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Case Series

Clinicopathological case series on ocular surface squamous neoplasia (OSSN) in a rural tertiary care centre

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Abstract

Ocular surface squamous neoplasia (OSSN) is a common malignancy globally, which affects the conjunctiva. It has a varied clinical spectrum and thus presents diagnostic and therapeutic challenges. This case series evaluates the clinical presentation, risk factors, diagnostic strategies, and management outcomes of OSSN. Four cases of histologically confirmed OSSN managed at a tertiary care hospital in North India (UPUMS, Saifai, Etawah) were taken. Data on patient demographics, clinical features, diagnostic techniques, treatment modalities, and follow-up outcomes were collected and analysed. Patients ranged from 40–70 years, with key risk factors including UV exposure. Clinical presentations varied from localised to diffuse conjunctival lesions. Treatment included topical chemotherapy and surgical excision. They were followed for a mean duration of 30.75 months without any recurrence. This case series highlights that OSSN can have a wide variety of clinical presentations and can sometimes mimic pterygium. Impression cytology is used to confirm the diagnosis (it reveals mild, moderate, or severe dysplasia of squamous cells). Treatment requires a tailored approach, including chemotherapy and the 'no-touch technique' of surgical excision, to manage neoplasia while preserving the patient's vision and eye function as much as possible. Regular follow-up is needed to improve outcomes and decrease recurrence rates.

Keywords: OSSN, Histopathology, Mitomycin, Cryotherapy, No touch technique, Interpalpebral area.

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1. Introduction

"Ocular surface squamous neoplasia (OSSN) denotes a variety of dysplastic changes that affect the conjunctiva, cornea, and limbus". Although these tumours are uncommon, they are notable due to their potential to cause significant ocular and systemic morbidity and mortality. OSSN includes conditions such as "squamous dysplasia, carcinoma in situ (also known as conjunctival and corneal intraepithelial neoplasia), and squamous cell carcinoma". The earliest case of OSSN was recorded in 1860, and was documented by Von Graefe.[1]

The main risk factor for OSSN is ultraviolet (UV) B ray exposure.[2] Non-modifiable risk factors include age and male gender.[2] Modifiable risk factors comprise smoking, chronic trauma or inflammation, exposure to chemicals, vitamin A deficiency, and local immunosuppression.[2] There is also a strong association between OSSN and infections with human papillomavirus (HPV) and human immunodeficiency virus (HIV).[2] Predominantly, HPV serotypes 16 and 18 are considered cofactors in OSSN development.[2] OSSN typically presents unilaterally, emphasizing the importance of clinical suspicion for diagnosis, which may be confirmed through various modalities such as multimodal imaging, cytology, or histology.[3]

The grading system for OSSN, as coined by Lee and Hirst,[4] includes benign dysplasia (e.g., papilloma, pseudoepitheliomatous hyperplasia), pre-invasive OSSN (conjunctival/corneal carcinoma in situ), and invasive OSSN (squamous carcinoma, mucoepidermoid carcinoma). Gold

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standard for diagnosis of OSSN is Histopathology. The 'no-touch technique,' introduced by Shields et al.[5] in 1997, is the preferred method for surgically removing small OSSN lesions. This approach aims to excise the tumour with clear margins and decreasing the risk of microscopic seeding. However, there is no consensus on the optimal margin during surgery.

2. Case Series

2.1. Case 1

A seventy-year-old female presented in the eye OPD with a mass encroaching the right eye for one year. At the time of presentation, vision in the right eye was 6/12. A clinical examination of the right eye showed a papilliform type of conjunctival lesion involving 9 clock hours around Limbus with a high risk of intraocular extension. (**Figure 1**) Before planning the excision of the mass, impression cytology was performed, which showed mild to moderate dysplasia of squamous cells. Later, the mass was excised with 4 mm margins and sent for histopathological examination. The diagnosis of papilliform OSSN was finally confirmed. Preoperatively, she received 6 cycles of mitomycin C followed by surgery, and 3 postoperative cycles were given. The patient has been following for 1 year without any recurrence.

