

A Series of Two Cases of Intraoral Malignancies in Patients with Xeroderma Pigmentosa

Ankit Dilip Mahuvakar, Darshan Premdas Meshram, Shaikh Mohsin Ahmed Abdul Nabi, Vijayalaxmi Kishanrao Ambulgekar, Mohammad A Sammer

ABSTRACT

Xeroderma pigmentosum (XP) is an autosomal recessive genetic disorder characterized by an increased frequency of skin cancer following minimal sunlight exposure.

Multiple basal cell carcinomas and other skin malignancies frequently occur at a young age in those with XP. In fact, metastatic malignant melanoma and squamous cell carcinoma are the two most common causes of death in XP victims.

This series represent rare presentations of malignancies in non-sun-exposed areas in such patients.

Keywords: Xeroderma pigmentosum, Intraoral malignancy, Non-sun-exposed areas.

How to cite this article: Mahuvakar AD, Meshram DP, Nabi SMAA, Ambulgekar VK, Sammer MA. A Series of Two Cases of Intraoral Malignancies in Patients with Xeroderma Pigmentosa. *Int J Otorhinolaryngol Clin* 2013;5(2):111-114.

Source of support: Nil

Conflict of interest: None declared

INTRODUCTION

Xeroderma pigmentosum (XP) is an autosomal recessive genetic disorder of DNA repair in which the ability to repair damage caused by ultraviolet (UV) light is deficient.¹ This disease involves both sexes and all races with an incidence of 1:250,000 in US more common in Japan.² The most common defect in XP is an autosomal recessive genetic defect in which nucleotide excision repair (NER) enzymes are mutated, leading to a reduction in or elimination of NER. If left unchecked, damage caused by UV light can cause mutations in individual cell's DNA. This buildup of mutations will lead to malignancy.¹

CASE REPORTS

Case 1

A 16 years old female patient, brought by parents with complaints of:

1. Blackish papules all over the body, since she was 1 month old.
2. Severe pain in the eyes on exposure to light since childhood.
3. Swelling on the tip of tongue since 3 months.
4. Swelling in the midline neck since 1 month.

Patient's relatives give history of multiple small swellings all over the body, which finally busted and later

developed into blackish papules. No history of pain in the papules. No history of seasonal variation in the number and size of the papules. No history of itching in the papules, followed by bloody discharge. No history of similar complaints in family members (Fig. 1).

She has severe pain in the eyes, when exposed to light and hence always keeps them shut, constant watering from both eyes and lost vision from right eye. She refrains from going out and is always at home. She also complains of severe burning pain when exposed even to bulb light.

She complained of swelling at the tip of tongue since 3 months. Painless, gradually increasing, occasionally bleeding from the swelling while chewing. Now the swelling has increased to such an extent that she has severe difficulty



Fig. 1: Freckles on sun-exposed areas (case 1)



Fig. 2: Mass on the tip of tongue



Fig. 3: Lateral profile showing submental lymphadenopathy

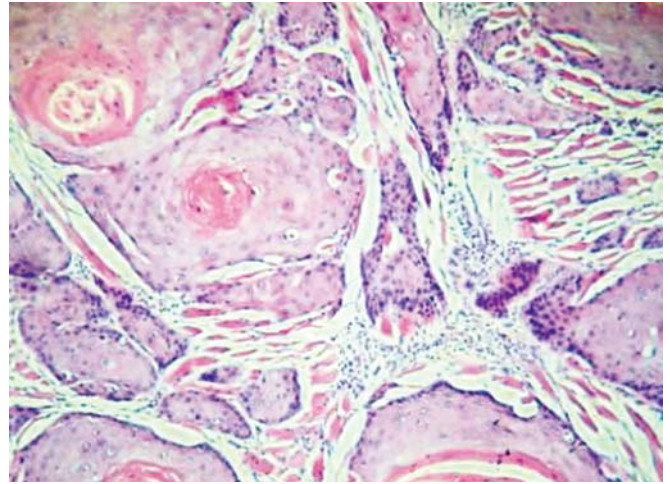


Fig. 4: Histopathology showing keratin pearls of squamous cell carcinoma

in swallowing solid food, now is on liquid diet. She also has difficulty in speaking and has altered speech, but is still intelligible (Fig. 2).

She had a swelling in the midline neck since 1 month which was gradually and progressively increasing, painless in submental region (Fig. 3).

Following are the reports of investigations done:

Punch biopsy: Suggestive of squamous cell carcinoma, well differentiated (Fig. 4).

