Ipsilateral presentation of ocular surface squamous neoplasia and conjunctival melanoma in xeroderma pigmentosum: A rare occurrence

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A case of a 16-year-old male with xeroderma pigmentosum (XP) who presented with multiple pigmented and nonpigmented conjunctival lesions in both eyes is reported. He had a keratinized lesion at the limbus and a pigmented lesion in bulbar conjunctiva in the left eye and multiple pigmented bulbar conjunctival lesions and a keratinized limbal nodule in the right eye. Excision biopsy confirmed the diagnosis of ocular surface squamous neoplasia (OSSN) and conjunctival intraepithelial melanocytic neoplasia-2 (CIMN-2) in the right eye and OSSN and conjunctival melanoma *in situ* (CIMN-5) in the left eye. Two malignant conjunctival lesions occurring simultaneously in the same eye of a patient with XP have not been reported earlier.

Key words: Conjunctival melanoma, ocular surface squamous neoplasia, xeroderma pigmentosum

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Xeroderma pigmentosum (XP) is a rare autosomal recessive inherited disorder characterized by deficiency of the enzymes responsible for repairing ultraviolet-radiation-induced DNA damage.[1] Persistence of unrepaired DNA damage results in somatic mutations, leading to neoplasia of the skin and ocular surface. Ocular surface squamous neoplasia (OSSN) and rarely conjunctival melanoma have been reported in patients with XP. However, simultaneous presentation of both malignancies in the same eye has not been reported.

Case Report

A 16-year-old previously diagnosed male patient with XP presented with chief complaint of slowly progressive, painless, nonpigmented and pigmented nodular opacities in the left eye noticed since the past 2 months. His parents had history of consanguineous marriage and his younger sibling was also diagnosed with XP. On general physical examination, he had hyperpigmented skin macules diffusely affecting the whole body. All data for this report are collected according to the Declaration of Helsinki, and prior permission was taken from the patient or parents for publication of photographs.

His best-corrected visual acuity (BCVA) in both eyes was 6/6. On slit-lamp examination, the right eye showed a pearly white plaque-like lesion at the temporal limbus measuring 2 × 2 mm and areas of flat, dark brown pigmented lesions inferonasal and inferior bulbar conjunctiva, occupying 4'o clock hour area around the limbus [Fig. 1a, c and d]. The left eye showed a pearly white, raised nodular, keratinized lesion 4 × 3 mm in size located at the temporal limbus with areas of pigmented conjunctiva around it and a 5 × 3.5 mm elevated, dark brown inferonasal bulbar conjunctival lesion, 0.5 mm away from the limbus with surrounding flat conjunctival pigmentation [Fig. 1b, e and f]. There was congestion in the adjoining conjunctiva in both eyes and inferior corneal scarring in left eye. Rest of the anterior segment and fundus examination was within normal limits in both eyes.

Anterior segment optical coherence tomography (AS-OCT) of the right and left eyes showed a raised hyper-reflective thickened epithelium with abrupt transition of normal and thickened epithelium with central back shadowing corresponding to the white nodular lesions with central area of keratin and hyper-reflective thickened epithelium with back shadowing corresponding to the pigmented lesion in the left eye.

A clinical diagnosis of OSSN with primary acquired melanosis in the right eye and XP with OSSN and conjunctival melanoma in the left eye was made. There was no regional lymphadenopathy. Wide margin excision biopsy of both lesions along with alcohol-assisted keratoepitheliectomy and cryotherapy to conjunctival edges and amniotic membrane grafting was done in both eyes.

Histopathological examination of the nonpigmented keratinized nodules showed mild squamous dysplasia of the conjunctival epithelium in the right eye [Fig. 2a] and moderate squamous dysplasia in the left eye [Fig. 2b] with uninvolved margins of excision. Histopathology of the pigmented lesions showed conjunctival intraepithelial melanocytic neoplasia (CIMN) grade 2 with atypia in the right eye [Fig. 2c] and CIMN grade 5 with atypia [Fig. 2d] in the left eye. A diagnosis of OSSN in both eyes and CIMN-2 in the right eye and conjunctival melanoma *in situ* (CIMN-5) in the left eye was made.

On his second week postoperative follow-up, a 1 × 1 mm gelatinous nonpigmented nodule was noted at the edge of the excised conjunctival OSSN in the left eye [Fig. 3a]. AS-OCT corresponding to the nodule revealed hyper-reflective thickened epithelium with abrupt transition suggestive of OSSN recurrence [Fig. 3b]. The patient was started on topical interferon alpha2b eye drops four times daily in the left eye. At 4 months of follow-up, the recurrent OSSN in the left eye had regressed completely. His ocular surface was stable in both eyes with minimal conjunctival scarring and inferior corneal scar in the left eye [Fig. 3c and d]. No further recurrence of OSSN or conjunctival melanoma was noted at last follow-up visit.