2.2. Case 2

A sixty-year-old female presented to the eye OPD complaining of redness and a mass encroaching on the cornea of her right eye for the past six months. The best corrected visual acuity in the right eye was 6/9. During the slit lamp examination, we suspected gelatinous type carcinomatous mass and diagnosed it as OSSN. (**Figure 2**) Preoperative chemo reduction was done using 4 weekly cycles of topical Mitomycin-c. Later, she underwent successful excision of the mass, followed by postoperative mitomycin C administered in 6 cycles. Patient followed up for 15 months without any signs of recurrence.

2.3. Case 3

A 40-year male patient presented with a pterygium-like mass in his left eye for the past three months, there was corneal involvement too (1mm onto the cornea). His best corrected visual acuity was 6/6 in both eyes. Upon slit lamp examination, there was suspicion of OSSN. Impression cytology was performed, revealing dysplastic changes. (**Figure 3**) The patient was directly taken for surgery without preoperative cycles of mitomycin C. Mass excision was performed, and postoperatively, the patient commenced 6 cycles of topical mitomycin C (0.04%) along with mild steroids.

2.4. Case 4

A 45-year-old female presented with a mass in her left eye for the last 6 months. Upon slit lamp examination, she was suspected of having a leucoplakic type carcinomatous lesion, prompting impression cytology. (**Figure 4**) The reports revealed severe dysplasia of squamous cells. The patient was scheduled for excision of the mass along with preoperative and postoperative courses of 6 cycles of topical mitomycin C (0.04%). The patient followed up for 3 year without any recurrence.

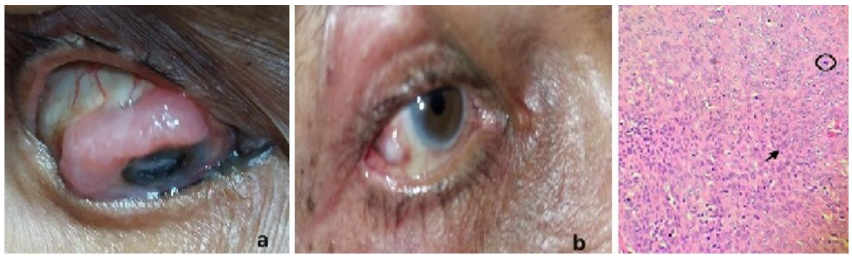

Figure 1: a): Large papilliform OSSN involving 9 clock hours around Limbus; **b**): Post op picture Day 30 after In toto excision; **c):** Photomicrograph illustrating atypical squamous epithelial cells displaying moderate nuclear pleomorphism, hyperchromatic nuclei (Arrow)Atypical mitotic figures(circle)

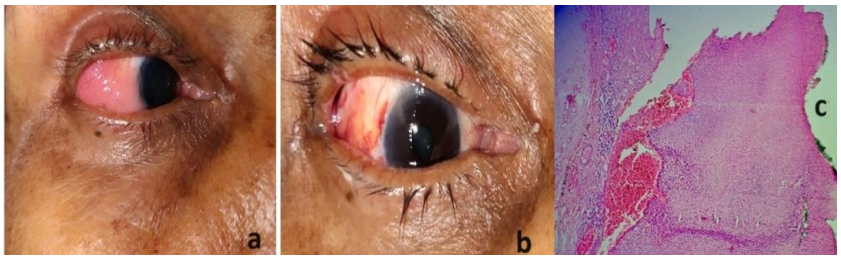

Figure 2: a): Gelatinous type OSSN arising from lateral canthus reaching upto Limbus; **b):** Post op pictures on day 15 after complete excision; **c):** Photomicrograph illustrating marked acanthosis of lining epithelium and full thickness dysplasia. No invasion seen (H&E ×100)

