Case Report

Limbal carcinoma: Common malignancy at uncommon site

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ABSTRACT

Limbus is the region of the eye between the cornea on one side and the sclera on the other. Limbus houses the stem cells. Neoplastic growths in limbus are the most common among growths of cornea and conjunctiva owing to the transition nature of the limbus. Although squamous cell carcinoma (SCC) is the most common carcinoma of limbus, its incidence is only 0.2–3.5/100,000. We present a 65-year-old patient with a limbal growth over a long period initially diagnosed as limbal stem cell deficiency. The patient sequentially developed epithelial dysplasia and then SCC. The complete excision of eyeball had to be done due to the recurrent nature of the lesion. The need for early detection of limbal mass and its prompt treatment cannot be overemphasized. Limbal growths have a good prognosis when treated early since they do not invade cornea and conjunctiva readily. Treatment is both surgical and medical. We present this case because of its rarity with a review of literature.

Key words: Limbal stem cell deficiency, limbus, squamous cell carcinoma

INTRODUCTION

Limbus is the transition region between cornea and sclera.[1] Corneal and conjunctival growths usually begin at the limbus. Squamous cell carcinoma (SCC) is the most common malignancy of the limbus. Limbal growths are superficial and do not invade cornea or sclera readily owing to tough Bowman's membrane of the cornea and tough layers of the sclera.[2] We present a case of a 65-year-old female patient diagnosed as having limbal stem cell deficiency and ultimately developed SCC.

CASE REPORT

A 65-year-old female patient presented redness and irritation in the right eye for 2 years. On examination, a fibrovascular growth was seen at the medial limbus encroaching over the cornea. The patient was diagnosed as having a local limbal stem cell deficiency after performing dye test and was put on medical treatment. After 6 months, the fleshy mass appeared at the base of the limbus, so an excision biopsy was performed. Histopathological examination (HPE) of the mass showed epithelial dysplasia and the patient was kept on close follow-up. After 6 months, the patient again presented with similar mass but refused any surgical intervention.

The mass increased in size for the next 1 year. At this time, the mass was painful, multilobulated, and encroached the two-third of cornea medially. It was adherent to the eyelids on the medial side and was associated with a mucus discharge. The visual acuity had worsened from 6/60 to only light perception. The cornea was visible in the upper part, but no further detail of anterior segment was visible. An imprint smear and edge biopsy of the lesion was allowed by the patient. Imprint smears revealed a few clusters of malignant epithelial cells with a polygonal shape, high nucleocytoplasmic (N/C) ratio, hyperchromatic nuclei, and prominent nucleoli consistent with SCC [Figure 1a].

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HPE revealed superficial ulceration, inflammatory cell infiltrate, and nests of malignant cells invading the stroma. The malignant cells showed pleomorphism, high N/C ratio, hyperchromatic nuclei, conspicuous nucleoli, increased mitotic activity, moderate amount of eosinophilic cytoplasm, and occasional keratin pearl formation [Figure 1b and c]. The mass was diagnosed as moderately differentiated SCC, right limbal growth. Clinically, there was no metastasis to regional or distant metastasis. The patient was planned for excision of the eyeball and partial lid excision with lower lid reconstruction in two stages. The excised eyeball showed a moderately differentiated SCC extending superficially from the limbus to adjacent cornea. The deeper layers of the cornea and underlying structures - ciliary body and pigmented epithelial layer of the iris were free from tumor invasion [Figure 1d].

DISCUSSION

Limbus is 1-mm broad area between the cornea on one side and the episcleral tissue and sclera on the other. It consists of two structures, namely, epithelium and stroma, and is characterized by the presence of blood vessels, lymphatics, and nerves.[1] Limbus has been shown to house the limbal epithelial stem cells (LESCs). LESCs replenish the squamous epithelial cells of the cornea which are constantly being shed during each blink. The evidence of limbal stem cells was first experimentally proven by Mann in 1944.[3] Partial or full LESC deficiency leads to deleterious effects on corneal wound healing and surface integrity.[4,5]

