CASE REPORT

Keratoacanthoma with Xeroderma Pigmentosum
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Abstract
Xeroderma Pigmentosum is a rare autosomal recessive genodermatosis, characterized by photosensitivity, freckled pigmentation and patchy pigmentation of skin, neurologic changes and premature skin aging. This paper report a case of keratoacanthoma in a twenty year old female patient of Xeroderma Pigmentosum.

Key Words: Xeroderma Pigmentosum; Keratoacanthoma, UV light; Squamous Cell Carcinoma.

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Introduction
Xeroderma Pigmentosum, a condition first described by Hebra and Kaposi in 1874, is a rare autosomal recessive genetic disorder which starts in early childhood and is characterized clinically by cutaneous photosensitivity, pigmentary, ocular & neurologic changes, photophobia and propensity for early development of malignancies in sun exposed mucocutaneous and ocular structures.(1) Primary defect lies in inability of cells to repair ultraviolet light induced DNA damage. These patients are more prone to develop skin cancers than normal individuals.(2) Though these patients more commonly develop cutaneous malignancies, benign tumors such as papillomas and keratoacanthoma etc. Keratoacanthoma is a self-limiting epithelial proliferation with a strong clinical and histopathological similarity to well differentiated squamous cell carcinoma, presumably arising from hair follicles and associated with sunlight induced damage.(3) Here we report a case of keratoacanthoma in a patient with Xeroderma Pigmentosum.

Case Report
A 20 year old female patient presented to Oral medicine and radiology department of College of Dental Sciences, Davangere, Karnataka with a chief complaint of a growth on the left side of upper lip since last 20 days with pain. Patient had noticed a small sized growth 20 days back which gradually increased to the present size.(Fig 1a,1b, 1c) It was associated with pain of sudden onset, which was intermittent, dull aching and mild in nature. The pain was localized and not associated with secondary changes. There was no history of similar growth in the same region or anywhere else in the body. No other constitutional symptoms were present.

Patient was a diagnosed case of Xeroderma Pigmentosum with corneal opacification and was under medical care. Her parents had consanguineous marriage, but other family members were not affected. Upon examination freckled pigmentation was present over the face with hypopigmented areas over the nose and right malar region and generalized skin hyperpigmentation. The skin over the lips was atrophied with a restricted mouth opening of 3 cm. A well-defined solitary, sessile and ovoid growth of approximately 1.5 cm x 1cm was present over the left side of the face on the skin of upper lip extending medio-laterally from midline to 0.5 cm short of the corner of the mouth and superio-inferiorly from 1 cm short of ala of the nose to transitional zone of upper lip involving the vermilion border of the lip. The skin over the growth was atrophic and pigmented with encrustation and had an irregular surface. There were no visible pulsations or any other secondary changes. Upon palpation it was tender, soft to firm in consistency, non-indurated and fixed to underlying structures. Based on history and clinical features, a provisional diagnosis of squamous cell carcinoma was given as it is the most common lesion occurring in Xeroderma Pigmentosum patients at the rate of 1000 to 4000 times more than be expected in people under 20 years of age.(4) Also squamous cell carcinoma occurs in these patients with more propensity to lips and tongue, undoubtly related to ultraviolet light induced DNA damage. Moreover the lesion was exophytic and rapidly developing. Keratoacanthoma was considered under the differential diagnosis. It is a benign self-limiting tumour which has about 95% occurrence on the sun exposed areas and about 8% on the outer edge of the vermilion border of the lips. The lesion is similar to squamous cell carcinoma except for the central plug of keratin with irregular crusted surface. These lesions are occasionally tender.(3)
The lesion was surgically excised and the histopathologic examination of the specimen revealed parakeratinised epithelium with acanthosis and increased individual cell keratinisation, keratin pearl formation and occasional sebaceous elements focally with inflammatory cell infiltrate (Fig 1d, 1e). These features were suggestive of keratoacanthoma and hence upon compilation of the data obtained from history, clinical and histopathological examination a final diagnosis of keratoacanthoma was made.

