Journal of Pathology of Nepal (2013) Vol. **3**, 472 -475

Journal of
PATHOLOGY
of Nepal

www.acpnepal.com

Original Article

Myrid of histopathological features of malignancy in Xeroderma pigmentosum

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Keywords:

Basal cell carcinoma;
Squamous cell carcinoma;
Xeroderma Pigmentosum

ABSTRACT

Background: Xeroderma pigmentosum is a rare autosomal recessively inherited disorder affecting 1 in 2,50,000 population. It shows genetic heterogeneity with at least ten different complementation groups identified which have different clinical presentations. They tend to have a more than 1000 fold increased risk of developing cancers in sun-exposed areas as a result of a DNA repair defect. This study presents a myriad of histopathological features of malignancies seen in individuals with this rare.

Materials and Methods: Biopsies received from patients with a clinical diagnosis of Xeroderma Pigemntosa at the department of pathology, Institute of Medicine, Tribhuvan University Teaching Hospital, Kathmandu, from April 2008 to June 2012 were included in the study. Hematoxylin and eosin stained sections were examined. Clinical history was retrieved from the computer data base of the department.

Results: During the study period, a total of eleven cases of Xeroderma pigmentosum presented with a biopsied lesion. All of these were malignant lesions. No benign lesions were seen. The age range of these patients was 6-30years with a mean of 18.8 years. The male to female ratio was 4.5:1. The most common malignancy seen was squamous cell carcinoma 7/11 (63.6%) followed by basal cell carcinoma 2/11 (27.2%). A single case presented with basal cell carcinoma of face and melanoma of trunk. The frequently observed site of malignancy was skin of the face followed by conjunctiva.

Conclusion: In our population, non melanotic skin cancers affecting the face are more common in young individuals with Xeroderma pigmentosum.

INTRODUCTION

Xeroderma pigmentosum (XP) is a rare autosomal recessively inherited disorder affecting 1 in 2,50,000 population.[1] It shows genetic heterogeneity with at least ten different complementation groups identified which have different clinical presentations.[2] They tend to have a more than 1000 fold increased risk of developing cancers in sun-exposed areas as a result of a DNA repair defect.[3-5] This study presents a myriad of histopathological features of malignancies seen in individuals with this rare disease in our experience.

MATERIALS AND METHODS

Biopsies of patients received at the Department of Pathology, Institue of Medicine, Maharajgunj,TUTH, with clinical diagnosis of Xeroderma Pigmentosum presenting between April 2008 to June 2012 were included in the

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Table 1: Clinicopathological features of patients with malignancies in Xeroderma Pigmentosum

S. N	Age	Sex	Site	Diagnosis
1	21	M	Face	BCC*
2	20	M	Face	SCC**
3	22	M	Face	SCC
4	14	F	Conjunctiva	SCC
5	20	M	Face/trunk	BCC and Melanoma
6	20	M	Face	BCC
7	6	M	Face	SCC
8	18	M	Face	SCC
9	17	M	Conjunctiva	SCC
10	28	F	Face	SCC
11	21	M	Face	BCC

* - Basal Cell Carcinoma, ** - Squamous Cell Carcinoma

study. Hematoxylin and eosin (HE) stained sections were examined. Clinical history was retrieved from the computer data base of the department and analyzed.

RESULTS

During the study period, a total of eleven cases of Xeroderma pigmentosum presented with a biopsied lesion. All of these were malignant lesions. The age range of these patients was 6-30 years with a mean of 18.8 years. The male to female ratio was 4.5:1. The most common malignancy seen was squamous cell carcinoma (n=7/11; 63.6%) followed by basal cell carcinoma (n= 2/11; 27.2%). A single case presented with basal cell carcinoma of face and melanoma of trunk. The frequently observed site of malignancy was skin of the face followed by conjunctiva. Details of the patients are presented in Table 1.

DISCUSSION

In 1968, Cleaver first reported that skin cells of patients with XP have an impaired ability to repair DNA damage induced by UV radiation.[6] Defective repair replication was later reported in dermal fibroblasts, lymphocytes in peripheral blood and conjunctival cells.[7] Pyrimidine-pyrimidine dimers of two juxtaposed thymidines are created by exposure to UV radiation. Normal DNA replication can subsequently take place only if such dimers are excised and the DNA strand repaired by the series of enzymatic reactions.[8] Repair is either by excision or photoactivation.[9] Cells cultured from patients with XP have low activity for photoreactivation[9] and DNA excision process is complex in Xeroderma Pigmentosum. Owing to impaired ability to repair, damaged DNA is retained which leads to heritable chromosomal mutations and cell death which possibly cause neoplastic and atrophic clinical abnormalities in XP.[10] Kraemer KH et al reported malignant skin cancers in 45% of XP patients[5] and Goyal JL et al observed these malignant changes in 60% of their patients.[10]

