

Cutaneous manifestations of Xeroderma Pigmentosum-ten cases

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Abstract

Background: Xeroderma pigmentosa (XP) is rare inherited autosomal recessive disorder. The defect is in DNA repair mechanism which is induced by ultra violet rays. It is characterized by photosensitivity, freckles, telangiectasia, xerosis, actinic keratosis, erythema, lentiginous macules and malignant lesion in sun-exposed areas. The malignancy seen are BCC, SCC and malignant melanoma.

Methods: We report ten cases XP of different age group with dermatological manifestations of varied severity at MGM Medical College and hospital Aurangabad and Sir Aurobindo Medical college institute Indore (MP). This is one of the largest case series we are reporting.

Conclusion: XP patient have shorter life span because of recurrent malignancies. It is important to have proper follow up and evaluation of the patient for early diagnosis and treatment of malignancies. Genetic counseling is important where siblings are affected to prevent further transmission of XP in familial cases.

Keywords: Xeroderma pigmentosa, BCC, SCC, Cutaneous manifestations

Introduction

Xeroderma pigmentosa (XP) is autosomal recessive disorder, caused by defect in nucleotide excision repair (NER) mechanism. Exposure to ultra violet rays is suggested etiology.⁽¹⁾ It was first described by Herba and Kaposi in 1974.⁽¹⁾ Diagnostic clinical features are photosensitivity, abnormal pigmentation, skin atrophy and carcinoma of skin or eye in the form of basal cell carcinoma (BCC), squamous cell carcinoma (SCC) and melanoma.⁽²⁾ There are ten types of XP described on the basis of chromosomal defects.⁽³⁾ Individuals with the disease are often colloquially referred to as Children of the Night. Multiple cutaneous and internal malignancies frequently occur at a young age in XP. Individuals with XP have a one-thousand-fold risk of developing skin cancer than the normal population and manifest before age of twenty years.^(5,6,7,8)

Materials and Method

It is a retrospective observational study of ten cases of xeroderma pigmentosa (XP) with cutaneous and other system involvement. Photosensitivity, pigmentation and skin malignancy were the main

features. Out of ten four were siblings from two families, with history of second degree consanguineous marriage. Age at presentation was between five to twenty-five years, out of which five were males and five were females. All patients have photosensitivity, xerosis, erythema & hypo and hyper pigmentation. (Table 1, 2).

Table 1: Demographic data

Case No	Age in Years	Sex
1	25	Female
2	14	Female
3	13	Male
4	19	Male
5	5	Male
6	8	Female
7	8	Female
8	18	Female
9	5	Male
10	7	Female

Table 2: Cutaneous manifestation of XP

Symptoms	Patient									
	1	2	3	4	5	6	7	8	9	10
Photosensitivity	+	+	+	+	+	+	+	+	+	+
Erythema	+	+	+	+	+	+	+	+	+	+
Xerosis	+	+	+	+	+	+	+	+	+	+
Telangiectasia	-	+	-	+	-	-	+	+	+	+
Poikiloderma	+	+	+	+	-	-	+	+	+	+
Mottled Pigmentation	+	+	+	+	+	+	+	+	+	+

Freckles	+	+	+	+	-	-	+	+	+	+
Premature graying of hair	-	-	-	-	-	-	-	-	-	-
Alopecia	-	-	-	-	-	-	-	-	-	+
Skin Atrophy	+	-	-	+	-	-	+	+	+	+
Ocular involvement	+	+	+	+	-	-	+	+	+	+
Photophobia	+	+	+	+	+	+	+	+	+	+
BCC	-	-	+	+	-	-	+	-	+	+
SCC	-	-	-	+	-	-	+	-	+	-
malignant melanoma	-	-	-	+	-	-	-	-	-	-

The additional clinical manifestations and unique features are mentioned below.

Case 1: Is female of age twenty-five years with minimal dermatological manifestations amongst ten cases may be because of wearing burkha so she was protected from sun exposure.

