

# Invasive Acantholytic Ocular Surface Squamous Neoplasia: A Rare Case

Avi Sharma <sup>1</sup>, Sachin Daigavane <sup>1</sup>, Arvind Bhake <sup>2</sup>

Received 01/01/2023

Review began 01/10/2023

Review ended 05/16/2023

Published 05/19/2023

© Copyright 2023

Sharma et al. This is an open access article distributed under the terms of the Creative Commons Attribution License CC-BY 4.0., which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

1. Ophthalmology, Jawaharlal Nehru Medical College, Datta Meghe Institute of Higher Education and Research, Wardha, IND 2. Pathology, Jawaharlal Nehru Medical College, Datta Meghe Institute of Higher Education and Research, Wardha, IND

**Corresponding author:** Avi Sharma, avik95@gmail.com

## Abstract

Ocular surface squamous neoplasia (OSSN) is a spectrum of intraepithelial and invasive neoplastic lesions of the conjunctiva and cornea. OSSN is a rare but potentially sight-threatening ocular malignancy that can be challenging to diagnose due to its clinical and histopathological resemblance to benign ocular surface lesions. However, OSSN can lead to significant ocular and systemic morbidity, including vision loss and metastasis. Various risk factors have been identified, including ultraviolet radiation exposure, human papillomavirus infection, and immunosuppression. The histopathological analysis of the lesion is of utmost importance in diagnosing and further managing squamous cell carcinoma. The acantholytic variant of squamous cell carcinoma is uncommon. Here, we present the case of a 69-year-old male who presented with an invasive mass of progressive growth on the left eyeball extending into the visual axis. The patient underwent extended enucleation, and a histopathological analysis demonstrated a rare acantholytic variant of squamous cell carcinoma.

**Categories:** Ophthalmology, Pathology, Oncology

**Keywords:** invasive carcinoma, malignancy, histopathology, acantholytic variant, squamous cell carcinoma

## Introduction

An ocular surface squamous neoplasia (OSSN) is a precancerous or cancerous lesion afflicting the conjunctival epithelium and cornea [1]. A variety of dysplasias, squamous cell carcinomas, and carcinomas in situ are included in this classification [2]. OSSN is more commonly prevalent among blacks. Those who live in regions in proximity to the equator and are exposed to more sunlight are more likely to suffer from this condition. The OSSN of the conjunctiva and cornea is estimated to affect 0.13 to 3.5 people in every 100,000 population [3]. There is an association between OSSN and exposure to solar ultraviolet radiation, but human papillomavirus (HPV) and human immunodeficiency virus (HIV) are also believed to play a significant role [4-8]. Squamous cell carcinoma development is associated with several mutations in p53 caused by ultraviolet B radiation [4-8]. Tumors usually develop in the nasal sector of the interpalpebral region. The acantholytic variant of OSSN is a rare subtype of OSSN characterized by intraepithelial and invasive neoplastic lesions with marked acantholysis and atypical keratinocytes [9]. A rare case of invasive acantholytic OSSN is presented here with an emphasis on the importance of histopathological analysis in establishing the diagnosis.

