CASE REPORT

Bilateral recurrent ocular surface squamous cell cancer associated with epidermodysplasia verruciformis

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SUMMARY

A 17-year-old boy, presented with a 2-year history of bilateral, recurrent ocular surface mass. Dermatological evaluation revealed the presence of multiple hypopigmented macules over his body. Skin biopsy showed features typical of epidermodysplasia verruciformis. Topical mitomycin C (0.02%) was administered in both eyes for 6 weeks (three 1-week cycles over 6 weeks). While the mass in the left eye regressed, the mass in the right eye was excised under guidance of intraoperative frozen section. Triple-freeze thaw cryotherapy of the surrounding conjunctiva along with placement of amniotic membrane graft was performed. Postoperative mitomycin C (0.02%) was administered for another 6 weeks (three 1-week cycles over 6 weeks) in both eyes. At 4 years of follow-up, no recurrence has been noted.

was excised twice in the past 2 years but showed repeated growth. No family members had a similar affliction. Both eyes had a best-corrected distance visual acuity (BDVA) of 20/20. On slit-lamp biomicroscopy, the right eye ([figure 1A](#)) showed an ill-defined, elevated, gelatinous nodular mass (6×4 mm) at temporal limbus (7–10 o'clock hours). Another similar mass (2×2 mm) was present at the nasal limbus (5 o'clock hours). Feeder vessels were also visible. Left eye examination showed a similar gelatinous mass (4×4 mm) at the nasal limbus (6–8 o'clock hours) with ill-defined edges and feeder vessel. Conjunctivalisation of the cornea was appreciable along all the masses. Gonioscopy did not show any abnormality in either eye. Lens and retinal examination of both eyes was normal. No lymphadenopathy was present.

BACKGROUND

Ocular surface squamous neoplasia (OSSN) encompasses the entire spectrum of dysplastic and carcinomatous lesions of the ocular surface.¹ OSSN may represent abnormal maturation of corneal and conjunctival epithelium as a result of a combination of factors such as ultraviolet B irradiation and human papilloma virus. Other reported risk factors include exposure to petroleum products, heavy cigarette smoking, chemicals such as trifluridine, arsenicals and beryllium, and ocular surface injury, vitamin A deficiency, light pigmentation of the hair and eyes, and HIV infection.

Epidermodysplasia verruciformis (EV) is a rare hereditary disease. The exact prevalence of EV is unknown but more than 200 cases have been reported in the literature so far. In early childhood, scaly macules appear on the trunk, shoulders, neck, arms and face. They may, however, be more widely distributed. The lesions are brown, red or white and in darkly pigmented skin they may appear black. The appearance and distribution of these lesions has been likened to pityriasis versicolor.² Seborrheic keratosis, actinic keratosis and squamous cell carcinoma arise in sun-exposed areas, most commonly on the forehead. Malignant conversion of the benign lesions occurs in more than half of patients who have had the disease for 20 years or more and can occur on any sun-exposed area.^{2 3}

CASE PRESENTATION

A 17-year-old Indian boy presented with a history of recurrent growth of mass in both eyes. The mass

INVESTIGATIONS

Impression cytology from the masses in both eyes showed features of mild squamous epithelial cell dysplasia along with neutrophilic infiltration. Ultrasound biomicroscopy (UBM; Paradigm Medical Industries, Salt Lake City, Utah, USA) examination of the eyes did not show any deep infiltration of the mass into the sclera.

Dermatological evaluation revealed multiple hypopigmented macules (approximately 0.5 mm) over the patient's forearms, arms and chest with hyperpigmentation over his cheeks ([figure 2](#)). A diagnosis of EV was made based on histopathology of the skin biopsy ([figure 3](#)). PCR analysis from the skin lesions was positive for β -1 human papillomavirus (HPV-5). An ELISA test for HIV was negative.

