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Case Study

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MULTIPLE METACHRONOUS MALIGNANCIES IN XERODERMA PIGMENTOSA: TOO MANY CANCERS IN ONE BODY

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ABSTRACT

Introduction: Xeroderma Pigmentosa is a rare autosomal recessive genetic disorder characterised by defective DNA repair. Clinical features are skin photosensitivity, xerosios, hyperpigmented lentiginous macule. Patient with this condition are at higher risk of developing malignancies throughout their life as compared to general population. **Case Report:** we report a case of a 21 year old boy suffering from Xeroderma Pigmentosa who developed multiple malignancies over time and was treated with multiple surgeries and radiation therapy. Till the last follow up the patient is doing well and tolerated well to radiation therapy. **Conclusion:** At present there is no permanent cure for Xeroderma Pigmentosa. Avoiding sun exposure by chemical or physical sunscreen is important. Early detection of premalignant and malignat lesions is important to avoid morbid surgery and radiotherapy. Though literature report different reaction to radiation therapy but our patient tolerated well to radiation therapy twice radiated.

KEYWORDS: Xeroderma pigmentosa; head and neck cancer; multiple malignancies.

INTRODUCTION

It is an established fact that Xeroderma Pigmentosa is one of the major risk factor for development of multiple cutaneous malignancy.[1] These malignant tumours most commonly occur in the sun exposed face, head and neck. The basic defect in XP is deficiency of Nucleotide Excision Repair (NER) enzyme which leads to impairment in repair of DNA damage by Ultra Violet (UV) rays. It was first described by Hebra and Kaposi in 1874.[2,3] Important clinical features are skin photosensitivity, actinic keratosis, xerosis, poikiloderma, hyperpigmented lentiginous macule, and malignant lesion in sun exposed area. XP patients are at increased risk of developing malignancy under 20years old. Squamous cell carcinoma, basal cell carcinoma and melanoma are commonly associated.[1,2,4] The incidence of XP varies across the globe with some reported incidence as: in United State 1:250,000, in Japan 1:40,000 and approximately 2.3 per millions in western Europe.[5,6,7] In India the incidence of multiple malignancy in XP is not yet significantly reported. The highest number of case report came from Halkud R et al.[8] The objectives of reporting this case is it may add up to the incidence of such cases to our regional reported system and to highlight the importance of frequent follow up and early detection of malignancy at early stage.

CASE REPORT

We have a 21 year old boy presented to us in outdoor department with a proliferative growth on the right side of parotid region. The patient had multiple blackish spot and rash on his face and chest and was diagnosed with Xeroderma Pigmentosa. He had been diagnosed and treated with multiple malignancies in the past. He developed the blackish lesions when he was 3 year old. On October 2013 he was diagnosed with a squamous cell carcinoma of nasal cavity for which he was treated with radiation therapy 60 Gy. The patient tolerated well with the dose and had no significant reaction. On May 2015 he was again diagnosed with basal cell carcinoma on the right side of face below the eye. The lesion was small (1.5x2cm) and he underwent wide local excision with advancement flap repair. On December 2016 he was diagnosed with squamous cell carcinoma on the left lateral canthus for which he was treated with wide excision and advancement flap repair. On March 2017 he was again diagnosed with squamous cell carcinoma of right orbit for which he underwent right orbital exenteration with post- operative adjuvant radiation therapy of 30 Gy. Again on October 2018 he developed a proliferative growth on right side of parotid region and small ulcerative lesion on left nasal alar region and left side of face below the lower eyelid (Figure 1 and 2).

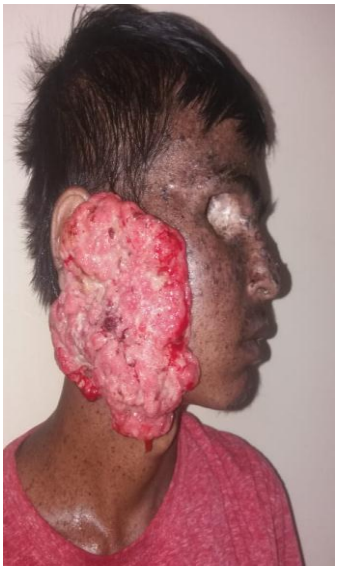

Fig. 1: Proliferative growth in parotid region.