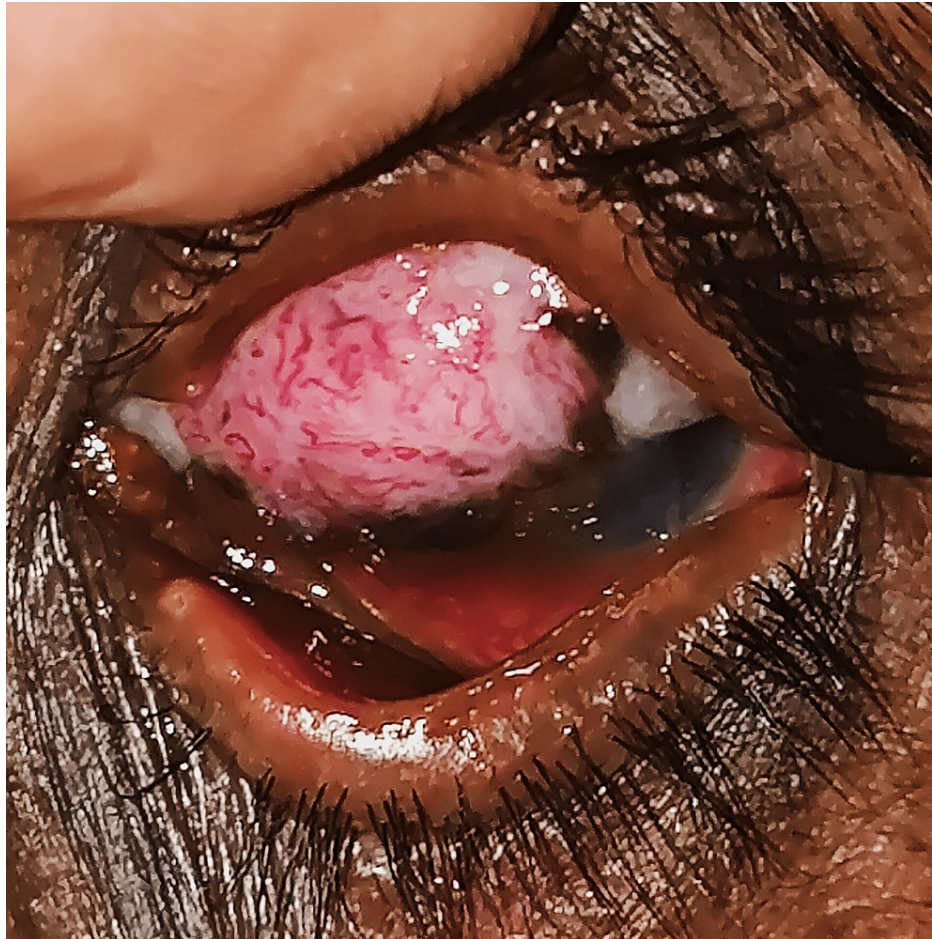
## Case Presentation

A 69-year-old male, a farmer by occupation, reported to the department of ophthalmology with the chief complaints of a fleshy mass growing in front of the left eye for the past six months, which had an insidious onset and was gradually progressive in nature. It was associated with pain, blepharospasm, watering, and gradual diminution of vision in the left eye, which reduced to visual acuity of hand movements close to the face.

On slit-lamp examination, a fibrovascular papillomatous conjunctival lesion extending from 7 o'clock to 12 o'clock in the nasal interpalpebral fissure was observed. The mass encroached the cornea with stromal infiltration encroaching the visual axis. Medial caruncular involvement was evident with surface keratinization and feeder vessels, intrinsic vascularity, and surface pigmentation. The examination of the right eye was normal (Figure 1).

### How to cite this article

Sharma A, Daigavane S, Bhake A (May 19, 2023) Invasive Acantholytic Ocular Surface Squamous Neoplasia: A Rare Case. Cureus 15(5): e39219. DOI 10.7759/cureus.39219

