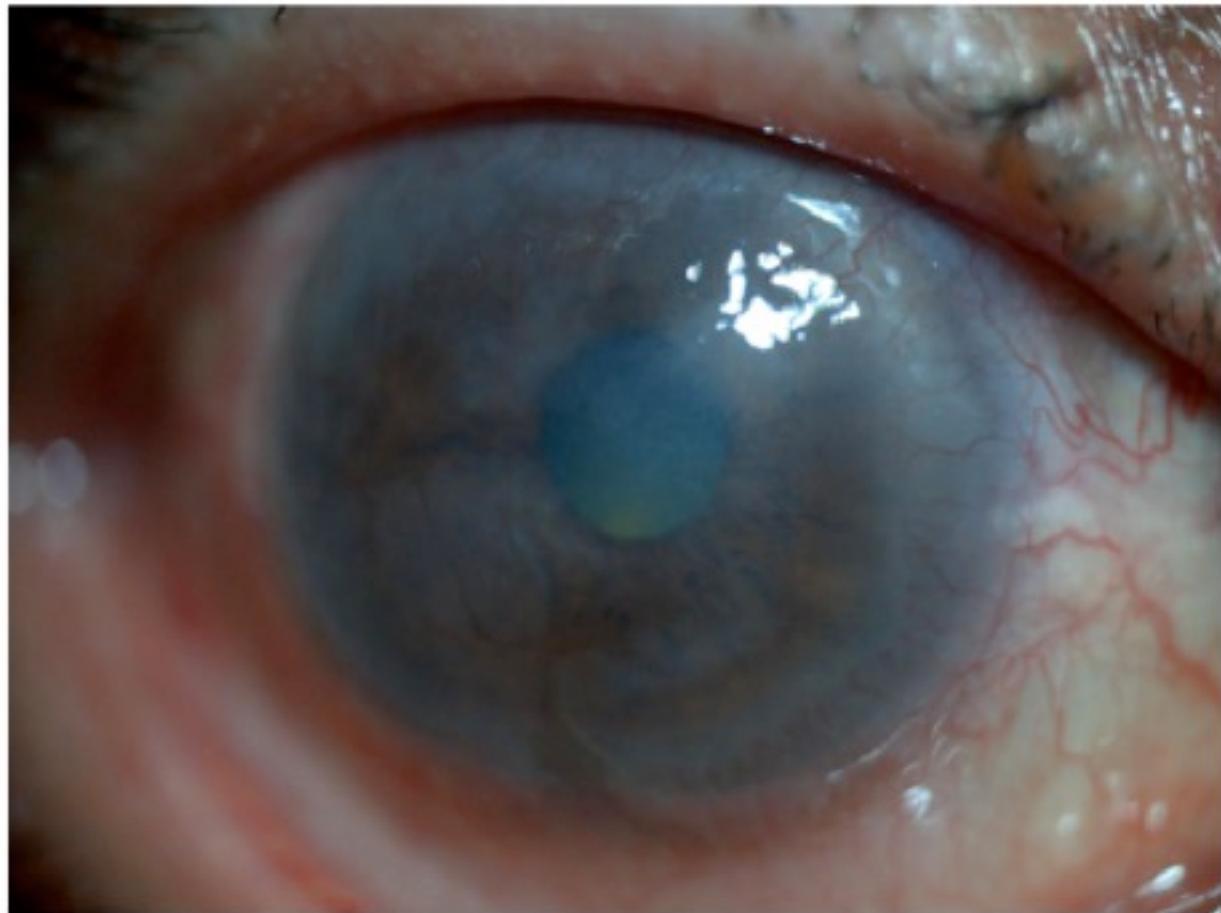


Figure 2. Persistent irregular epithelium with patchy stromal edema.

