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Case Report

Ophthalmology Section

Conjunctival Ocular Surface Squamous Neoplasia with Spheroidal Degeneration: A Rare Case of UV-B Associated Ocular Neoplasia and Keratopathy

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ABSTRACT

Ocular Surface Squamous Neoplasia (OSSN) is an umbrella term that includes a broad spectrum of conjunctival and corneal malignancies, ranging from mild epithelial dysplasia to invasive squamous cell carcinoma. These are uncommon ocular surface lesions but harbour the potential to cause significant ocular morbidity and rarely mortality. Human Papilloma Viruses (HPV) and Ultraviolet-B light (UV) have been identified as important risk factors in aetiopathogenesis. The present OSSN patient is a 48-year-old male with redness, growth, and a foreign body sensation in his left eye over the past four months. Examination of the left eye revealed a growth in the nasal limbus with a feeder vessel measuring 0.9×0.3×0.1 cm in size. Diagnosis was confirmed by anterior segment Optical Coherence Tomography (OCT). The patient was admitted for an excision biopsy accompanied by intraoperative Mitomycin-C. The lesion's histopathology revealed grade 2 in situ carcinoma with spheroidal formation. This case is considered rare due to the infrequent association between Conjunctival Intraepithelial Neoplasia (CIN) and spheroidal degeneration.

Keywords: Corneal malignancies, Epithelial dysplasia, Mitomycin-C, Optical coherence tomography

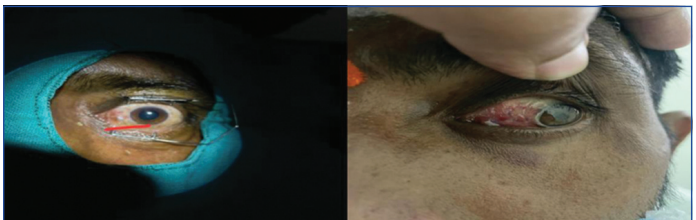
CASE REPORT

A 48-year-old male patient, a farmer by occupation, presented to the tertiary care eye hospital with complaints of an ocular mass, watering from the eyes, and a foreign body sensation for the last four months. There was no history of decreased vision, pain, and photophobia. The patient was non-diabetic, non-hypertensive, and negative for Human Immunodeficiency Virus (HIV) infection and HPV virus infection. There was no history of alcohol intake and smoking.

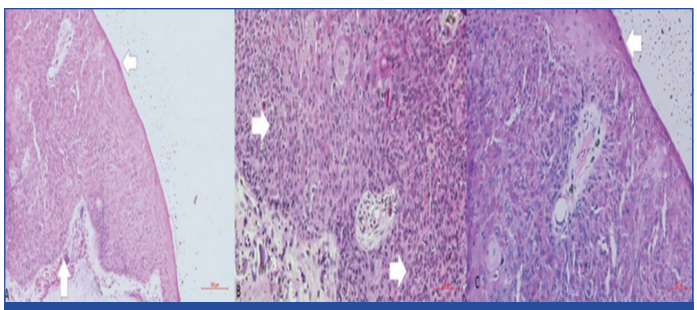
On examination, the best-corrected vision was 6/9 and 6/6 in the left and right eyes, respectively. Both eyes were orthophoric. A slit lamp examination revealed a whitish growth of size 0.9×0.3×0.1 cm on the nasal aspect of the bulbar conjunctiva of the left eye for four months [Table/Fig-1]. Routine blood investigations, clotting time, bleeding time, and systematic investigations were normal. A detailed serological workup was done, and the patient was found negative for HIV, Hepatitis B Virus (HBV), and Hepatitis C Virus (HCV). A provisional diagnosis of CIN was made based on high clinical suspicion and confirmed by anterior segment OCT.

The case was scheduled for a no-touch excision biopsy. OSSN was excised with 4 mm clear margins, and mitomycin C 0.02% was applied to the surgical bed for two minutes and washed with normal saline. A conjunctival limbal graft was taken from the superotemporal quadrant and placed with 6-0 vicryl (polyglactin 910) sutures to cover the excised area. Two cycles of topical chemotherapy with mitomycin-C (MMC) 0.04% were administered postoperatively. Each cycle consisted of one week on and one week off treatment. The patient was followed-up at three months and six months postoperatively, and no recurrence of the lesion was noted.

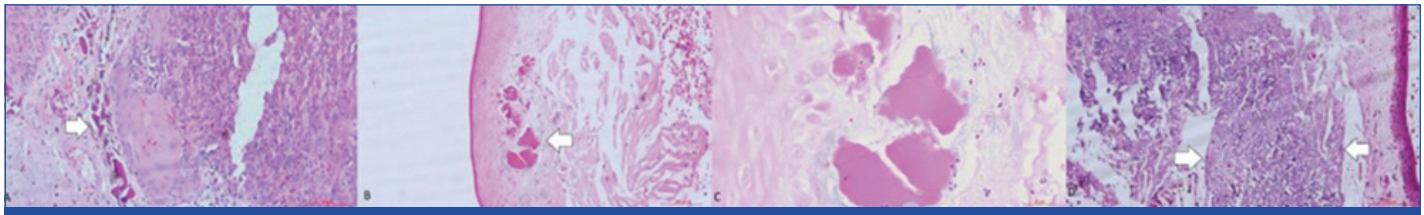
Histology of the lesion revealed the following findings: Conjunctival surface epithelium showed a sharply demarcated intraepithelial proliferation and thickening of the epithelium. There was a loss of maturation extending up to the lower two-thirds of the epithelial thickness, suggestive of CIN 2. Surface maturation was intact [Table/Fig-2]. Homogenous mauve-coloured confluent globular deposits were observed in the substantia propria adjacent to the CIN2 lesion. They were also seen underneath the uninvolved epithelium. These deposits lacked the fine quality and deep purple colour of calcium crystals, suggestive of Spheroidal degeneration (Labrador keratopathy). Solar elastotic change was observed in the collagen fibers of the substantia propria due to UV-B associated damage [Table/Fig-3].