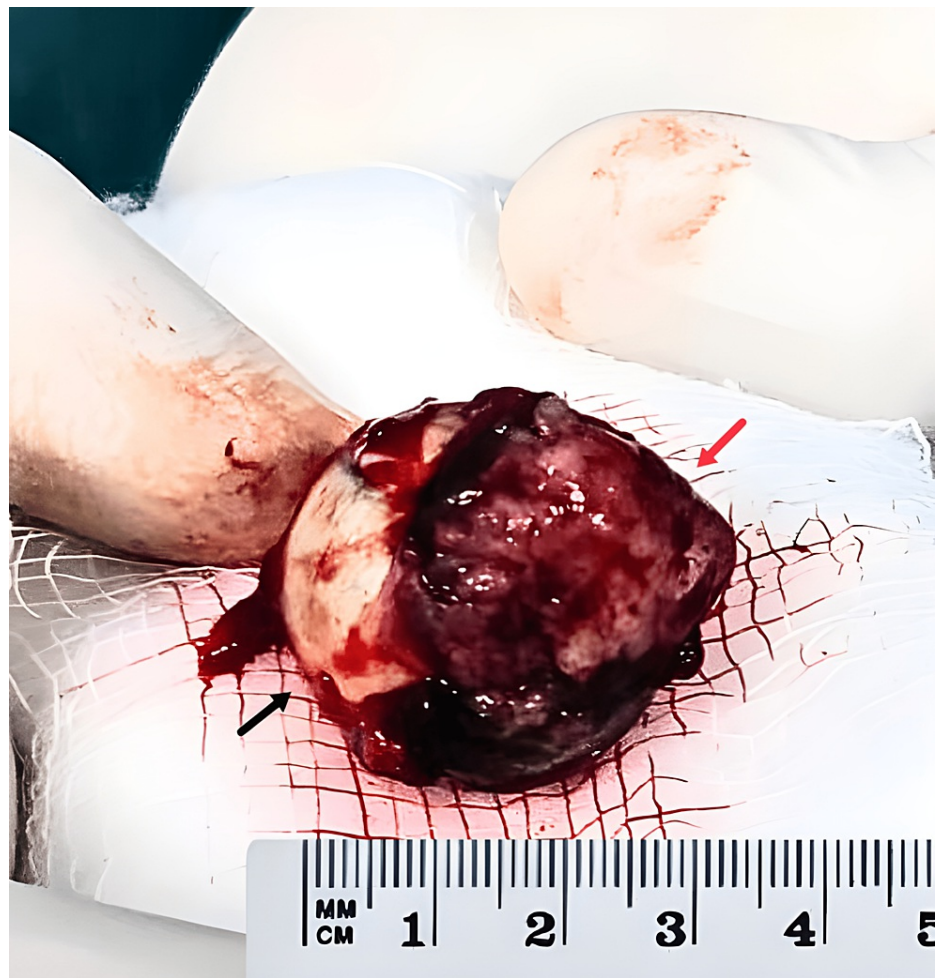


**FIGURE 1: Slit-lamp examination showing a fibrovascular papillomatous conjunctival lesion extending from 7 o'clock to 12 o'clock in the nasal interpalpebral fissure.**

Routine blood testing and serological testing were negative for HIV and HPV. A diagnosis of ocular squamous cell carcinoma was suspected based on the clinical findings, such as a fleshy sessile lesion adjacent to the limbus in the interpalpebral region involving the cornea and bulbar conjunctiva, and the patient underwent extended enucleation with mass excision. The specimen was sent for histopathologic analysis. Postoperatively, the patient was started on topical 1% 5-fluorouracil.

### **Gross examination of the enucleated eye**

An eyeball measuring 3 cm in longest diameter was evaluated with pericorneal and corneal (7 o'clock to 12 o'clock) areas which showed apparent growth. The growth measured 1.75 cm × 2 cm, appearing variegated, irregular, and ulcerated. The growth in the part showed a white, fragile, cauliflower-like area. The growth showed no well-defined margins and invaded the cornea, anterior chamber, and sclera on cut section examination. The posterior chamber lacked infiltration by the growth, and the optic nerve stump was free of evident tumor involvement (Figure 2).



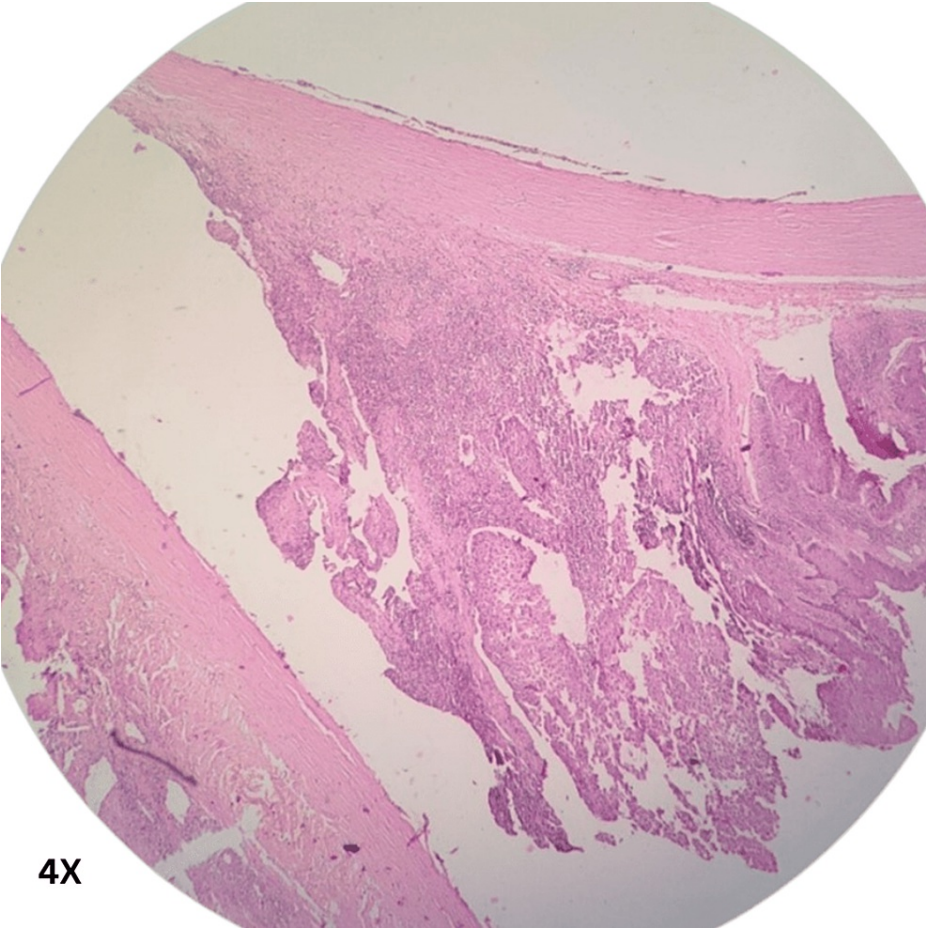
**FIGURE 2: Gross examination of the enucleated specimen.**