Discussion

Oculocutaneous malignancies in XP mainly comprise basal cell carcinomas which are slow-growing and rarely metastasize and squamous cell carcinomas (SCC) which are fast-growing, invasive, and can metastasize.[2] These malignancies are seen in 50% of the patients with XP in the first decade of life. Oculocutaneous SCC in XP has double (4%) metastatic potential compared with the non-XP-associated SCC (2%).[3] Conjunctival melanoma has been reported rarely in patients with XP.

Patients without XP present with nonmelanocytic oculocutaneous malignancies at a mean age of 67 years and oculocutaneous melanomas at 55 years.[4] However, in the patients with XP, the median age at diagnosis of nonmelanocytic oculocutaneous malignancies is 9 years (range 1–32 years) and oculocutaneous melanoma is 22 years (range 2–47 years).[5]

In patients with XP, the inability to repair the ultraviolet-light-induced DNA damage leads to somatic mutations and the development of cancerous growth. This inherent defect, in turn, accounts for the increased susceptibility of such patients to OSSN at a younger age.[6]

OSSN in XP is frequently bilateral, more aggressive (recurrence rate = 64.3%) than usual, and the prognosis is poor when compared with the normal population.[7] This is evident in our case as well where the patient presented with OSSN recurrence in the early postoperative period despite tumor-free margins on histopathology.

Patients with XP can also develop melanocytic neoplasms of ocular surface, particularly seen in (but not limited to) UV-exposed areas. In a longitudinal study that evaluated ocular features in patients with XP, conjunctival melanosis was seen in 20% of patients and conjunctival melanoma in only 1 out of 87 patients with XP.[8] Uveal and orbital melanoma has also been reported in patients with XP. Two cases of malignant melanoma involving iris and ciliary body in patients with XP have been reported which necessitated enucleation in both patients.[9,10] Primary orbital melanoma, including amelanotic variant, has also been reported in patients with XP.[11,12]

However, simultaneous occurrence of OSSN and conjunctival melanoma in patients with XP is reported rarely.

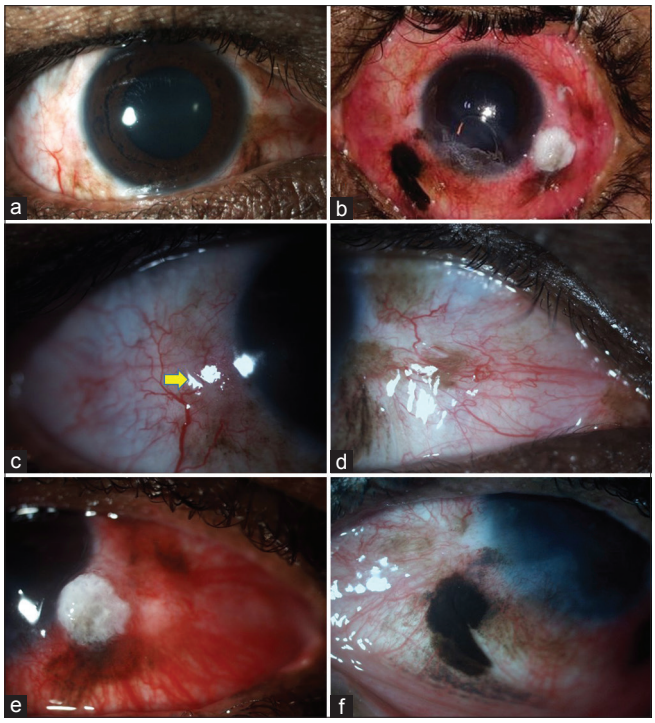

Figure 1: Clinical photograph showing OSSN and conjunctival melanocytic lesion in the (a) right eye and (b) left eye. High-magnification photograph of the right eye showing (c) placoid area (yellow arrowhead) with surface keratin at temporal limbus and (d) areas of flat brown conjunctival melanocytic lesion of the nasal bulbar conjunctiva. High-magnification photographs of the left eye showing (e) OSSN at the temporal limbus and (e) dark brown thickened pigmented conjunctival lesion in nasal bulbar conjunctiva

