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**Case Report**

# Ocular surface squamous neoplasia misdiagnosed as corneal opacity and dry eye: a case report

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## ABSTRACT

Ocular surface squamous neoplasia (OSSN) represents a spectrum of ocular surface epithelial neoplasms ranging from conjunctival intraepithelial neoplasia (CIN) to invasive squamous cell carcinoma. We report a case of a 75-year-old man initially misdiagnosed with corneal opacity and dry eye, whose symptoms persisted despite lubricant therapy. Detailed ophthalmic examination revealed a suspicious lesion extending across the temporal cornea with sentinel vessels and corneal invasion. Histopathological analysis confirmed high-grade intraepithelial dysplasia consistent with CIN, while immunohistochemistry for p16 was negative. The patient underwent surgical excision with wide margins, adjunctive cryotherapy, and postoperative topical 5-fluorouracil therapy. This case illustrates the diagnostic challenges of OSSN due to its ability to mimic benign ocular surface conditions. Prompt recognition, appropriate histopathological confirmation, and timely treatment are essential to prevent progression and preserve vision. Clinicians should maintain a high index of suspicion for atypical or persistent ocular surface lesions, particularly in elderly patients with risk factors such as ultraviolet exposure and diabetes.

**Keywords:** Ocular surface squamous neoplasia, Conjunctival intraepithelial neoplasia, Corneal lesion, 5-Fluorouracil

## INTRODUCTION

Conjunctival intraepithelial neoplasia (CIN) is a precancerous lesion affecting the conjunctival epithelium and represents the most common manifestation of ocular surface squamous neoplasia (OSSN), a spectrum of dysplastic and malignant conditions of the ocular surface.[1,2] It typically presents as a fleshy, elevated, or leukoplakic lesion at the limbus and can resemble more benign entities such as pterygium or chronic conjunctivitis, which often leads to diagnostic delays.[1]

Risk factors for CIN include chronic ultraviolet radiation exposure, infection with high-risk human papillomavirus (HPV), immunosuppression (including HIV), and environmental exposures such as smoking.[1,2] Although it is non-invasive, CIN carries the potential for progression into invasive squamous cell carcinoma if left untreated, emphasizing the need for early recognition and appropriate management to reduce the risk of metastasis.[1]

Diagnosis is primarily clinical, supported by slit-lamp examination and confirmed histologically. Treatment typically involves surgical excision with clear margins and adjunctive cryotherapy or topical agents like 5-fluorouracil or interferon alpha-2b to reduce recurrence risk.[2]

## CASE REPORT

A 75-year-old man presented to his local primary health care center with complaints of discomfort in his left eye. He has a 20-years history of poorly controlled type 2

diabetes mellitus, managed with Janumet (sitagliptin/metformin), with fasting point-of-care glucose readings consistently ranging from 5.5 to 11.5 mmol/l. His past medical history also includes hypertension, dyslipidemia, and hypermetropia. On examination, his visual acuity was 6/24 in the right eye and 6/12 in the left eye. A preliminary diagnosis of corneal nebula and dry eye was made, and he was prescribed ocular lubricants with instructions to continue use and follow up regularly. At his one-month follow-up, there was no improvement in symptoms, and alternate lubricants were prescribed.

Nearly a year later, in April 2025, during his routine diabetic eye screening, the patient reported a two-months history of pain, tearing, and reduced vision in the left eye. He was also scheduled for bilateral cataract surgery the following week. At this visit, his left eye visual acuity had declined to 6/18. Slit-lamp examination revealed a suspicious lesion extending from 3 to 7 o'clock, with sentinel vessels, surface degeneration, and invasion of the temporal corneal epithelium, involving both superficial and deep corneal vessels. A central corneal epithelial ulcer was also noted (Figures 1a and b). CIN was suspected, and the patient was urgently referred to an ophthalmology oculoplastic specialist.