Red arrow: surface growth. Black arrow: eyeball.

### Histopathological assessment of the enucleated eye

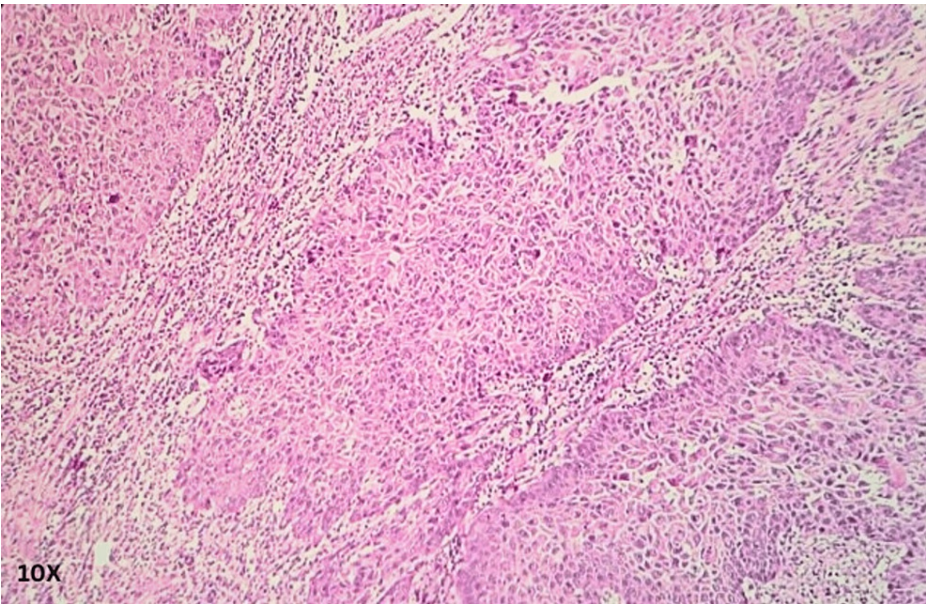
Sections from various areas of the eye and the tumor were taken per the standard reporting protocol. Section from the tumor showed solid sheets, a few finger-like extensions of sheets, some cords, and a pseudo-glandular structure, and the papillary structure of squamous cells was noted. The squamous cells contained low-grade malignant nuclei, and their cytoplasm showed partial-to-complete keratinization. The intercellular cracking creating the windows was prominent (acantholytic change). The intercellular bridges were prominent but present in a few cells. No squamous pearls, whorls, or nests were identified. The tumor, at places, showed lymphoid cell infiltrate. The invasion was noticed in scleral tissue below the choroid, but the posterior chamber and optic nerve were free from tumor invasion. A diagnosis of an acantholytic variant of squamous cell carcinoma was offered (Figures 3-6).