Case 3: Malignant melanoma at limbus along.

Case 8: Crusting oozing from the scalp lesion, patchy cicatricial alopecia, erosion.

Case 9: Severely affected child among all cases. Extensive nodules on nose and malar area. Biopsy showed basi-squamous malignancy. Right side scalp showing large ulcerative lesion with destruction of bony tissue and exposing brain matter.

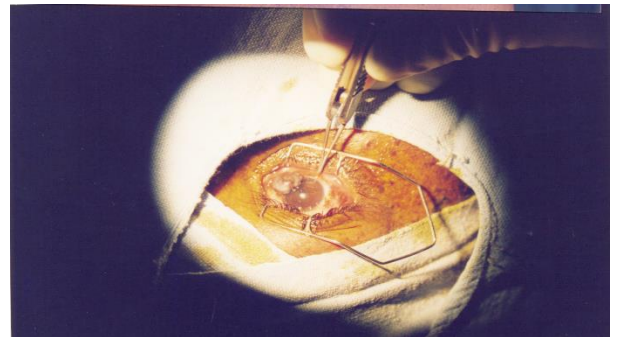


Fig. 3: Malignant melanoma at limbus



Fig. 1: Minimal dermatological manifestations



Fig. 4: Invasive BCC



Fig. 2: Ocular manifestations



Fig. 5: Extensive nodular lesions



Fig. 6: Ulcer eroding bone

Discussion

Xeroderma pigmentosa is an autosomal recessive disorder caused by defects in normal repair of DNA of various cutaneous damage by exposure to sunlight.^(6,9,10) In our case study, there were five males and five females of age group five to twenty-five years. Male to female ratio in our study is equal which corresponds with case series reports by Sankha Khaoly and Arun Kumar.^(1,2) Over all worldwide incidences is one to four percent per million and more common where consanguineous marriage is seen. We report similar incidence in two families with history of consanguineous marriage & four siblings affected.

In patients with XP at birth, the skin appears normal. Onset of the disease usually begins at around six months and generally progresses through three stages.⁽⁴⁾

Stage one: Is usually demonstrated by about six months with the following signs: Areas exposed to the sun show.

Stage two: Presented as poikiloderma, which is a result of an accumulation of actinic changes. Often it appears at the median age of two and is characterized by the following: Solar lentigines, Skin atrophy and thinning, telangiectasia, patches of hypo pigmentation and hyper pigmentation.

Stage three: as the development of actinic keratoses and skin cancer. This stage may occur as early as four to five years or as late as adolescence

In our study all patients had classical skin lesions freckles, telangiectasia, poikiloderma, xerosis, actinic keratosis, acute burning under minimal sun exposure, erythema.

There are ten different variants of XP resulting from defects in different change depending on DNA defects they are classified as A to I and tenth XP variant.^(6,9,11,12,13) The defect in DNA repair is either due to deficient in nucleotide excision repair or defective post replication repair.⁽¹⁴⁾ These defect in DNA repair causes deficiency of fibroblast to repair UV induced damage. This intern leads to cutaneous manifestation of XP.^(6,15,16,17)

Other systemic involvement is mainly ocular and neurological. Ocular manifestations in our patient were- all the patients were having photophobia, two patients had SCC and one patient had malignant melanoma.

Neurological manifestations are around thirty to forty percent of the patients.^(6,18) Neurological abnormalities are may be mental retardation, spasticity, seizures, abnormal speech hyporeflexia.^(19,6,18) The most severe form is known as Desanctis – cacchione syndrome which is group A XP. In our study only one patient i.e. ten percent had neurological involvement in the form of malignancy.