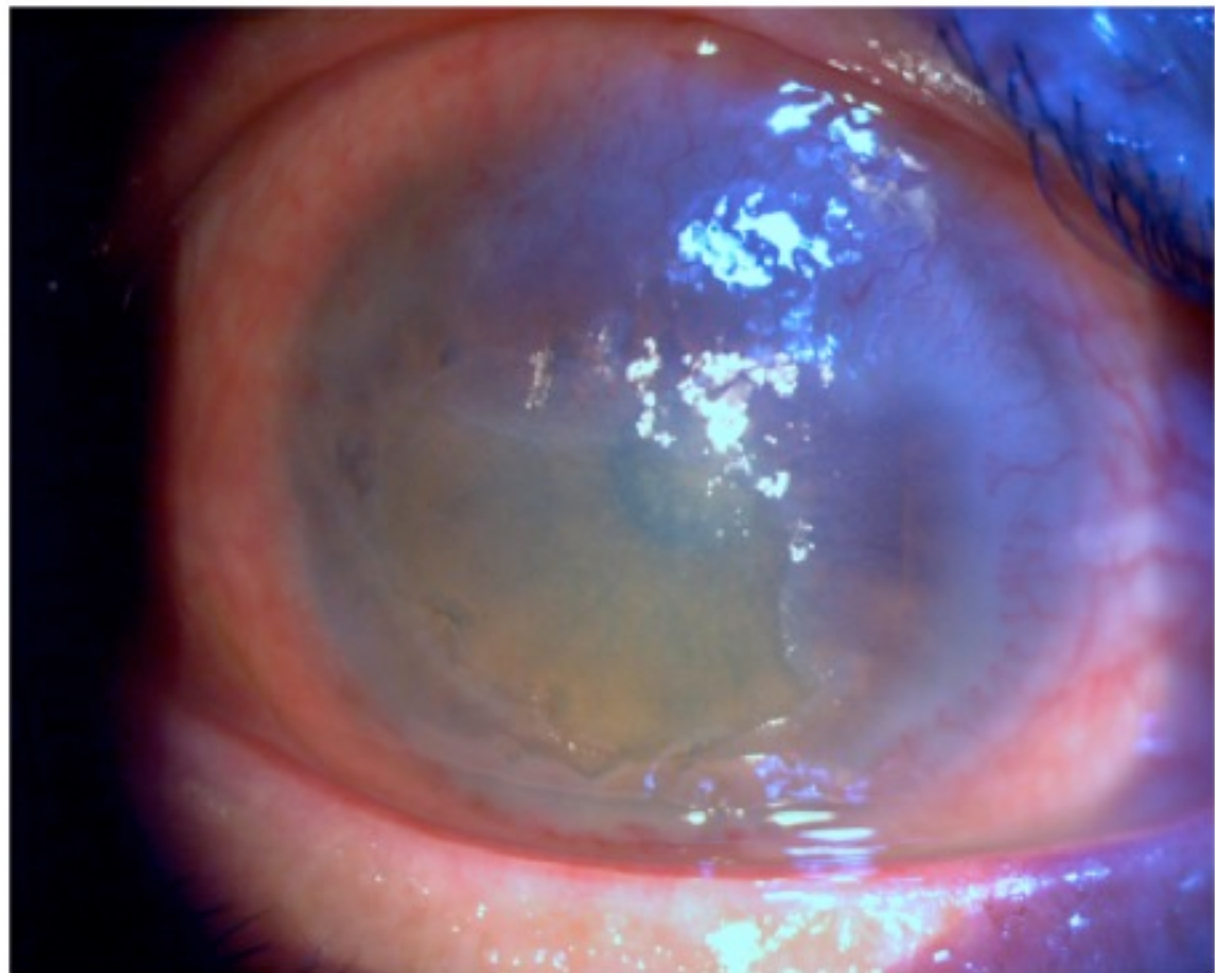


Figure 1. Corneal epithelial defect before treatment adjustment.