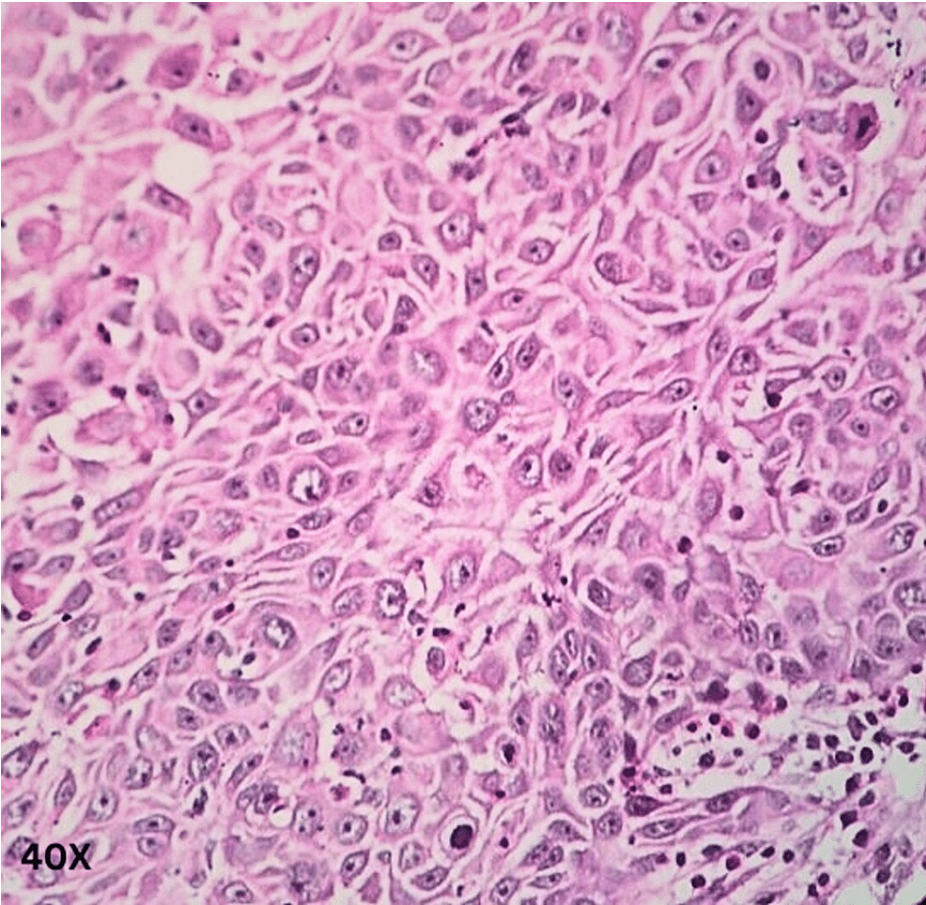
4X

**FIGURE 3: Histo-morphological appearance of an acantholytic variant of ocular squamous cell carcinoma showing papillaroid architecture (magnification 4×).**