Fig. 2: Ulcerative lesion in left facial region.

Biopsy from parotid mass showed a squamous cell carcinoma and he underwent wide local excision of the primary tumour with modified neck dissection along with pectoralis major myocutaneous flap repair. The patient also at the same time had excision of left nasal alar lesion and repair with median forehead flap and excision of ulcerated lesion on left cheek below the eyelid with mustarde flap repair. After the last operation the patient is seen on 4th month 10 days and is doing well with no new malignancy detected till this time as shown in figure 3 and 4. His younger sister (12 year old now) also developed similar blackish spots from the age of 1 year and till present she has not been diagnosed with any cancer. No other family members or relatives developed such lesion.

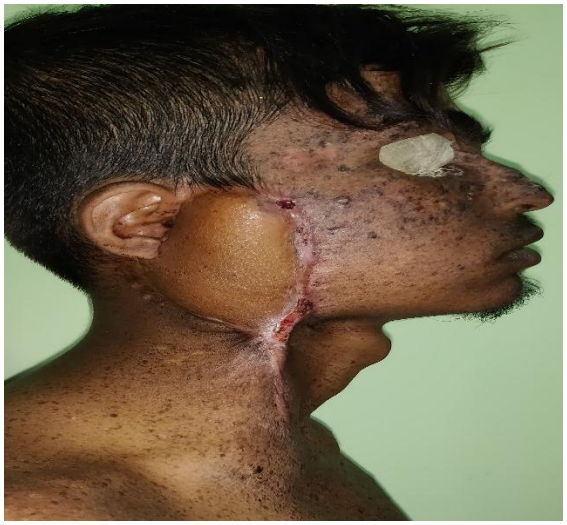

Fig. 3: Reconstruction done with Pectoralis Major Myocutaneous flap.

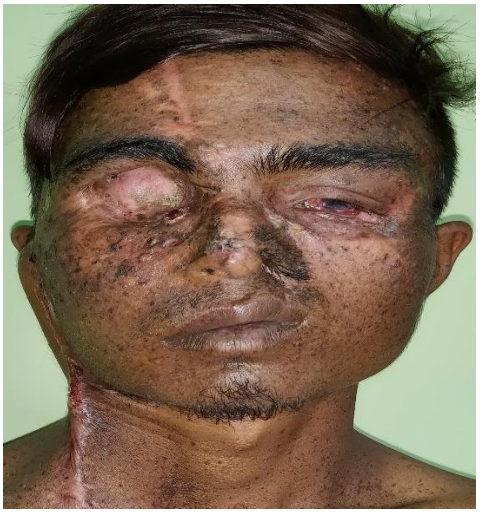

Fig. 4: Four months post operative.

DISCUSSION

Xeroderma Pigmentosa is a rare autosomal recessive disorder of DNA repair characterised by increased sensitivity to ultraviolet radiation, early development of pigmentary changes and ultraviolet radiation induced skin cancers.[9] Based upon the specific gene effected, XP can be divided into seven subgroup Group A (XPA) through G (XPG) and Xeroderma Pigmentosa Variant (XPV).[9] Subtype XPA to XPG have NER defect whereas subtype XPV is associated with defect in post replication repair.[10] Subtype XPA, XPB, XPD, XPF, XPG experience severe sunburn on exposure to sun, in contrast subtype XPC, XPE, XPV have normal sunburn response.[11] It has been shown that patients without an abnormally severe sunburn response are paradoxically developing skin cancer earlier than those who experience sunburn.[12]

Patients with XP are found to be at more risk of developing cutaneous cancer than the general population. In a 40 year follow up study by National Institute of Health in 106 XP patients, the risk of nonmelanoma skin

cancer (NMSC) and melanoma were found to be 10,000-fold and 2000-fold higher, respectively, than the general population.[13] The average age of onset is 9 years for NMSC and 22 years for melanoma. Besides cutaneous lesion and malignancy XP patients also develop ophthalmic changes in 40-100%[14] and central nervous system changes in approximately 25%.[12] The diagnosis is based upon clinical presentation, a family history consistence with autosomal recessive inheritance, and/or confirmatory genetic testing.