Skin cancers are more prevalent in sun exposed areas of skin such as the face, neck and forearms. Individuals with XP have a one-thousand-fold risk of developing skin cancer than the normal population and manifest before age of twenty years.^(5,6,7,8) There is also a ten to twenty-fold increase in the likelihood of developing cancer or tumour's affecting internal organs. In our study five patients had BCC, three patients had SCC and one patient had malignant melanoma. One patient had invasive malignancy in brain.

Management

Mainly prevent measures to minimize skin and eye damage. Strict sun protection. Regular screening of the patients for early diagnosis and management of malignancies.

Conclusion

XP patient have shorter life span because of recurrent malignancies. It is important to have proper follow up and evaluation of the patient for early diagnosis and treatment of malignancies. Genetic counseling is important where siblings are affected to prevent further transmission of XP in familial cases.

References

1. Sankha khaoly, Sanjiv V. Choudhari, Soumen Choudhari, Shilpi sharma et. al 2012. Xeroderma pigmentosum: report of two cases and review of the literature. Journal of Pakistan association of dermatologist.
2. Arun kumar S. Bilodi and M.R. Gangadhar 2013 xeroderma pigmentosa-a rare clinical entity. Indian Journal of medical case Reports 2013;2(1);January-March.
3. Jeffrey freedman 1977. Xeroderma pigmentosum and band – shaped nodular corneal dystrophy. British journal of ophthalmology.
4. Fitzpatrick book for general medicin third edition page no 1794.
5. Halpern, J.; Hopping, B.; Brostoff, J. 2008. "Photosensitivity, corneal scarring and developmental delay: Xeroderma Pigmentosum in a tropical country".
6. Kraemer KH. In: Xeroderma Pigmentosum. Pagon RA, Bird TC, Dolan CR, Stephens K, editors. Seattle, WA: University of Washington, Seattle; 2008. Gene Reviews.

7. Levin PS, Green WR, Victor DI, MacLean AL. Histopathology of the eye in Cockayne's syndrome. *Arch Ophthalmol.* 1983; 101:1093–1097.
8. Sevel D. Xeroderma Pigmentosum with Ocular Complications. *Br J Ophthalmol.* 1963;47.
9. Duke-Elder S. St. Louis: C V Mosby; 1974.
10. Giller H, Kaufmann WC. Ocular lesions in xeroderma pigmentosum; a case report of carcinoma of the cornea. *AMA Arch Ophthalmol.* 1959;62:130–133.
11. Cleaver JE. Defective repair replication of DNA in xeroderma pigmentosum. *Nature.* 1968;218:652–656.
12. El-Hefnawi H, Mortada A. ocular manifestations of xeroderma pigmentosum. *Br J Dermatol.* 1965;77:261–276.
13. Fitzpetricz book for general medicin page no 1794.
14. Mehta C, Gupta CN, Krishnaswamy M. Malignant melanoma of conjunctiva with xeroderma pigmentosa--a case report. *Indian J Ophthalmol.* 1996;44:165–166.
15. Kraemer KH, Patronas NJ, Schiffmann R, et al. Xeroderma pigmentosum, trichothiodystrophy and Cockayne syndrome: a complex genotype-phenotype relationship. *Neuroscience.* 2007;145:1388–1396.
16. Limawararut V, Leibovitch I, Sullivan T, Selva D. Periocular squamous cell carcinoma. *Clin Experiment Ophthalmol.* 2007;35:174–185.
17. Lindenbaum Y, Dickson D, Rosenbaum P, et al. Xeroderma pigmentosum/cockayne syndrome complex: first neuropathological study and review of eight other cases. *Eur J Paediatr Neurol.* 2001;5:225–242.
18. McKinnon PJ. DNA repair deficiency and neurological disease. *Nat Rev Neurosci.* 2009;10:100–112.
19. Kleijer WJ, Laugel V, Berneburg M, et al. Incidence of DNA repair deficiency disorders in western Europe: Xeroderma pigmentosum, Cockayne syndrome and trichothiodystrophy. *DNA Repair (Amst)* 2008;7:744–750.