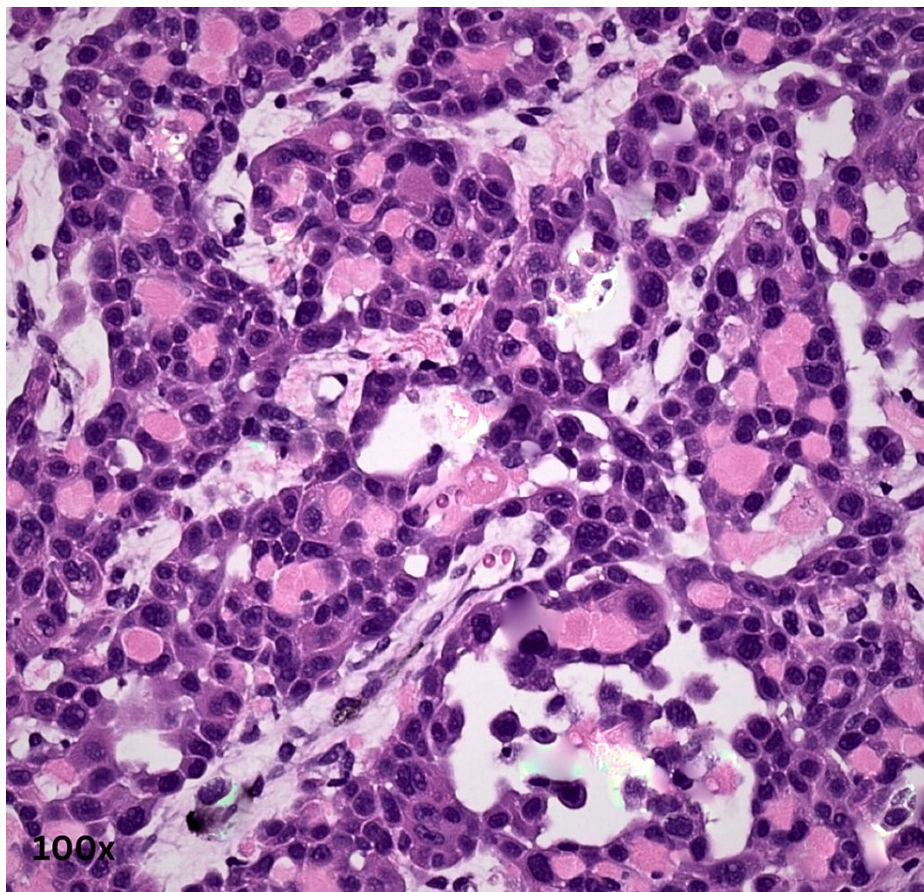
10X

**FIGURE 4: Histo-morphological appearance of an acantholytic variant of ocular squamous cell carcinoma (magnification 10×).**



**FIGURE 5:** Histo-morphological appearance of an acantholytic variant of ocular squamous cell carcinoma (magnification 40×).





**FIGURE 6: Acantholytic squamous cell carcinoma with multiple acantholytic cells (magnification 100×).**

### Follow-up

On the follow-up visit after one month, the orbital socket was healthy, and there was no discharge. The patient was referred to the Department of Prosthodontics, where a clear polymethyl methacrylate ocular prosthetic was designed for the patient (Figures [7A-7C](#)).



**FIGURE 7: Pre and post-enucleation and orbital prosthesis. Follow-up after one month.**

A: pre-enucleation. B: immediate postoperative day after extended enucleation. C: After one month of enucleation with an orbital prosthetic.

## Discussion

In this case report, we examined a case of OSSN, a classification encompassing a range of malignancies affecting the eye surface. These neoplasms include intraepithelial neoplasia as well as invasive squamous cell carcinomas. Early diagnosis is crucial as they can often mimic benign lesions such as pterygiums and chronic conjunctivitis [10]. Other differential diagnosis includes pseudo-epitheliomatous hyperplasia, squamous papilloma, actinic keratosis, pyogenic granuloma, benign epithelial dyskeratosis, chronic inflammation of the ocular surface, corneal pannus, Mooren's ulcer, corneal epithelial dystrophies and fatty degenerations, keratoacanthoma, conjunctival nevus, and conjunctival malignant melanoma [11-13].

The terminology associated with this condition is varied, including epithelioma, epidermalization, conjunctival and corneal intraepithelial neoplasia, dyskeratosis, Bowen's disease, and ocular surface epithelial dysplasia [10].

Several factors contribute to the etiology of OSSN, including exposure to chemical carcinogens, ultraviolet radiation, viral infections such as HIV and HPV, and mutations in the p53 tumor suppressor gene [14-16]. Our patient was a farmer at risk for malignancy due to chronic exposure to ultraviolet light. These lesions are commonly found within the interpalpebral fissure, particularly near the limbus, although they may occur at any location on the conjunctiva and cornea [17].

The clinical manifestations of OSSN often involve growth at the limbus and a cluster of blood vessels in the interpalpebral region, similar to our patient who presented with a fibrovascular papillomatous conjunctival lesion in the nasal interpalpebral fissure [5]. However, it is worth noting that the literature rarely reports histological variants, such as acantholytic squamous cell carcinoma. We observed similarities in clinicopathological and histopathological features between our case and the case reported by Julius et al. [18].

OSSN presents with three primary lesion types, namely, gelatinous (papilliform or leukoplakic), nodular, and diffuse [10]. The gelatinous form is characterized by a well-defined sessile papillomatous lesion with dilated conjunctival arteries, while the nodular type appears as elevated mulberry-like masses. On the other hand, the diffuse form is poorly demarcated and exhibits a radial pattern of growth [10]. Our patient presented with a papillomatous vascular mass on the ocular surface.