Treatment of XP is still unsatisfactory and is primarily limited to avoiding sun exposure by chemical or physical sunscreen. Early diagnosis and extensive sun protection may prolong the life expectancy of the patient or prevent early occurrence of malignancy. Eye care consist of sunglasses, artificial tears, bland ointment at night. Keratoplasty and corneal transplantation has been used to restore vision in individual with severe keratitis.[15] Premalignant and small malignant lesion had been treated nonsurgically with cryotherapy,[16] photodynamic therapy[17] and topical application of fluoruocil and imiquimod.[18] genetic counselling is also an important component in managing XP patient especially in a family that has an affected child and is considering having more children.

The ideal treatment of XP should be aimed at replacing the deficient repair enzyme or repairing the defective pathway. Two such modalities had been investigated. Daily topical application of a lotion containing endonuclease V in a liposome vehicle (T4N5 lotion) or placebo had been studied in 30 patients with XP.[19] At the end of the study the annual number of actinic keratosis and basal cell carcinoma were found to be low in study group as compared to those treated with placebo. Few studies had explore the option of gene therapy in XP like introduction of wild type XPC gene into clogenenic human primary XPC keratinocyte using a retroviral vector,[20] correction of mutated XPC gene using an engineered nucleases.[21]

Management of malignant tumour in XP is a troublesome as the patient may need multiple treatments due to development of multiple cutaneous malignancies in a subsequent period of time. The principle of management follow the same oncology principle of management. Surgical excision of the lesion is generally preferred wherever possible. One has to keep in mind as well as counsel the patients that wide excision of the tumour does not prevent the development of new tumour in the same field.[22] To reduce the surgical defect Mohs micrographic surgery can be helpful but can be impractical in patients requiring frequent and recurrent surgical excision.[22] Use of radiation is still controversial as review of literature showed that patients of XP show difference in sensitivity to ionising radiation. Rogers et al[23] evaluate the 4 children (out of 2000 radiated cases) who had severe reaction to radiation therapy and found only one who is diagnosed with XP. Arlet et al[24] reported a case of XP with angiosarcoma of the scalp treated with surgical excision and radiation therapy who developed severe desquamation and necrosis of the underlying bone after receiving 38Gy in 19 fractions with 6-MeV electron. DiGiovanna JJ et al treated a XP patient with astrocytoma successfully with radiation and did not have recurrence after 9 years of follow up.[25] Our patient received radiation therapy twice but no such toxicity was manifested in his subsequent follow up. This give us a glimpse that radiation therapy is a potential mode of treating malignancies in XP as primary or adjuvant therapy though at present we do not have any guidance about who are prone to develop radiation therapy toxicity.

Xeroderma pigmentosa is ultimately fatal, but life can be prolonged by simple preventive measures to minimise sun exposure and frequent follow up to detect early malignancies.[8] Devastating surgeries can be prevented when malignancies are detected at an early stage. In our case when basal cell carcinoma on right side of face was detected at early stage, it could be treated by simple excision and advancement flap. But when malignancies on right parotid region was detected at late stage more comprehensive surgeries with reconstruction has to be done. Hence frequent follow up and early detection of malignancies is essential.

CONCLUSION

Xeroderma pigmentosa is a devastating disease as there is no permanent cure at present and the worst is patient may have to undergo multiple treatments for malignancies. Early detection of premalignant or malignant lesions by close clinical follow up and regular skin and eye examination can prevent destructive surgery when patients can be treated with simple excision when diagnosed early. Radiation therapy can be a potential mode of treating malignancies in XP as primary or adjuvant though we don't have guidance at present about who are prone to develop radiation therapy toxicity.

Compliance with Ethical Standard

Conflict of interest: The author declare that they have no conflict of interest.

Source of funding: None.

Informed consent: Informed consent was taken from all the participant included in the study.

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