TREATMENT

The patient was started on topical mitomycin C (0.02%) four times a day for 6 weeks (three 1-week cycles over 6 weeks). The mass in the left eye showed substantial reduction in size whereas the right eye failed to show improvement. Therefore, excision of mass with frozen section analysis and cryotherapy of conjunctival margins was planned in the right eye. The temporal and nasal mass were both excised along with a 3 mm conjunctival margin and sent for frozen section analysis. Frozen section analysis of the temporal mass revealed malignant infiltration of the inferior and temporal margins of the conjunctiva, therefore a further 3 mm conjunctival excision was performed infero-laterally. Margins of nasal mass were free from

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Figure 1 (A) Preoperative clinical photograph of right eye showing ocular surface squamous neoplasia with feeder vessel. (B) Postoperative day one clinical photograph showing ocular surface free from mass and covered with amniotic membrane graft.

infiltration. Three cycles of freeze-thaw cryotherapy were applied to the remaining conjunctival margins and amniotic membrane graft was sutured on bare sclera (figure 1B). Postoperatively the patient was continued on topical MMC (0.02%) for 6 weeks (three 1-week cycles over 6 weeks) in both eyes. Topical moxifloxacin hydrochloride (0.5%) and lubricants were also given. Histopathological examination revealed well-differentiated squamous cell carcinoma with tumour cells infiltrating into the underlying stroma.

OUTCOME AND FOLLOW-UP

The patient did not show any signs of recurrence at 4 years of follow-up. Repeat impression cytology failed to show any evidence of squamous dysplasia.

DISCUSSION

EV is a rare, inherited disorder that predisposes patients to widespread HPV infection and cutaneous squamous cell carcinomas.^{4 5} The most common inheritance pattern is autosomal recessive, though rarely, autosomal dominant and sporadic patterns may be seen. The disease is characterised by chronic

infection with β -HPV. Widespread skin eruptions of flat-to-papillomatous, wart-like lesions and reddish-brown pigmented plaques on the trunk, hands, upper and lower extremities and face, are typical.

More than 30 HPVs have been identified in EV lesions. HPV-5 and HPV-8 have been isolated in more than 90% of EV-associated squamous cell carcinomas. Treatment of EV is limited and aimed mainly at preventing the progression of benign lesions into malignant ones. No therapy for EV is definitive. Treatment of EV includes preventive measures, the most important of which is strict sun avoidance and protection, beginning as soon as the diagnosis is made.

The association of OSSN and EV has been reported only once in the literature. Partridge and Pariser⁶ reported a case of ocular and cutaneous squamous cell carcinoma in an African-American man with EV resulting in blindness and death. Despite multiple local excisions, that patient experienced several recurrences with invasion of the cornea. Exenteration was required to prevent further local invasion but involvement of the parotid gland was observed after a few months. Parotidectomy was performed, but the patient died of metastatic disease after 6 years of follow-up. Multiple recurrences occurred on excision in that patient as well as in ours.

Patients with EV are prone to having multiple malignant lesions and their prognosis is worse as compared to older individuals without any systemic disease. Although no recurrence has been detected in our patient during 4 years of follow-up, the nature of the disease and the need for lifelong follow-up has been explained to him.

Figure 2 Hypopigmented macules over arms and chest.

Figure 3 Histopathology of skin lesion showing acanthosis and hypergranulosis of epidermis with presence of large cells with abundant basophilic cytoplasm, slightly enlarged nuclei and peripheral margination of chromatin.

This case report highlights the fact that occurrence of OSSN in younger age groups (<25 years) should arouse suspicion of any systemic predisposing disease such as xeroderma pigmentosum and HIV infection. EV, though rare, is associated with OSSN. A thorough dermatological evaluation and follow-up will help rule out such association.

Learning points

- Occurrence of ocular surface squamous neoplasia in younger age groups (<25 years) should arouse suspicion of systemic predisposing diseases.
- A thorough dermatological evaluation and follow-up will help rule out association with epidermodysplasia verruciformis.
- Lifelong follow-up is necessary to rule out any evidence of recurrence.

Competing interests None.

Patient consent Obtained.

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