Histopathologically, OSSN can be classified based on the predominant cell type, such as spindle cell type and mucoepidermoid and adenoid squamous subtypes [10]. High-grade lesions are often associated with male gender, temporal location, multifocality, increased mitotic activity, and low-grade cellular differentiation [19]. Although conjunctival and corneal squamous neoplasia are less likely to undergo systemic metastasis, they can invade local areas.

The acantholytic variant is characterized by histopathological features that involve a non-solid component containing either single or grouped acantholytic and dyskeratotic epithelial cells or cellular debris beneath the conventional squamous cells. This non-solid component is also known to create pseudo-glandular or pseudo-vascular structures [20]. Our histopathological specimen showed solid sheets, finger-like extensions of sheets, cords, a pseudo-glandular structure, and a papillaroid structure of squamous cells. The squamous cells showed intercellular cracking and low-grade malignant nuclei in the form of acantholytic changes. The intercellular bridges were prominent but present in a few cells. Thus, a diagnosis of acantholytic OSSN was made.

Histopathological evaluation is essential to establish a definitive diagnosis and differentiate between the various lesions within the broad spectrum of OSSN. Treatment approaches for primary OSSN have traditionally involved surgery. However, topical chemotherapy is increasingly gaining traction among corneal specialists [20]. A recent study on the standard of care in treating OSSN revealed that while 66% of corneal specialists previously relied solely on surgery for primary OSSN, this percentage decreased to 51% in 2012, with more doctors opting for medical treatments instead [21,22].

It is essential to acknowledge that our findings align with previous reports, further contextualizing our case within the existing literature. This strengthens the evidence supporting the diagnosis and management of OSSN in line with established knowledge. Moreover, our findings contribute to understanding the histological variant of acantholytic squamous cell carcinoma, which has rarely been reported in the literature. By documenting this rare occurrence, we provide valuable information that adds to the body of evidence surrounding OSSN.

## Conclusions

This is a case of a 69-year-old farmer diagnosed with a rare acantholytic variant of invasive ocular squamous cell carcinoma on biopsy. The patient underwent extended enucleation with excision of the mass and was started on topical 5-fluorouracil. Histopathology is the gold-standard method for diagnosing the various types of ocular surface squamous carcinomas. This case report highlights the importance of histopathological analysis in diagnosing and managing rare cases of ocular squamous cell carcinoma. The patient was managed by interdepartmental collaboration between oncology and pathology.

## Additional Information

### Disclosures

**Human subjects:** Consent was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

## References

1. Lee GA, Hirst LW: Ocular surface squamous neoplasia. *Surv Ophthalmol.* 1995, 39:429-50. [10.1016/s0039-6257\(05\)80054-2](#)
2. Grossniklaus HE, Green WR, Luckenbach M, Chan CC: Conjunctival lesions in adults. A clinical and histopathologic review. *Cornea.* 1987, 6:78-116. [10.1097/00003226-198706020-00002](#)
3. Patel S, Pokharel BB, Shah A, Goda MS, Thapa SK: Clinico-pathological study of ocular surface squamous neoplasia in a tertiary care centre of western region of Nepal. *J Univ Coll Med Sci.* 2019, 7:9-13. [10.3126/jucms.v7i1.24677](#)
4. Pizzarello LD, Jakobiec FA: Bowen's disease of the conjunctiva. A misnomer. *Ocular and Adnexal Tumors.* Jakobiec FA (ed): Aesculapius, Birmingham, UK; 1978.
5. Templeton AC: Tumors of the eye and adnexa in Africans of Uganda. *Cancer.* 1967, 20:1689-98. [10.1002/1097-0142\(196710\)20:10<1689::aid-cnrcr2820201019>3.0.co;2-f](#)
6. Erie JC, Campbell RJ, Liesegang TJ: Conjunctival and corneal intraepithelial and invasive neoplasia. *Ophthalmology.* 1986, 93:176-83. [10.1016/s0161-6420\(86\)33764-3](#)
7. Ash JE, Wilder HC: Epithelial tumors of the limbus. *Am J Ophthalmol.* 1942, 25:926-32. [10.1016/S0002-9394\(42\)90592-0](#)
8. Clear AS, Chirambo MC, Hutt MS: Solar keratosis, pterygium, and squamous cell carcinoma of the conjunctiva in Malawi. *Br J Ophthalmol.* 1979, 63:102-9. [10.1136/bjo.63.2.102](#)
9. Kane CL, Keehn CA, Smithberger E, Glass LF: Histopathology of cutaneous squamous cell carcinoma and its variants. *Semin Cutan Med Surg.* 2004, 23:54-61. [10.1016/s1085-5629\(03\)00088-9](#)



