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Squamous Cell Carcinomas of the Cornea: A Case Rreport

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ABSTRACT

Squamous cell carcinomas of the cornea are rare tumours. After excision, adjuvant treatment in the form of topical Interferon is commonly used to prevent recurrences and also for margin positive excisions. Ours is a chronic hepatitis B patient who underwent excisional biopsy and presented as corneal perforation while on topical adjuvant Interferon therapy. It can be secondary to previous surgery or unusual presentation, such as tumour perforation. The secondary role of initiating IFN therapy causing perforation is a possibility, and the complication needs to be assessed further. It may be prudent to avoid interferon drops in patients with compromised ocular surface tectonic stability and immune-compromised individuals. Plaque brachytherapy would be a better adjuvant in these cases.

Keywords: Squamous Cell Carcinoma Eye, Corneal Perforation on Interferon Therapy, Squamous Cell Carcinoma Perforation, OSSN.

INTRODUCTION

Ocular surface squamous neoplasia (OSSN) encompasses a wide spectrum of diseases ranging from conjunctival intraepithelial neoplasia (CIN) to squamous cell carcinoma (SCC). Literature suggests that occurrences of such malignancy are rare. Out of these, about 39% are CIN. The Incidence of SCC ranges from 0.02 to 3.5/100,000 population. The majority occur in older males, with the limbus being the most common site. The resistance of the Bowman's membrane limits the disease to the conjunctival portion of the lesion, which can be managed with wide local excision or topical chemotherapy.[1] We report a rare presentation of corneo-conjunctival OSSN, which presented as corneal perforation while on adjuvant interferon therapy. Rare incidences of SCC unusually presenting as perforation due to diffuse growth, advanced lesions, Herpes Simplex Virus, and topical chemotherapy with mitomycin have been reported. The secondary role of Hepatitis B and initiation of interferon (IFN) therapy, as in our case, causing perforation remains unclear until further evidence are available.

CASE HISTORY

A 46-year-old gentleman had a history of a lesion in his left eye for one month. He had a documented history of a nodular lesion at the limbus on the nasal side, for which he underwent an excisional biopsy. He presented to us after two months, and on examination, there was a lesion at the limbus of the left eye in the superomedial quadrant. The lesion was 6*5mm in size extending from 8 to 11 o'clock position extending on to cornea for 4mm from the limbus and extending to the bulbar conjunctiva for 2mm and involving sclera with its thinning at the periphery of the lesion. Visual acuity was 6/6 on both eyes. On evaluation, he was found to be Hepatitis B positive. He does not have significant past history or family history. The excisional biopsy report was suggestive of well-differentiated SCC of size 1*0.4cm with the involvement of excised margin with tumour. Ultrasound biomicroscopy (UBM) was not done due to recent surgery. The postoperative MRI of the eye reported a 0.4*0.2 cm irregularity in the superomedial aspect of the left eyeball, which was suggestive of residual disease. CT Scan of the neck and thorax did not show any metastasis.

After a multispecialty board discussion, possible treatment options were discussed with the patient. As the patient insisted on preserving his vision and due to the non-availability of

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plaque brachytherapy facility in our center, the patient was started on topical Interferon alpha 2b (IFN α2b) eye drops. Four weeks after initiation of interferon therapy, the patient presented with a corneal perforation (Figure1). Perforation had occurred towards the choroidal ciliary junction with prolapse of iris and suspected intraocular extension. Hence, a decision for enucleation was made. The patient promptly accepted the decision when the contingency of progressive disease was explained. Final histopathology was moderately differentiated SCC involving cornea & sclera-corneal junction. The patient has been on regular follow-up for the past two years and is happy being disease-free.

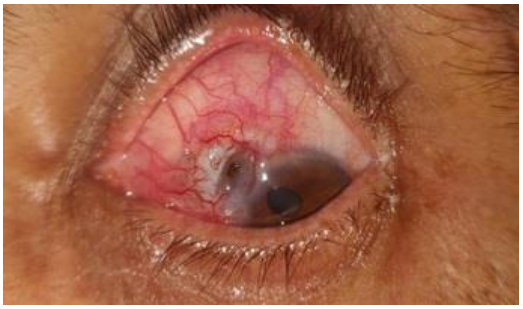

Figure 1: Corneal perforation with iris prolapse and eccentric pupil after starting interferon therapy

DISCUSSION

Ocular surface squamous neoplasia (OSSN) includes a spectrum of malignancy ranging from clinically subtle intraepithelial neoplasia to more ominous invasive tumors. An invasion of epithelial basement membranes differentiates them. OSSN prefers the corneoscleral limbus, a transition zone with the greatest mitotic activity. [1] These are rare tumours with an incidence of 0.02 to 3.5/100,000 populations and are seen in the middle to old-age groups. [1]The majority of the lesions occur at the limbus. The lesion may be flat or elevated and associated with the feeder's vessels. Lesions can be gelatinous or plaque-like, or white lesions. Lesions in the conjunctiva tend to be immobile and more raised. Large feeder vessel, when seen, is suggestive of violation of the epithelial basement membrane. Rarely presentation as bilateral lesions can also occur, typically keratinized and papillary. Imaging modalities like Optical coherence tomography (OCT), Confocal microscopy, and High-frequency ultrasound may help determine the extent of the disease [1].