- *FNAC submental LN:* Metastasis from squamous cell carcinoma
- *Dermatology opinion:* Xeroderma pigmentosa
- *Skin biopsy:* Suggestive of XP
- *Ophthalmology opinion:* XP with severe corneal and conjunctival xerosis, vision could not be checked due to severe photophobia even after instilling anesthetic eye drops
- *Adv:* Lubricant eye drops.

Case 2

Patient is 19 years old male, brought by relatives with complaints of:

1. Gradually and progressively developing skin discoloration since 3 years of age.
2. Gradual loss of vision in both eyes.
3. Swelling in oral cavity since 3 months.

Relatives noticed gradually progressive discoloration of the skin and increased roughness, when he was 3 years old. This now has progressed over time to reach the present condition where these lesions are present all over the body (Fig. 5).

He complains of severe pain and pricking sensation in the eyes from childhood, which has increased. Now, he has very poor vision and relies on support from others to mobilize.



Fig. 5: Freckles on sun-exposed areas (case 2)



Fig. 6: Mass on the gums and extending onto hard palate

He complains of gradually progressive swelling in oral cavity on the upper part since 3 months, swelling has now increased to such extent that he is having difficulty in swallowing and in speaking. He also complains of intermittent bleeding from the swelling even on minimal manipulation (Fig. 6).

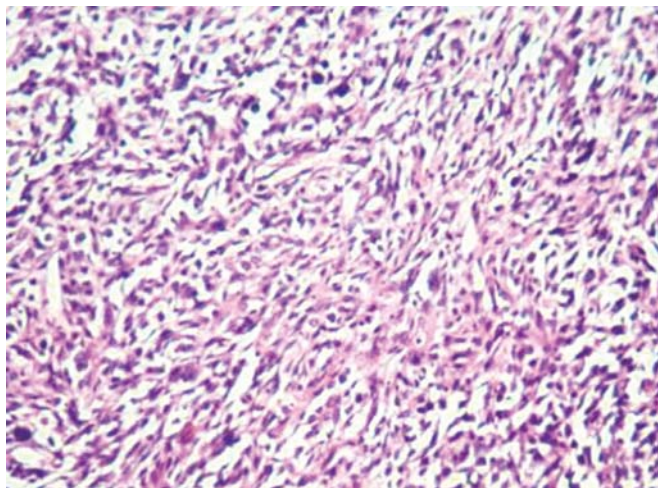


Fig. 7: Histopathology showing spindle-shaped tumor cells s/o sarcoma

He has no other obvious skin ulcerations, swelling.

No history of similar complaints in past, no similar complaints in family members.

On examination: He has severe photophobia, due to severe corneal ulcerations.

Patient had 2 × 3 cm globular, irregular mass on the hard palate, arising from the lingual surface of the incisors to anterior one-third of hard palate. Swelling was nontender, noninflamed, immobile, soft and rubbery.

Investigation Done

Punch biopsy from the swelling confirmed it to be soft tissue sarcoma (Fig. 7).

Dermatology opinion regarding skin pathology was that it was a case of XP.

DISCUSSION

XP is a rare disease. It was first described in 1874 by Hebra and Kaposi in 1882.³ As previously mentioned, its incidence is 1:2,50,000. This disease usually presents with skin malignancies. Oral malignancies though present are very rare. Mostly oral malignancies are restricted to lower lip and tip of tongue, as they are comparatively more sun exposed.⁴ These two patients with XP presented with intraoral malignancies and both had a different histopathological diagnosis; one is consistent with XP while other is not. We had the opportunity to see and analyze these two rare cases in a short interval of time. While deciding upon the management of these patients we came across many obstacles, beginning from the use of imaging, as only CT scan is available in our institute, and the consequences it will have on the sensitive tissues.^{5,6} Postoperative radiotherapy to these patients was even bigger

problem as both the lesions were midline, and both side of the neck needed adequate management.⁷ As expert management for treating such patients are not available in our institute we referred the patients to higher center.