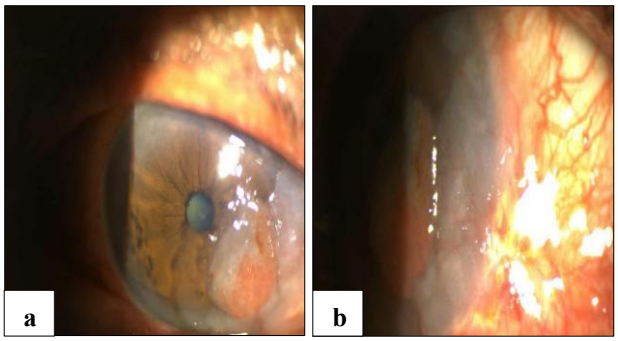


**Figure 1 (a and b): Picture of the left eye.**

Further examination revealed an elevated lesion on the ocular surface of the left eye, extending temporally and inferiorly onto the sclera. The lesion had an irregular elevation ranging from 0.4 mm to 0.7 mm over the cornea and was minimally elevated over the sclera. It extended beyond the limbus into the temporal and inferotemporal sclera; the total extension of the lesion from the corneal center was approximately 7.6 mm. There was no evidence of intraocular mass. Given the high clinical suspicion for OSSN, the patient was admitted for surgical excision with wide margins, cryotherapy, and topical 5-fluorouracil (5-FU). The excised tissue was sent for histopathological evaluation. Microscopic analysis revealed marked epithelial thickening, loss of cellular polarity, disorganized maturation, nuclear pleomorphism, frequent mitotic figures, and dyskeratosis—features consistent with high-grade intraepithelial dysplasia. These findings supported the provisional diagnosis of CIN. Immunohistochemistry for p16, a surrogate marker for high-risk HPV, was negative.

## DISCUSSION

A variety of epithelial tumors are included on the spectrum of OSSN, which ranges from CIN to invasive squamous cell carcinoma. Although relatively rare, it remains the most common non-pigmented ocular surface malignancy. It typically affects elderly males and is strongly associated with chronic ultraviolet (UV) light exposure, immune-suppression, and HPV infection. Our patient, a long-term uncontrolled diabetes, also had additional risk factors such as old age and chronic UV exposure.[1,3]

He presented with a progressive conjunctival lesion initially misdiagnosed as corneal nebula and dry eye. This misdiagnosis delayed appropriate interventions, a challenge also reported in other case reports. Hawthorne et al described a similar case where initial symptoms were mistaken for chronic irritation before a suspicious lesion was later identified.[2,5] The variable and often subtle presentation of OSSN, including gelatinous, papilliform, or leukoplakic appearances, demands a high index of suspicion. In our case, the presence of sentinel vessels and corneal involvement on slit-lamp examination raised concern for a more serious etiology.[4]

Histopathological confirmation remains the gold standard for diagnosis. In our case, biopsy showed high-grade dysplasia consistent with CIN, and was negative for high-risk HPV on p16 immunostaining. However, Höllhumer et al reported that p16 status is helpful but not definitive in confirming HPV involvement in OSSN.[4]

Treatment approaches vary depending on lesion size, location, and degree of invasion. Surgical excision with safety margins and cryotherapy, as done in this case, remains the mainstay of treatment for localized disease. However, several case reports have displayed excellent results with topical chemotherapeutic agents. Han and Karp reported successful use of topical 5-FU in OSSN cases, highlighting its affordability, efficacy, and lower toxicity compared to mitomycin C.[5] Similarly, Sepulveda et al supported the use of topical agents to target subclinical disease and reduce recurrence post-operatively.[6]

Comparatively, Hawthorne et al opted for using interferon alpha-2b to manage their case, achieving full resolution without recurrence over six months.[2,5] Although interferon has a favorable side effect profile, its availability and cost can be limiting factors. In contrast, our patient's regimen of excision followed by adjuvant 5-FU offered a practical and effective strategy with a good short-term outcome.

Prognosis for OSSN is generally favorable with early detection and management. However, recurrence rates remain significant, ranging from 5% to 33% depending on initial treatment adequacy and follow-up rigor.[4,7] The presence of high-grade dysplasia, as in our case, necessitates close monitoring due to higher recurrence risk. Regular follow-up, including slit-lamp examinations

and possibly impression cytology, is critical for long-term surveillance. In our case, long-term follow-up data are not yet available, limiting the ability to comment on recurrence rates or treatment durability.

## CONCLUSION

This case highlights the diagnostic challenges and therapeutic options in OSSN. Prompt recognition and management are key to optimizing visual outcomes in patient with OSSN. The presentation of OSSN is nonspecific and may mimic common benign conditions, which may further delay the diagnosis. In patients with high clinical suspicion, prompt referral and appropriate interventions are essential to prevent progression and preserve vision. Comparative case studies support both surgical and non-surgical approaches, and ongoing research continues to refine the role of adjuvant therapy in reducing recurrence.

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