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Review Article

Ocular surface squamous neoplastic disease: A major review

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Abstract

Ocular surface squamous neoplasia (OSSN) has a varied presentation. The etiopathogenesis is still not clearly understood, although various factors such as exposure to UV rays, viral infections and chemical carcinogens have been implicated. The number of patients with human immunodeficiency virus has increased which is reflected in an increase of this tumor with a poorer prognosis. Anterior segment OCT and confocal microscopy have become powerful tools to aid the diagnosis of OSSN.

Keywords: OSSN, Squamous cell carcinomas, Conjunctival intraepithelial neoplasia.

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1. Introduction

Ocular Surface Squamous Neoplasia (OSSN) is a spectrum of abnormal cell growths affecting the conjunctiva, cornea, and limbus. It encompasses various stages, including Simple dysplasia which has Mild cellular abnormalities, Conjunctival intraepithelial neoplasia (CIN) which has Abnormal cell growth within the conjunctival epithelium, Carcinoma in situ (CIS) which has Abnormal cell growth that hasn't invaded deeper tissues, Invasive squamous cell carcinoma (SCC) which has Cancerous cells that have invaded deeper tissues.[1]

OSSN typically affects older adults but is increasingly seen in younger individuals, particularly those with weakened immune systems. Early detection and treatment are vital to prevent local invasion, preserve vision, and avoid complications.[2]

2. Etiology

The pathogenesis of OSSN is complex and multifactorial. Ultraviolet rays, particularly UV-B radiation has been implicated as the most significant environmental risk factor for OSSN. It causes DNA damage of the limbal epithelial stem cells.[3] A higher incidence of OSSN has been noted in the equatorial regions, probably due to more UV exposure.[4]

Human Papilloma Virus infection, particularly types 16 and 18 have also been implicated in the pathogenesis of OSSN. There may be an underlying viral oncogenic mechanism similar to cervical neoplasia.[5]

The role of tumour suppressor gene p53 overexpression has been studied as a possible prognostic factor, immunohistochemical analysis has shown that it could occur with disease progression, as observed in other solid tumors, however its significance remains unclear.[6]

It has been noted that retroviral positive individuals have a higher prevalence of OSSN which may be due to immune dysregulation and an increased susceptibility to oncogenic viruses.[7] Likewise young patients with HIV and AIDS are also at higher risk of OSSN which is sometimes the first presentation of HIV.[8] The lesions are more aggressive with thicker tumors and a higher incidence of corneal, scleral and orbital invasion. These have a poor ocular prognosis and higher need for extended exenteration.[9]

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Xeroderma pigmentosum (XP) is a rare genetic disorder with multiple oculocutaneous manifestations, including a high risk of OSSN, which tends to be multiple, recurrent, and bilateral. While OSSN is a disease of aging, children with XP are prone to develop OSSN.[10]

Other risk factors include ocular irritation and exposure to petroleum products.[8]

3. Clinical Features

OSSN typically presents as a slow growing, unilateral lesion on the interpalpebral conjunctiva, usually near the limbus. They appear gelatinous, papillomatous, leukoplakic or nodular. The presence of a sentinel vessel, which is a large feeder vessel, is often noted.[11] Presence of such lesions in older patients should be marked as suspicious and warrant cytological evaluation.

Symptoms are non-specific in early stages and include redness, irritation and in cases where the cornea is involved, decreased vision. In very advanced cases, it invades the orbit or intraocular structures.

4. Diagnosis

It is challenging to diagnose OSSN due to overlapping features with benign ocular surface lesions such as pterygia or papillomas. Hence a high index of suspicion is needed to diagnose OSSN in its early stages. Impression cytology is an invaluable diagnostic modality.[12] Anterior segment optical coherence tomography allows non-invasive imaging and may reveal thickened, hyperreflective epithelium.[13]

Histological examination after biopsy gives us the definitive diagnosis. Impression cytology and in vivo confocal microscopy are useful adjunctive diagnostic tools but lack the ability to distinguish between in situ and invasive disease.[14]

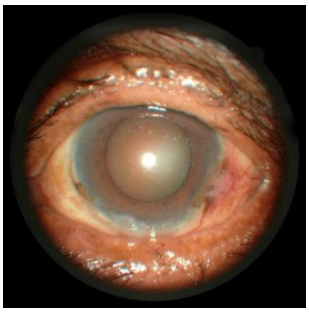

Figure 1: Anterior segment photograph of ocular surface squamous neoplasia.

5. Management

Treatment of OSSN depends on the size, location and the extent of the lesion and aims to completely destroy or remove the abnormal cells while preserving vision.

The standard of care for carcinoma in situ is topical chemotherapy and is the first line of treatment in many cases. Topical mitomycin 0.02% QID is effective but may cause irritation, keratitis or limbal stem cell deficiency. The cycle consists of one week on mitomycin followed by one week off, allowing the epithelium to heal. This is repeated for 2-4 cycles depending on the response.[15]

The standard of care for limbal lesions has been surgical excision via Shields' no-touch technique and wide margins (4mm), along with cryotherapy to surgical margins to minimize recurrence.[11] However, surgery alone is associated with recurrence rates of 5-33%. Symblepharon, limbal stem cell deficiency and conjunctival scarring are complications encountered after surgery.[12]

Role of Chemotherapy: This is a useful modality which can be a standalone therapy for intraepithelial neoplasia and subclinical lesions. It is often given after excision and for early recurrences. Topical chemotherapy has gained popularity due to its non- invasive nature and the ability to treat subclinical disease. Antimetabolites such as 5-fluorouracil (5-FU), mitomycin C (MMC) and interferon alpha-2b (IFN-a2b) have proved efficacious. IFN-a2b when administered as eye drops or subconjunctival injections is preferred due to its low toxicity and high success rates.[16,17] Mitomycin is effective, but has been associated with serious side effects such as limbal stem cell deficiency and scleral thinning.[18] 5 -FU is generally well tolerated, with only minor side effects like transient irritation and hyperemia.[19] Adjuvant topical chemotherapy reduces the post operative risk of tumour recurrences, and is an example of chemoprevention.[20]

For extensive or recurrent OSSN, combined therapy with surgery and topical agents is often used. Radiotherapy and photodynamic therapy may need to be considered.[20]

Role of radical surgery: In rare situations as in extensive orbital invasion complete excision is not feasible and exenteration may be only option, particularly for advanced cases resulting from late presentation, delayed diagnosis or incomplete excision. Unfortunately such eyes often have useful vision and the decision to remove the eye should be the last option done in consultation with the patient.[6,20]

6. Prognosis and Follow Up

The prognosis for OSSN is generally favourable with appropriate treatment. Regular follow up is essential due to the risk of recurrence, especially within the first two years after treatment. Retroviral positive patients have more aggressive disease and higher recurrence rates.[20]

7. Conclusion

OSSN is a potentially sight – threatening and locally invasive ocular surface malignancy. Early recognition and an aggressive approach to treatment, including surgery and topical chemotherapy offer excellent control rates with minimal morbidity. Future research into targeted therapies

and preventive strategies especially in high-risk populations is warranted.

8. Source of Funding

None.

9. Conflict of Interest

None.

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