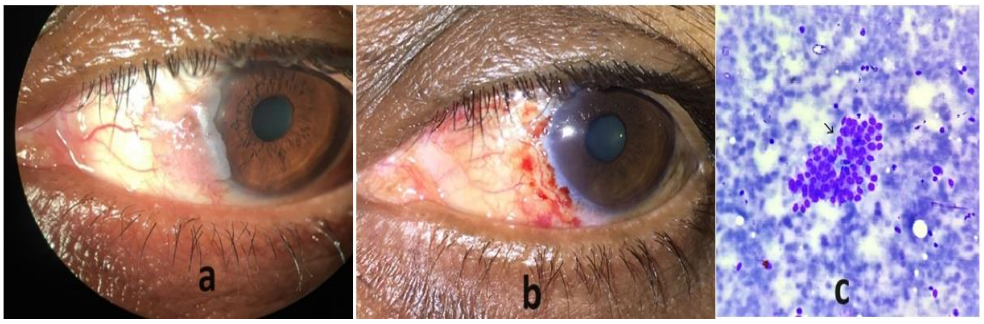

Figure 3: **a)**: OSSN mimicking temporal Pterygium showing corneal invasion also; **b):** Post op day 7 after surgery; **c):** Smear shows cluster of atypical squamous epithelial cells (Arrow) displaying moderate anisonucleosis (MGG×100)

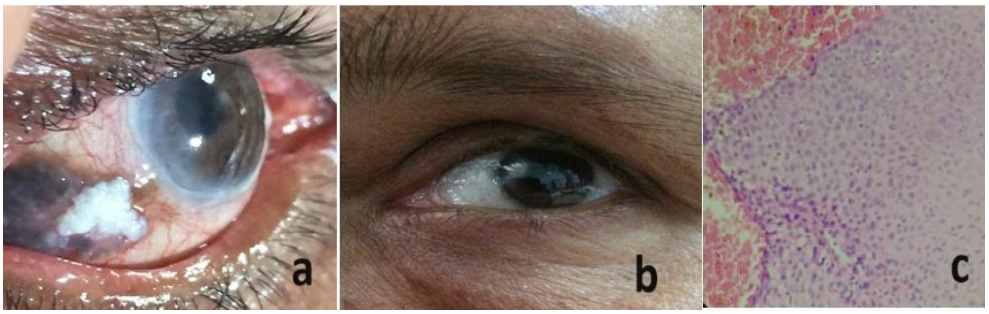

Figure 4: a): Leucoplakic type OSSN with feeder vessel; **b):** Post surgery after 6 months; **c**): Photomicrograph showing squamous epithelial lining having loss of polarity

3. Discussion

Ocular surface tumours are relatively rare, it's occurs at a rate of 0.13 to 1.9 per 100,000 individuals.[1] The term "ocular surface squamous neoplasia" (OSSN) refers to a broad category of dysplastic alterations in the conjunctival or corneal squamous epithelium. These alterations include conjunctival-corneal intraepithelial neoplasia (CIN), squamous papilloma, carcinoma in situ (CIS) and invasive squamous cell carcinoma (SCC). OSSNs can have a wide range of clinical presentations; they are categorized according to the degree of stromal and epithelial invasion. Mild to severe infiltration is possible with this. Dysplasia (mild, moderate or severe) to full-thickness epithelial dysplasia (CIS) to invasive SCC in which the tumor cells penetrate into the basement membrane of the epithelium. Thankfully, invasive SCC is the rarest variation of these ailments.[1,4]

In above case series, the patients were between 40-70 years and female dominance was also seen as females also go for outdoor farming works here in rural areas so exposure of UV B rays are high, however in the earlier studies the incidence of OSSN was found to be highest among men aged between 50 and 75 years.[1,2] A history of skin cancer in the past, fair skin, pale irises, and a propensity to sunburn easily are risk factors linked to this disorder.[6] Chronic infections including trachoma, HIV, or HPV (human papilloma virus), chronic irritants, xeroderma pigmentosum, vitamin A insufficiency, and chronic epitheliopathies are additional risk factors for OSSN.[1,6] ELISA for HIV was negative in all the patients. In younger patients, the presence of an OSSN lesion may indicate an underlying immunodeficiency. Research conducted in Kenya found OSSN was strongly associated with HIV infection.[6] Therefore, HIV testing is essential, along with a comprehensive evaluation for other potential causes of immunodeficiency. Visual acuity was quite good in all 4 cases because according to literature also lesions rarely affect vision prior to presentation.[7] The lesion was located in interpalpebral area in all the patients. It is also supported by literature. More than ninety-five percent of OSSN cases start at the limbus, and they often appear in the interpalpebral region (at positions about 3:00 or 9:00 O clock on the bulbar conjunctiva).[3] This tendency is believed to be caused by elements such a high mitotic index, strong UV exposure, and a transitional type of epithelium.[5] These lesions can have a variety of appearances, with colors ranging from pearly gray to pigmented (reddish brown). On the surface of the lesion white plaque, or leucoplakia, may develop, signifying secondary hyperkeratosis because of malfunctioning squamous cells, which gives rise to worries regarding invasive disease.[8] There may be noticeable feeder vessels,[7] but that doesn't assist in narrowing down the differential diagnosis.[9] Clinically, symptoms can vary from none at all to a persistently irritated, red eye. Initially, masses are mobile; but in advanced stages, the conjunctiva become, fixed to the globe due to a deeper scleral invasion. The extent of the lesion can be determined with the use of rose bengal staining. Histopathology specimens for small lesions can be extracted in to using excision biopsies.[9] When significant invading lesions occur, impression cytology can be performed to verify the diagnosis before going to a surgical excision.[10] Papilloma's show on histology the papillary fibrovascular

