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Case Report

Squamous Cell Carcinoma of the Cornea

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In this paper, a case of corneal squamous cell carcinoma is reported. Invasive squamous cell carcinoma of the cornea is a rare disorder and has not been previously described in the Korean literature. In this case, the invasive squamous cell carcinoma of the cornea was treated by complete excision and cryotherapy. No evidence of metastasis or recurrence has been found since the procedure. Complete excision and adjunctive cryotherapy has become the treatment of choice because of the higher recurrence rate following a simple excision.

Key Words: Cornea, squamous cell carcinoma

INTRODUCTION

Neoplastic lesions of the squamous epithelium in the ocular surface include actinic keratosis, dysplasia, carcinoma in situ, and invasive squamous cell carcinoma. Recently, Lee et al. suggested using the term, Ocular Surface Squamous Neoplasia (OSSN), which includes dysplastic and carcinomatous lesions of the cornea as well as the conjunctiva.[1] They reported the incidence of OSSN as being 1.9/100,000 in Metropolitan Brisbane, Australia, between 1980-1989.[2] Templeton et al. investigated tribal groups in Uganda between 1961 and 1966, reporting an average incidence of 0.13/100,000.[3]

OSSN predominantly occurs in older males, with an average age of 56 years ranging from 4 to 91 years old.[1] It is most often presented as a growth on the ocular surface or as a foreign body sensation, redness or irritation. Diminished vision is less common.[1] Squamous cell carcinoma of the cornea is generally a slow growing tumor that remains localized.

Squamous cell carcinoma of the cornea has not yet been described in the Korean literature. Here, we report a case of a 73-year-old man with corneal squamous cell carcinoma who was treated with complete excision and cryotherapy.

CASE REPORT

On August 5, 1999, a 73-year-old man visited the Yonsei University Medical Center because of a mass found on his right eye 15 days prior. He felt no irritation or pain. Upon examination, the visual acuity was 20/200 in the right eye and 20/50 in the left. Using a Goldmann applanation tonometer, the intraocular pressure was 16 mmHg in the right eye and 13mmHg in the left eye.

Using slit-lamp biomicroscopy, there was an elevated fixed nodular mass at the nasal limbus of the cornea in the interpalpebral area of the right eye. The pinkish lesion consisted of dilated feeding vessels on the surface along with a hyperpigmented patch on its medial side. The mass involved the epithelial layer of the cornea without a noticeable extension to the adjacent ocular tissues (Fig. 1). The left eye was normal. The preoperative diagnosis was a limbal tumor. For diagnostic and therapeutic purposes, an elective excision biopsy under local anesthesia was performed on August 6, 1999. Under a surgical microscope, the first incision was made in the normal conjunctiva 1.5 mm distal to the lesion,

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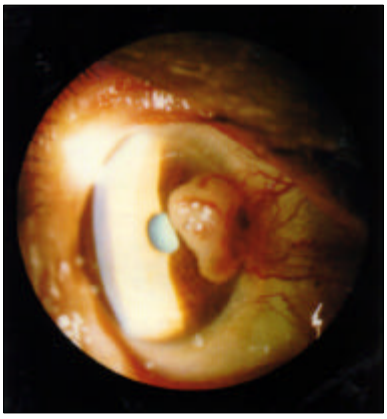

Fig. 1. Elevated nodular mass at the nasal quadrant of the corneal limbus in the right eye.

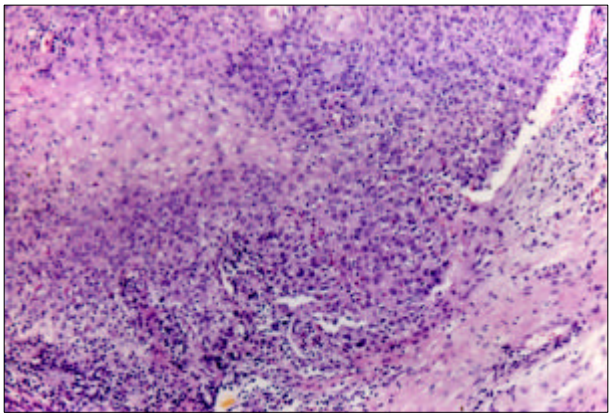

Fig. 2. Histologic section showing well differentiated squamous cell carcinoma with high cellularity, and a loss of polarity (H&E stain, ×100).

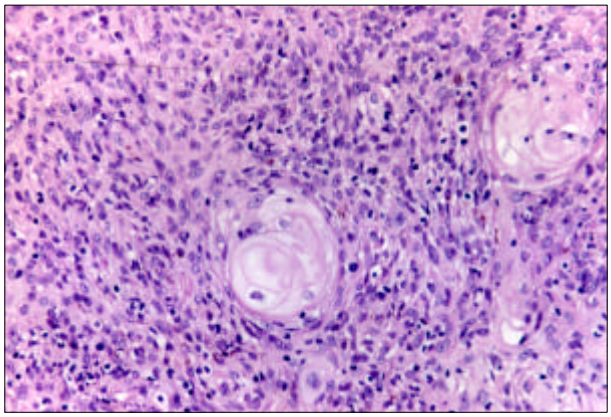

Fig. 3. Another histologic section showing malignant epithelial cells forming keratin pearls representing an invasive squamous cell carcinoma (H&E stain, ×200).

and a corneal sample was scraped forward to the limbus with a blade. A 1.5 mm normal corneal epithelium from the lesion was also included within the removed mass. The nodular mass was easily removed in one piece. The limbus, all adjacent tissue, and the scleral bed were treated with double freeze-thaw cryotherapy. There was no complication after the treatment.