**Discussion**

Xeroderma Pigmentosum is a group of rare autosomal recessive inherited disorders characterized by extreme skin sensitivity to ultraviolet light, abnormal skin pigmentation and high frequency of benign and malignant skin neoplasm development especially on sun exposed skin. The condition was first described in 1874 by Hebra and Kaposi. In 1882 Kaposi coined the term Xeroderma Pigmentosum for the condition referring to its characteristic dry pigmented skin.(1)

The basic defect lies in nucleotide excision repair, leading to deficient repair of DNA damaged by UV radiation. UV radiation induces cross linking between thymine nucleotides. After exposure to UV light normal cultured cells identify and excise the UV induced thymine dimers and insert undamaged nucleotides after DNA synthesis and ligation. It is this repair process (unscheduled DNA synthesis) which is deficient in Xeroderma Pigmentosum. In addition to this UV radiation also has immunosuppressive effects that may be involved in the pathogenesis of Xeroderma Pigmentosum. Although typical symptoms of immunodeficiency are not usually observed in patients, several immunological abnormalities have been described in the skin of Xeroderma Pigmentosum patients.

It affects about 1 in 250,500 persons with no sexual and geographic predilection. As with most autosomal recessive disorders, usually no family history is present, the being heterozygotes, are healthy, however a history of consanguinity may be elicited.

The disease typically passes through three stages. The skin is healthy at birth. The first stage appears after the age of six months and is characterized by diffuse erythema, scaling and freckle like areas of increased pigmentation seen over light exposed areas especially on the face. Gradually it involves the skin of other areas in the body. The second stage is characterized by poikiloderma, which consists of skin atrophy, telangiectasias, and mottled hyperpigmentation and hypopigmentation. The third stage is heralded by the appearance of numerous malignancies including squamous cell carcinoma, malignant melanoma, basal cell carcinoma, and fibrosarcoma. These malignancies may occur as early as the age 4-5 years with a mean age of 8 years. (1) In striking contrast the mean age for squamous cell carcinoma in general population is 58 years and for keratoacanthomas it is 45 years. (4) Keratoses, warty papillomas, keratoacanthomas, fibromas, neurofibromas, angiofibromas and angiomyomas may occur as benign tumors. (4) In the present case the tumor appeared at the age of 20 years with no previous history of any other neoplastic growth. The ocular changes include severe photophobia, conjunctivitis, corneal opacification, conjuctival nevi, epibulbar and lid neoplasms. The patient in our case had presented with corneal opacification.

Keratoacanthoma is a self-limiting epithelial proliferation with a strong clinical and histopathological similarity to well differentiated squamous cell carcinoma. (4) Chemicals, viruses like HPV, sunlight, trauma and altered immunity has been implicated as the causative agents. (4) With exposure to sunlight being the most common cause, and 95% of the solitary lesions are found on the sun exposed areas like face, head and extremities and 8% of all cases are found on the outer edge of the vermilion border of the lip. (4) This common etiology explains its association with Xeroderma Pigmentosum as in the present case. However incidence of...
Keratoacanthoma in patients with Xeroderma Pigmentosum is not recorded.

Keratoacanthoma appears as a firm, non-tender, well demarcated, sessile, dome shaped nodule with a central plug of keratin, which may be yellowish, brown or black and has an irregular, crusted often verruciform pattern. Rapid enlargement is typical, with the lesion usually attaining a diameter of about 1 to 2 cm within 6 weeks. This critical feature helps to distinguish it from the more slowly enlarging squamous cell carcinoma.(4) The patient in present case had developed the lesion of about 1.5 cm in duration of three weeks with typical clinical features. However its association with Xeroderma Pigmentosum in the present case makes it significant due to high incidences of malignancies in such patients. The keratoacanthoma may regress spontaneously with residual scarring. The adjuvant therapies used include excision, curettage and desiccation, cryosurgery, radiotherapy, podophyllin, intramuscular methotrexate, retinoids and intralesional or topical fluorouracil.(4) However in the present case we preferred to for a excisional biopsy due to its suspected malignant nature and esthetic reasons.

The overall life expectancy of a Xeroderma Pigmentosum patient is reduced by 30 years with 90% probability of surviving to age of 13 years, 80 % probability of survival till 28 years and only 70 % probability of survival till 40 years.(4) Hence, the early diagnosis, even prenatally by amniocentesis in families with affected members and lifelong protection and avoidance of sun and UV light may prevent or at least delay the popikilodermatic and neoplastic alterations of the skin and eyes.(1)

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