fronds coated in acanthotic epithelium. Although there are varying levels of dysplasia, the basal layers and normal polarity of the cell are often unremarkable. There are three categories for preinvasive OSSN: mild, moderate, or severe according to the dysplastic epithelium's level of involvement and the layers affected.[11]

Treatment for ocular surface squamous neoplasia (OSSN) varies based on the lesion's size and severity. Smaller, less invasive lesions may be addressed with topical chemotherapy or simple excision, while larger or invasive ones might require a mix of surgery, cryotherapy, and chemotherapy. During surgery, a margin beyond the visible disease is usually excised, and cryotherapy can be used to freeze any remaining cancer cells. In severe cases, treatments like radiation therapy or enucleation may be necessary.[2]

Chemotherapy, typically administered through eye drops, is often employed alongside surgery to reduce lesion size preoperatively and target any residual cancer cells postoperatively. This chemotherapy acts by damaging the DNA of cancer cells or inhibiting their growth. The most common drugs used are topical Mitomycin-c, 5-FU injections and interferon.[2,3]

The study by J.M. Manoher et al studied the use of MMC as a sole treatment for diffuse OSSN and in conjugation with surgical excision for localized OSSN.[12] MMC is a potent cytotoxic compound isolated from Streptomyces caespitosus. It becomes an alkylating agent upon metabolic activation, exhibiting cytotoxic effects on both proliferating and non-proliferating cells. It functions during all phases of the cell cycle, specifically aimed at fast dividing cells by blocking DNA synthesis, mostly in the G1 and S phases.[2,3]

Post-surgery, the patients are closely monitored, and they may undergo cycles of chemotherapy drops to aid recovery. However, these drops can sometimes lead to side effects like dry eyes or punctal stenosis.[3] Case 3 developed nasolacrimal duct obstruction a year after the surgery, which is likely side effect of chemotherapy.

Protocol for topical MMC in our study

1. 0.04% (0.4 mg/ml)
2. 4 times a day
3. One week on and one week off cycles given
4. 4-8 cycles were given depends on severity of lesion

Overall, treating OSSN requires a tailored approach to eliminate or manage the cancer while preserving vision and eye function as much as possible.

4. Limitations

There are some potential limitations for this case series: small sample size, only 4 cases were included in this study, so we cannot generalize the findings to a broader population and we cannot draw statistically significant conclusions also, all the cases were selected from outpatient department of UPUMS, Saifai, Etawah i.e. from a single centre, so the cases may not represent full spectrum of OSSN severity or variability in clinical presentation. These limitations can be acknowledged to provide context and emphasize the need for larger, multicentre studies to validate findings.

5. Conclusion

OSSN can have wide variety of clinical presentation, sometimes can mimic pterygium. Impression cytology is done to confirm the diagnosis (it reveals mild, moderate or severe dysplasia of squamous cells) before starting the treatment. Treatment requires a tailored approach including chemotherapy and ‘no touch technique’ of surgical excision to manage neoplasia while preserving the vision and eye function of the patient as much as possible. Regular follow up is needed to improve the outcome and decrease the recurrence rates.

6. Source of Funding

None.

7. Conflict of Interest

None.

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