10. Sethi S, Naik M, Joshi M, Gupta V: Ocular surface squamous neoplasia (OSSN). *DOS Times*. 2014, 20:65-70.
11. Winer LH: Pseudoepitheliomatous hyperplasia. *Arch Dermatol Syph*. 1940, 42:856. [10.1001/archderm.1940.01490170106009](https://doi.org/10.1001/archderm.1940.01490170106009)
12. Mittal R, Meena M, Saha D: Actinic granuloma of the conjunctiva in young women . *Ophthalmology*. 2013, 120:1786-9. [10.1016/j.ophtha.2013.01.071](https://doi.org/10.1016/j.ophtha.2013.01.071)
13. Kaliki S, Mohammad FA, Tahiliani P, Sangwan VS: Concomitant simple limbal epithelial transplantation after surgical excision of ocular surface squamous neoplasia. *Am J Ophthalmol*. 2017, 174:68-75. [10.1016/j.ajo.2016.10.021](https://doi.org/10.1016/j.ajo.2016.10.021)
14. Mittal R, Rath S, Vemuganti GK: Ocular surface squamous neoplasia - review of etio-pathogenesis and an update on clinico-pathological diagnosis. *Saudi J Ophthalmol*. 2013, 27:177-86. [10.1016/j.sjopt.2013.07.002](https://doi.org/10.1016/j.sjopt.2013.07.002)
15. Shields CL, Chien JL, Surakiatchanukul T, Sioufi K, Lally SE, Shields JA: Conjunctival tumors: review of clinical features, risks, biomarkers, and outcomes--the 2017 J. Donald M. Gass Lecture. *Asia Pac J Ophthalmol (Phila)*. 2017, 6:109-20. [10.22608/APO.201710](https://doi.org/10.22608/APO.201710)
16. Sayed-Ahmed IO, Palioura S, Galor A, Karp CL: Diagnosis and medical management of ocular surface squamous neoplasia. *Expert Rev Ophthalmol*. 2017, 12:11-9. [10.1080/17469899.2017.1263567](https://doi.org/10.1080/17469899.2017.1263567)
17. Tunc M, Char DH, Crawford B, Miller T: Intraepithelial and invasive squamous cell carcinoma of the conjunctiva: analysis of 60 cases. *Br J Ophthalmol*. 1999, 83:98-103. [10.1136/bjo.83.1.98](https://doi.org/10.1136/bjo.83.1.98)
18. Julius P, Siyumbwa SN, Moonga P, et al.: Clinical and pathologic presentation of primary ocular surface tumors among Zambians. *Ocul Oncol Pathol*. 2021, 7:108-20. [10.1159/000511610](https://doi.org/10.1159/000511610)
19. Kao AA, Galor A, Karp CL, Abdelaziz A, Feuer WJ, Dubovy SR: Clinicopathologic correlation of ocular surface squamous neoplasms at Bascom Palmer Eye Institute: 2001 to 2010. *Ophthalmology*. 2012, 119:1773-6. [10.1016/j.ophtha.2012.02.049](https://doi.org/10.1016/j.ophtha.2012.02.049)
20. Kim JE, Lee C, Oh KY, Huh KH: A rare acantholytic variant of squamous cell carcinoma of the maxilla: a case report and literature review. *Medicine (Baltimore)*. 2020, 99:e21631. [10.1097/MD.00000000000021631](https://doi.org/10.1097/MD.00000000000021631)
21. Adler E, Turner JR, Stone DU: Ocular surface squamous neoplasia: a survey of changes in the standard of care from 2003 to 2012. *Cornea*. 2013, 32:1558-61. [10.1097/ICO.0b013e3182a6ea6c](https://doi.org/10.1097/ICO.0b013e3182a6ea6c)
22. Stone DU, Butt AL, Chodosh J: Ocular surface squamous neoplasia: a standard of care survey . *Cornea*. 2005, 24:297-300. [10.1097/01.ico.0000138834.42489.ba](https://doi.org/10.1097/01.ico.0000138834.42489.ba)