On histopathologic examination, a well differentiated squamous cell carcinoma with an invasion of the basement membrane was noted (Fig. 2 and 3). The depth of invasion beneath the basement membrane was 1 mm, and the excision margin was clear.

A nasopharynx, orbit, chest, abdomino-pelvic computed tomogram, and a whole body bone scan showed no evidence of metastasis.

A slit-lamp examination showed that there was no evidence of recurrence since the procedure.

DISCUSSION

Squamous cell carcinoma most commonly occurs in the limbus.[1] The limbus is an area where the transition from conjunctiva to the corneal epithelium occurs. This area is predisposed to dysplasia, as a transformation zone of the uterine cervix.[4]

Excessive exposure to UVB causing DNA damage plays a major role in developing OSSN.[5] UV light can cause DNA damage by forming pyrimidine dimers. A failure in DNA repair may lead to fixed somatic mutations and a cancerous transformation. McDonnell et al. suggested that the human papilloma virus (HPV) type 16 might play a role in the development of dysplasia and carcinoma.[6] They used an in vitro gene amplification technique with PCR to identify the HPV 16 DNA in conjunctival premalignant and malignant lesions. Another pathogenic factor that has recently been suggested is the presence of a p53 gene mutation. Toth J et al. reported that there was frequent p53 gene overexpression in conjunctival squamous cell carcinoma (18 out of 23 cases; 78%), but the relation between p53 gene overexpression and a HPV infection within tumor tissue could not be determined.[7,8] In addition, other pathogenic factors such as dust, wind, lid closure causing trauma, ocular surface injury, petroleum exposure, and cigarette smoking has been suggested.[1]

OSSN appears to be related to some systemic and ocular disease. Squamous cell carcinoma shows a higher incidence in patients with acquired immunodeficiency syndrome (AIDS). Studies of large populations in Uganda and the United states have shown that AIDS patients carry a higher risk for developing conjunctival squamous cell carcinoma.[9,10] The odds ratio of a squamous cell carcinoma associated with a human immunodeficiency virus (HIV) infection was 13.1 in Uganda, and 78% of patients with conjunctival squamous cell carcinoma were found to be HIV positive in Malawi.[11] Since squamous cell carcinoma arises predominantly in eldery males, squamous cell carcinoma with histologic features of aggressive behavior in a young individuals should indicate the possibility of a HIV infection.[12] Furthermore, xeroderma pigmentosum has been associated with particularly young patients with OSSN. The cells from most people with xeroderma pigmentosum are unable to repair UV damaged DNA as rapidly as normal cells. Other ocular diseases such as pterygium, pingueculum, climactic droplet keratopathy, cataract, and corneal degeneration are thought to be related to UVB exposure, and also have a high association with OSSN.[1] In our patient, there was no associated systemic disease or eye disease.

Histologically, OSSN is divided into dysplasia (mild, moderate, and severe), carcinoma in situ, and invasive squamous cell carcinoma.[13] The histopathologic features of invasive squamous cell carcinoma are characterized by invasive malignant squamous cells that violate the basement membrane and grow in sheets or cords into the stromal tissue.[14] In this case, a microinvasive well differentiated squamous cell carcinoma forming keratin pearl was noted.

Excision of the lesion with a wide surgical margin of 2 - 3 mm was the standard treatment for squamous cell carcinoma of the cornea.[15] Rose bengal staining can be used to delineate the extent of the abnormal tissue. A deep corneal invasion may require deep lamellar keratoplasty and scleroplasty. The recurrence rates following excision range from 15 to 52%, with an average of approximately 30%.[1] The major risk factor for recurrence has been identified to be an inadequate excision margin.[16] Cryotherapy is also a commonly employed treatment modality. Cryotherapy may destroy cells by a thermal effect and by obliterating the microcirculation, resulting in an ischemic infarction of both the normal and tumor tissues. Complications following cryotherapy such as iritis, increased or decreased intraocular pressure, thermic inflammatory edema and lateral corneal scarring increase with more extensive freezing.[1] The recurrence rates after cryotherapy range from 7 to 22%, with an average of 12%.[1] Recently, a complete excision with adjunctive cryotherapy has become the treatment of choice because of the higher recurrence rate (28.5%) following a simple excision of an ocular surface squamous neoplasia when compared to an excision plus adjunctive cryotherapy (7.7%) from retrospective review of 28 patients.[17] Radiation therapy may be used for diffuse or spreading lesions in cases where the initial excision is likely to be too extensive.[1] In some cases DNCB (dinitrochlorobenzene), urea, topical mitomycin C, topical 5 - FU, and thiotepa has been used to treat OSSN. However, the use of these agents need further investigation to define their therapeutic role.[1,18] In our case, the corneal squamous cell carcinoma was treated by complete excision and cryotherapy.

Squamous cell carcinoma of the cornea is generally a slow progressing tumor. A further intraocular invasion, and a metastasis is uncommon. Tabbara et al. reviewed 10 patients from Saudi Arabia with regional and distant metastasis.[19] The sites of metastasis included the preauricular lymph nodes, the cervical lymph nodes, the parotid gland, the lung and bone. The development of regional metastasis is not related to a poor prognosis, whereas local invasion was more often related to a tumor-related mortality. In our patient, the nasopharynx, orbit, chest, abdominopelvic computed tomogram, and a whole body bone scan revealed no evidence of metastasis.

In our case a 73-year-old man with corneal squamous cell carcinoma was treated by complete excision and cryotherapy. There was no complication or recurrence since the procedure.

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