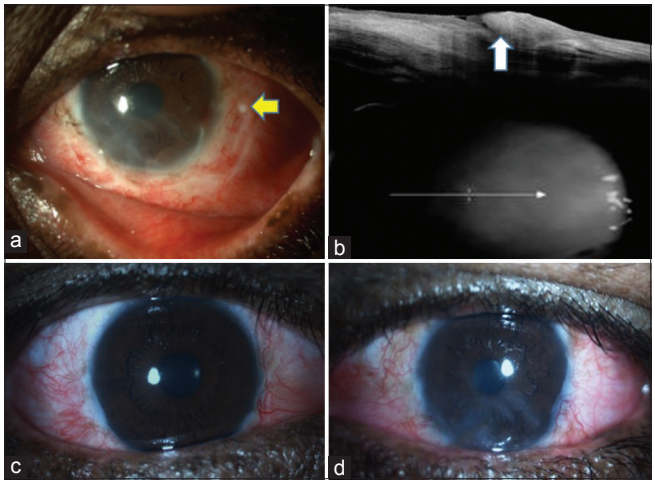

Figure 3: Postoperative photographs. (a) Slit-lamp photograph of the left eye at 2 weeks postoperative period showing a gelatinous nodule at the edge of conjunctival excision (yellow arrowhead) suggestive of OSSN recurrence. (b) AS-OCT through nodule showing localized thickened hyper-reflective epithelium with abrupt transition between the normal and thickened epithelium (white arrowhead). Postoperative photograph of the (c) right and (d) left eye at 1 year follow-up showing conjunctival scarring with no evidence of recurrence of OSSN or melanoma

Caso E R has recently reported a histopathology-confirmed OSSN in one eye and conjunctival melanoma in the other eye in an 18-year-old patient with XP.[13] Our patient adds to this literature evidence of melanocytic and nonmelanocytic conjunctival neoplasms developing simultaneously in patients with XP. In our patient, both OSSN and conjunctival melanoma were present simultaneously in one eye. This presentation was not reported earlier.

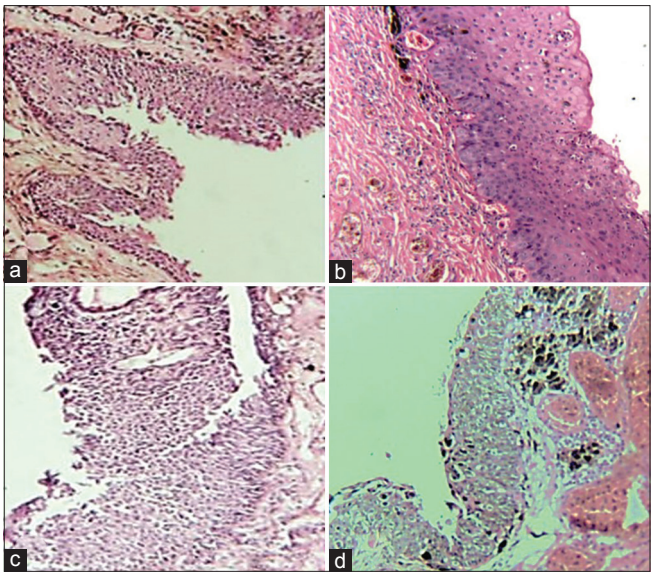

Figure 2: Histopathology of the excised conjunctival lesions. Hematoxylin and eosin (H and E, ×40)-stained tissue from the (a) right eye nonpigmented temporal bulbar conjunctiva showing stratified squamous epithelium with mild to moderate dysplasia and (b) nonpigmented temporal lesion in the left eye showing moderate squamous dysplasia. Histopathology (H and E, ×40) (c) from the right eye flat pigmented nasal bulbar conjunctival lesion showing CMIN with grade 2 atypia and (d) from pigmented left eye nasal bulbar conjunctival lesion showing CMIN with grade 5 atypia (melanoma *in situ*)

The management of ocular malignancy in a patient with XP should be focused on early detection. Detailed slip-lamp evaluation of ocular surface starting from early childhood and prompt biopsy of any suspicious lesion are required to prevent morbidity related to ocular surface tumors in these patients. Pigmented conjunctival lesions also need biopsy to rule out conjunctival melanoma or precursor lesions. Literature reports of the role of adjuvant topical therapy in these patients are scanty. However, high and early recurrence rate of OSSN in patients with XP as exemplified by our case emphasizes the need for close postoperative follow-up and possible role of topical adjuvant therapy with interferon alpha2b. Sun protection, long-sleeved clothing, scarfs, and sunglasses should be advised to all patients with XP to further minimize UV-radiation-induced DNA damage.

Conclusion

In conclusion, OSSN and conjunctival melanoma can coexist simultaneously in the same eye in patients with XP. All patients with XP should be thoroughly screened for OSSN and melanocytic conjunctival lesions, and prompt biopsy is indicated at earliest clinical suspicion Close postoperative follow-up is required to detect and treat tumor recurrence in these patients.

Declaration of patient consent

The authors certify that they have obtained all appropriate

patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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