[Table/Fig-1]: A gelatinous growth was present in the interpalpebral fissure (sun exposed area) of bulbar conjunctiva arising at the limbus (Right). Postoperative image with conjunctival graft (Left).



[Table/Fig-2]: (AX40) Conjunctival surface epithelium shows a sharply demarcated intraepithelial proliferation and thickening of epithelium. (BX100) There is loss of maturation extending upto the lower two third of the epithelial thickness suggestive of Conjunctival Intraepithelial Neoplasia 2 (CIN 2). (CX100) Surface maturation is intact.



[Table/Fig-3]: (AX100) Homogenous mauve coloured confluent globular deposits in substantia propria adjacent to the CIN2 lesion. (BX100 & CX100) They are also seen underneath uninvolved epithelium. Unlike calcification, they lack the granular quality and deep purple colour of calcium crystals suggestive of Spheroidal degeneration (Labrador keratopathy). (DX100) Solar elastotic change in the collagen fibres of substantia propria due to UV-B associated damage.

DISCUSSION

Lee GA and Hirst LW first coined the term OSSN in 1995 for a spectrum of ocular surface dysplasia, carcinoma in situ, and invasive squamous cell carcinoma. It is uncommon and primarily occurs in older males (78.5%) with an incidence between 0.03 and 1.9 per 100,000 individual [1].

Prolonged exposure to ultraviolet rays is considered a risk factor for OSSN. 43.8% of OSSN cases had Telomerase Reverse Transcription (TERT) promoter mutations [2]. Conjunctival squamous cell carcinoma usually presents in older age groups and arises in the interpalpebral fissure as a nodule, gelatinous mass, or leukoplakia [3]. It closely mimics common degenerative conjunctival and corneal surface pathologies such as pinguecula, pterygium, conjunctival granulomas, cysts, and sometimes other ocular malignancies like amelanotic nevus or melanoma.

There are three grades of OSSN:

1) Benign dysplasia, including papilloma, pseudotheliomatous hyperplasia, and benign hereditary intraepithelial dyskeratosis.
2) Preinvasive OSSN, including conjunctival/corneal carcinoma in situ.
3) Invasive OSSN, including squamous cell carcinoma and mucoepidermoid carcinoma [4].

OSSN typically manifests as a unilateral, vascularised limbal mass in the interpalpebral fissure, although it can also be bilateral or multifocal [4]. In rarer cases, the tumor may involve the tarsal conjunctiva or be associated with pterygia or other benign disorders, making the correct diagnosis more challenging.

Spheroidal degeneration, also known as Labrador keratopathy, Fisherman's keratopathy, climatic droplet keratopathy, actinic keratopathy, and Bietti's band-shaped nodular dystrophy, is a degeneration of the cornea and/or conjunctiva. It is characterised by amber-coloured homogeneous, translucent spherules of varying sizes in the corneal stroma, Bowman's membrane, and subepithelium. These granules are usually bilateral and appear at the peripheral cornea, coalesce, become nodular, and spread to involve the central cornea [5,6].

Spheroidal degeneration is a relatively common condition clinically characterised by oil deposits at the limbus. Histologically, it shows mauve globular degeneration of the subepithelial stroma. Under light microscopy, the lesions stain blue-green with toluidine blue, bright red with methyl green-pyronin, and variably pink with Gomori's aldehyde fuchsin (which demonstrates the collagenous component). They also stain eosinophilic with Haematoxylin and Eosin (H&E). Under electron microscopy, finely granular structures are observed on collagen bands. The deposited material in spheroidal degeneration is composed of protein [5,6].

McKelvie et al. reported 26 cases of CIN with spheroidal degeneration [7], while Yang et al. published 3 similar cases [8]. These findings are similar to the present case.

Diagnostic tests available include in-vivo confocal microscopy (IVCM) [9], high-resolution or ultra-high-resolution anterior segment optical coherence tomography (HR-OCT), and impression cytology [10]. HR-OCT is a noncontact method that provides clear images while patients sit comfortably in an upright position, making it user-friendly for operators.

Treatment options for OSSN include surgical excision with a no-touch technique and a clear margin of 2-4 mm, along with intraoperative application of 0.02% mitomycin-C [11]. Primary chemotherapy with topical 0.004% mitomycin eye drops [12] or topical 1% 5-fluorouracil alone [13] can also be used. Additionally, immunomodulatory drugs such as topical interferon-2b eye drops (1 million IU/mL) alone [14] are an option. The present case was treated with surgical excision, intraoperative mitomycin application, and postoperative mitomycin eye drops, resulting in a low recurrence rate.

Unique features of the present case include the disease occurring in a younger age without any immunocompromising status, which contrasts with it typically affecting elderly and immunocompromised individuals and being associated with spheroidal degeneration.

CONCLUSION(S)

Conjunctival ocular surface with secondary spheroidal degeneration is a rare condition. Early diagnosis and treatment prevents irreversible visual loss and the need for more advanced therapies.

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