Treatment for OSSN involves surgical excision with 4mm clinically clear margins with alcohol kerato-epitheliectomy with or without lamellar sclerotomy with double freeze-thaw cryotherapy to the edge and or base of the lesion is performed. If the intraocular extension is present, the patient may need enucleation.[2] Adjuvant treatment in the form of topical chemotherapy (mitomycin C and 5-fluorouracil) or immunotherapy agents (topical or injection IFN α2b) are used for extensive tumors, margin positive excision, or prevention of recurrence.[3] IFN α2b has various novel techniques of application like single-agent monotherapy, Immuno reduction to facilitate anticipated excision, and immunoprevention for tumors after surgical removal, especially when there is a positive surgical margin.[3,4] Plaque Radiotherapy with ruthenium-106 (RU-106) plaques is used in recurrent or incompletely excised SCC.

After excision alone, the microscopic disease is possible beyond the edge of the clinically visualized lesion. Hence, the recurrence rate after excision alone has been as high as 56%. Even if the pathological margins are clear, up to 33% reccurence have been reported. As a result, adjuvant therapies are often performed with excision, including cryotherapy or topical chemotherapy, with a reduction in recurrence rates. [5]Excision surgery carries risks of limbal stem cell deficiency and formation of symblephara. To avoid these risks and treat the entire ocular surface, medical treatment alone has gained popularity. Chemotherapeutic agents commonly used include mitomycin-C, 5-fluorouracil, and interferon-alpha-2b (IFNα2b). Topical IFNα2b has gained popularity for OSSN treatment because of its minimal toxicity. No difference in the recurrence rate of OSSN was found between surgical versus IFNα2b therapy alone. A 1-year recurrence rate of about 4% was reported in both groups [5]. In cases of positive surgical margins, recurrence rates increased to 100%. Studies showed that surgical excision followed by adjuvant topical IFN-α2b is the most effective strategy for minimizing persistence or recurrence in such cases. They reported the risk of positive margins following excision as 42%. After positive and negative margin status, recurrence rates were 52% and 11%, respectively. The rate of successful treatment with IFN-α2b was estimated to be 88%, and the subsequent risk of recurrence was only 6%. [5, 6]. When plaque

radiotherapy was used for positive margins, local tumor control was achieved in 100% of cases. Still, distant conjunctival tumor recurrence far away from the site of radiotherapy was seen in 25%.[7]

In this case, after following the described protocol, presentation as tumour perforation three months after surgery while on one month of IFN therapy made us search the possibility of per se tumour perforation and assess addendum of IFN therapy and Hepatitis B to previous surgery as causative for perforation.

There have been previously reported incidences of SCC unusually presenting as perforation without any gross tumor formation, due to diffuse growth causing inflammation leading to thinning and perforation and in advanced lesions as necrotizing scleritis with scleral perforation and uveal prolapse.[8,9] Herpes Simplex Virus has been described as a cause for corneal perforation, but there is no reported incidence of Hepatitis B as a causative factor. Topical chemotherapy with mitomycin has been associated with corneal perforation after pterygium excision but not for OSSN though epithelial defects are described.[10] With regard to IFN α2b flu-like symptoms, conjunctival hyperemia, follicular and papillary conjunctivitis are known side effects. There have been reported incidences of scleral/corneal melting and severe keratitis when IFN was used in rheumatoid arthritis patients on immunosuppressants. These patients have documented the incidence of complications during or immediately after completion of interferon therapy [11].

In our case, perforation may be secondary to previous surgery, which is a proven risk factor. Also, there have been unusual presentations of tumour perforation without a distinct mass due to diffuse growth. There is no proven causative link with Hepatitis B. The secondary role of initiation of IFN therapy causing perforation remains unclear until further evidence is available. A review of the literature showed such an anecdotal occurrence in immune-compromised individuals. [11] It may be prudent to avoid interferon drops in patients with compromised tectonic stability of the ocular surface. In retrospect, plaque brachytherapy would have been a better option in these cases.

CONCLUSION

This was a rare presentation of squamous cell carcinomas of the limbus in a chronic hepatitis B patient who underwent excisional biopsy and presented as corneal perforation while on topical adjuvant Interferon therapy. The secondary role of initiation of IFN therapy causing perforation is debatable. It can be secondary to previous surgery or unusual presentation, such as tumour perforation. It is better to avoid interferon drops in patients with compromised ocular surface tectonic stability and immune-compromised individuals. Plaque brachytherapy would be a better adjuvant in these cases.

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