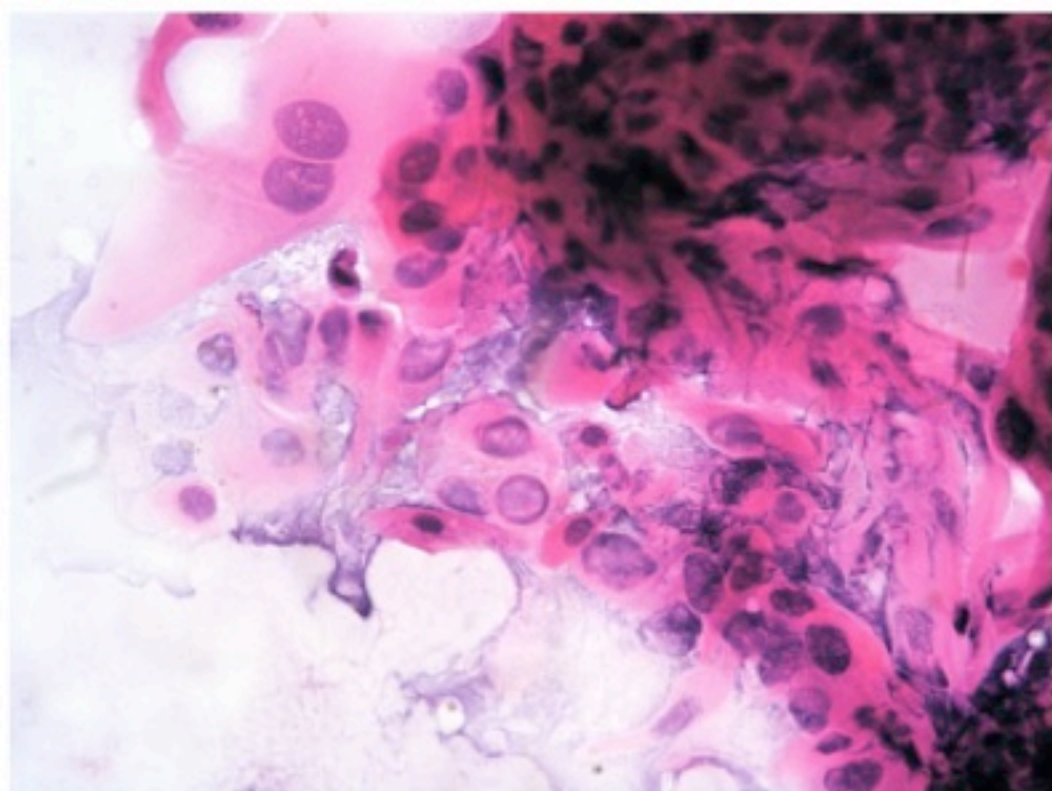
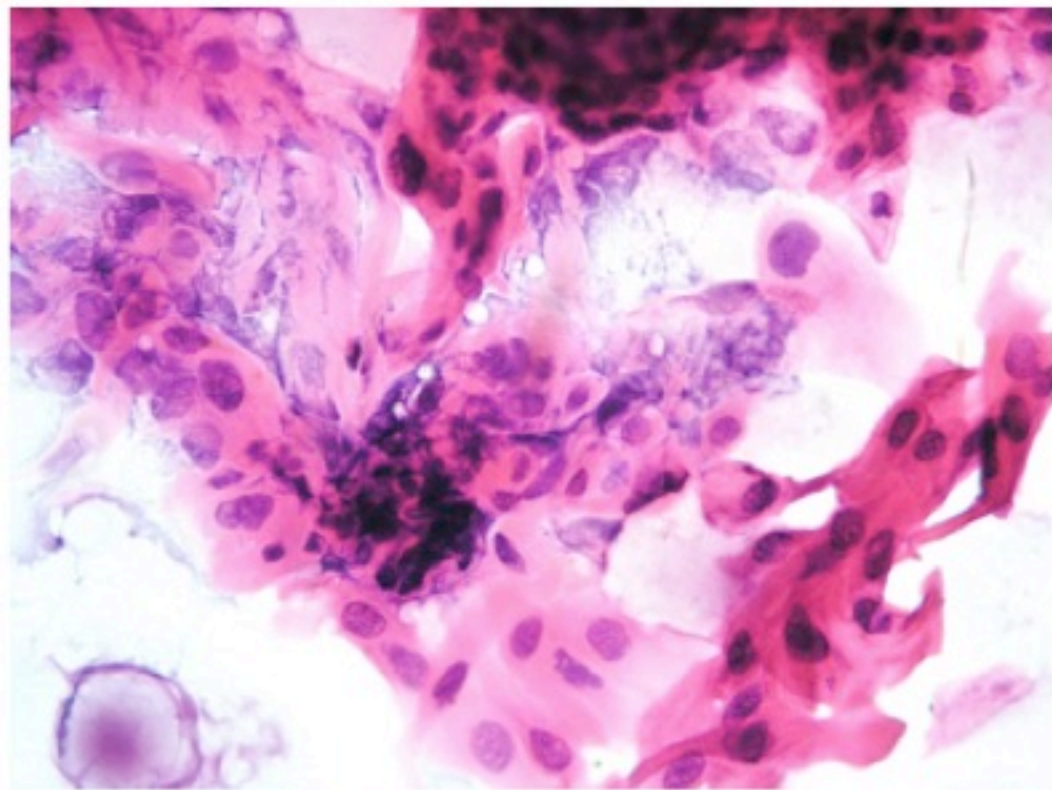


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