Association between squamous cell carcinoma, basal cell carcinoma, melanoma with XP is proved beyond doubt. But, there are few reports which suggest association between soft tissue sarcoma and XP. For instance, the loss of a single allele of ligase IV was shown to result in sufficiently reduced nonhomologous end-joining (NHEJ) activity to engender chromosomal alterations associated with sarcomas in a murine model.⁸ XPG locus is located on 13q22-33 and it has been reported that, among the various genetic anomalies in synovial sarcomas, loss of the 13q21-31 region is one of the most frequent. Genotyping of the tumor samples revealed indeed a high frequency of LOH for XPG in synovial sarcomas and in myxoid liposarcomas.⁹

There have been researches on the treatment with virus transduction. Retroviral vector (LXPDSN) containing the XPD (ERCC2) cDNA, which fully complements the DNA repair deficiency of primary skin fibroblasts.¹⁰ Similar transduction of viruses carrying mutations of XP, if done in malignant cells would make them extremely sensitive to radiation, even to UV rays. This can be a great boon in the management of cancer patients and also would prevent complications of radiotherapy seen so commonly.

OBJECTIVES

1. Rare case, presenting with inherit challenges for treatment.
2. Line of management is strictly conservative.
3. Genetic engineering is helping with development of the construction of a retroviral vector (LXPDSN) containing the XPD (ERCC2) cDNA, which fully complements the DNA repair deficiency of primary skin fibroblasts.

REFERENCES

1. Cleaver JE. Defective repair replication of DNA in xeroderma pigmentosum. *Nature* 1968 May;218(5142):652-656.
2. Robbins JH, Kraemer KH, Lutzner MA, Festoff BW, Coon HG. Xeroderma pigmentosum, an inherited disease with sun sensitivity, multiple cutaneous neoplasia and abnormal DNA repair. *Ann Inter Med* 1974 Feb;80(2):221-248.
3. von Hebra, FR.; Kaposi, M. On disease of skin including the exanthemata. London: The New Sydenham Society; 1874. 252-258 p.
4. Watkinson, J.; Gilbert, Ralph W. Stell and Maran's textbook of head and neck surgery and oncology. 5th ed. India: CRC Press; 2012. p574.
5. Arlett CF, Plowman PN, Rogers PB, Parris CN, Abbaszadeh F, Green MH, McMillan TJ, Bush C, Foray N, Lehmann AR. Clinical and cellular ionizing radiation sensitivity in a patient

- with xeroderma pigmentosum. *Br J Radiol* 2006 Jun;79(942): 510-517.
6. Arlett CF, Harcourt SA, Lehmann AR, Stevens S, Ferguson-Smith MA, Morley WN. Studies on a new case of xeroderma pigmentosum (XP 3BR) from complementation group G with cellular sensitivity to ionizing radiation. *Carcinogenesis* 1980 Sep;1(9):745-751.
 7. Watkinson, J.; Gilbert, Ralph W. *Stell and Maran's textbook of head and neck surgery and oncology*. 5th ed. India: CRC Press; 2012. p565, 844.
 8. Sharpless NE, Ferguson DO, O'Hagan RC, Castrillon DH, Lee C, Farazi PA, Alson S, Fleming J, Morton CC, Frank K, et al. Impaired nonhomologous end-joining provokes soft tissue sarcomas harboring chromosomal translocations, amplifications, and deletions. *Mol Cell* 2001 Dec;8(6):1187-1196.
 9. Szymanska J, Serra M, Skytting B, Larsson O, Virolainen M, Akerman M, Tarkkanen M, Huuhtanen R, Picci P, Bacchini P, et al. Genetic imbalances in 67 synovial sarcomas evaluated by comparative genomic hybridization. *Genes Chromosomes Cancer* 1998 Nov;23(3):213-219.
 10. Carreau M, Quilliet X, Eveno E, Salvetti A, Danos O, Heard JM, Mezzina M, Sarasin A. Functional retroviral vector for gene therapy of xeroderma pigmentosum group d patients. *Hum Gene Ther* 1995 Oct;6(10):1307-1315.

ABOUT THE AUTHORS

Ankit Dilip Mahuvakar (Corresponding Author)

Resident, Department of ENT, Dr Shankarrao Chavan Government Medical College, Nanded, Maharashtra, India, Phone: 09819782717
e-mail: ankitmahuvakar@gmail.com

Darshan Premdas Meshram

Resident, Department of Pathology, Dr Shankarrao Chavan Government Medical College, Nanded, Maharashtra, India

Shaikh Mohsin Ahmed Abdul Nabi

Resident, Department of ENT, Dr Shankarrao Chavan Government Medical College, Nanded, Maharashtra, India

Vijayalaxmi Kishanrao Ambulgekar

Head, Department of ENT, Dr Shankarrao Chavan Government Medical College, Nanded, Maharashtra, India

Mohammad A Sammer

Associate Professor, Department of Pathology, Dr Shankarrao Chavan Government Medical College, Nanded, Maharashtra, India