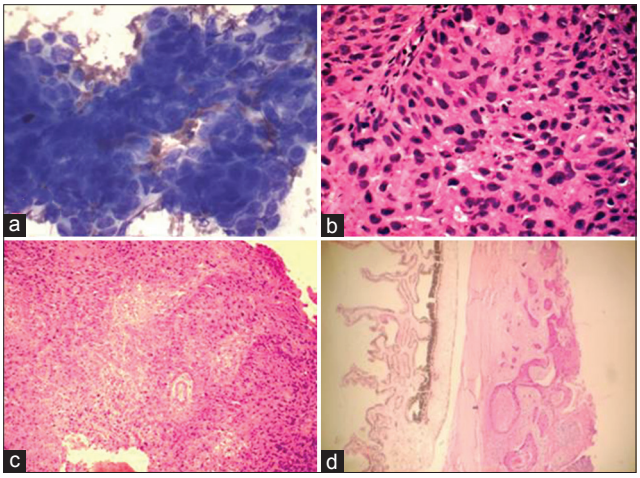

Figure 1: (a) Imprint smears from limbal mass showing a cluster of malignant epithelial cells with a polygonal shape, high N/C ratio, hyperchromatic nuclei, and prominent nucleoli (Giemsa, ×40). (b and c) Histopathological examination showing nests of malignant cells invading the stroma, malignant cells showing pleomorphism, high N/C ratio, hyperchromatic nuclei, conspicuous nucleoli, increased mitotic activity, moderate amount of eosinophilic cytoplasm, and occasional keratin pearl formation (H and E, ×10 and ×40). (d) Histopathological examination of excised eyeball showing moderately differentiated squamous cell carcinoma involving limbus and extending into adjacent cornea and underlying structures are free (H and E, ×10)

The incidence of SCC of limbus is 0.02–3.5/100,000.[6] The tumors that involve the cornea and conjunctiva arise at the limbus. Limbus is the site of epithelial transition; thus, it is common for the limbus to be the place of predilection of tumors. It is well known that SCCs in this location are less malignant than elsewhere in the body and grow as an exophytic mass, probably because of the difficulty of spread over tough structures such as the cornea and sclera.[2] The corneal Bowman's membrane offers considerable resistance to the deep invasion of the tumor, and even tumors involving the entire corneal surface may not have penetrated into the stroma. This feature is important from a therapeutic aspect as even very large tumors invading large areas of the cornea may be adequately removed by superficial keratectomy.

SCC has been reported to be more common in males by a study by Sunderraj *et al.*;[7] however, the present limbal SCC is seen in an elderly female. An increased incidence of malignancies of the cornea, conjunctiva, and eyelids has been observed in the patients with xeroderma pigmentosa.[8] Of these structures, limbus is the most common site and SCC is the most common histological type. The increased incidence is due to the fact that these structures have more exposure to ultraviolet radiations and shield the iris, lens, and retina from ultraviolet rays. Besides ultraviolet rays, HIV and human papillomavirus infection are also associated with limbal SCC.[9] Thus, an HIV test should be performed in all patients suffering from recurrent or bilateral SCC of the limbus, cornea, and conjunctiva. Our patient was HIV-negative.

A pigmented variant of limbal SCC has been reported by Shirzadeh[10] and Shields.[11] This variant is very rare and less than thirty cases have been reported in literature. Pigmented tumor is due to the presence of melanin granules in the neoplastic cells. Differential diagnosis of pigmented lesions in the limbal region includes pigmented SCC, malignant melanoma, and pigmented papilloma.

Besides SCC, a number of other neoplasms affect limbus, benign being more common than malignant.[7] Dermoid is the most common benign neoplasm reported by various studies[1,7] followed by papilloma, hyperplastic squamous epithelium, and nevus. Other less common tumors are lipoma, angioma, fibroma, neurofibroma, lymphoma, and fibroxanthoma.[7] The closest differential diagnosis of limbal SCC includes a papilloma and dermoid.

Ash and Wilder, in discussing limbal tumors, came to the conclusion that local excision with 1-mm healthy margin will suffice in the majority of cases and that enucleation is necessary only if recurrences are persistent.[12] Conservative management of intraepithelial SCC of conjunctiva-corneal by instillation of mitomycin C and interferon alpha-2b is

followed to prevent recurrence and where surgical resection is unfeasible. Instillation of mitomycin C following surgical excision has been shown to reduce recurrence rates.[13]

CONCLUSION

Any mass in the limbal region should be viewed with suspicion although malignancy is uncommon at this site. Early detection can prevent many radical treatments such as enucleation 1000.

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Conflicts of interest

There are no conflicts of interest.

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