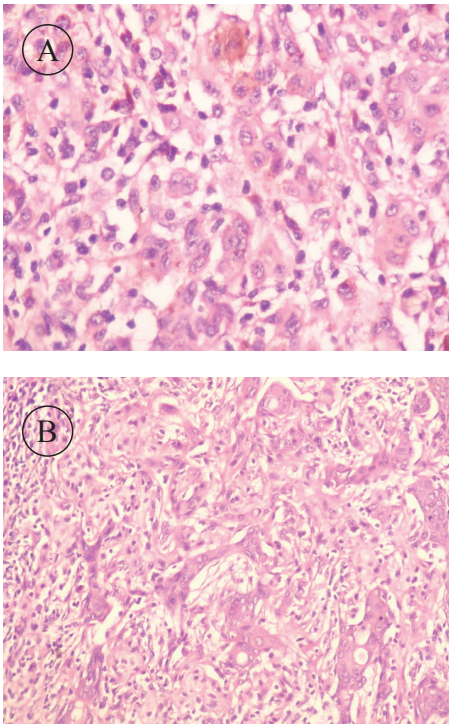

Figure 1: *Focus of melanoma (A) and basal cell carcinoma (B) in 20years-old male (HE Stain, X200).*

In the present study, the clinical age of presentation with malignancy was 6 to 30 years with mean age of 18.8 years. According to a study carried out in Pakistan, those with XP who developed cutaneous malignancies were young, between the ages of 3.5 – 14 years (mean 9.8 years).[11] The early mean age of presentation for malignancy in their study could be due to the fact that their study was carried out in Larkarna, Pakistan, where the temperature is extremely hot going up to 53°C. Xeroderma Pigmentosum patients are thought to have a close relationship to latitude and weather with respect to developing skin lesions.[12,13]

M: F ratio was 4.5:1 with a male predominance. A male predominance was seen in a study carried out by Goyal JL et al.[10] A history of consanguinity was seen in 4/10 cases of XP in their study.[10] Similarly, a history of consanguineous marriage within two generations was found in 19/26 cases of XP patients in a study carried out in Japan.[14] However, a similar history could not be found in any patients in this series of study.

A positive family history was available only in two of the cases, while family history couldn't be elicited in others as this was a retrospective study. A positive family history was found in 6/10 cases in a study by Goyal JL et al.[10]

In this study, the most common malignancy seen was squamous cell carcinoma (n=7; 63.6%) followed by basal cell carcinoma (n=3; 27.2%). Commonest site for developing these malignancies was face (n=8; 72.7%) followed by conjunctiva (n=2; 18.1%). In another study, the

most common malignancy was squamous cell carcinoma developing on exposed parts of the body i.e. head, neck, face and ears.[11]

A single case of 20 year-old male presented with basal cell carcinoma of face and melanoma of trunk (fig.1). Similarly, multiple cutaneous malignancies were reported in an individual with XP in a study by Mohanty P et al.[15] This patient developed squamous cell carcinoma of conjunctiva, basal cell carcinoma of nose and malignant melanoma of cheek.[15]

The incidence of internal malignancy is said to be 10-20 times higher in patients with XP than in normal individuals.[16] None of these patients had internal malignancy in our study. Similar result was seen in a study by Bhutto AM et al[11] and Goyal JL et al.[10] However, Goyal JL et al found a single case (1/10) of carcinoma tongue in their series of patients.[10] From 40 years literature Cairns J et al[17] could find only seven reports of internal neoplasms in XP patients; other cases have also been cited.[18] The absence of internal malignancies during a follow up of 192.8 person – year in one study, whilst numerous skin cancers occurred, indicates that the risk of internal malignancy in XP is lower than the risk of skin cancer.[19]

Only one case of malignant melanoma was seen in this series of cases (fig.1). In a study by English JSC et al[19] 3/32 patients with XP presented with malignant melanoma whereas it was seen in 1/10 cases in a study by Goyal JL et al.[10] In all these studies malignant melanoma was less commonly seen in patients with Xeroderma pigmentosum than non-melanoma skin cancers. This is in accordance with the findings of Bradford et al who noted > 10,000 fold increased risk of non-melanoma skin cancer and > 2000 fold increased risk of melanoma in patients with Xeroderma Pigmentosum.[20]

Though no benign skin lesions were seen in association with XP in this series, other authors have reported benign neoplasms like pilomatricoma in association with Xeroderma Pigmentosum.[21]

The second most common organ involved in XP is the eyes.[11] Ocular neoplasms and other abnormalities are usually limited to the conjunctiva, cornea and eyelids. Two cases (18.1%) of ocular malignancy were seen in this study. Kraemer KH et al[4] have reported 11% of cases as having ocular malignancies while Goyal JL et al reported 20% of cases of ocular malignancy.[10] However no ocular malignancies were seen in another study.[11]

The patients in this study were lost to follow-up. Other studies have found that mortality was high in XP, but from mental and neurological deterioration rather than from actinic tumors.[19] Kraemer KH et al reported a 70% probability of survival attainable at the age of 40, a 28 year reduction in comparision with the US general population.[5]

CONCLUSION

Non melanotic skin cancers affecting the face are more common in young individuals with Xeroderma pigmentosum in our population.

REFERENCES

1. Robbins JH, Kraemer KH, Lutzner MA, Festoff BW, Coon HG. Xeroderma Pigmentosum. An inherited disease with sun sensitivity, multiple cutaneous neoplasms and abnormal DNA repair. Ann Intern Med 1974;80:221-48.
2. Strutton G, Stenn KS. Tumors of cutaneous appendages. In: Symmers W. STC, Weedon D, editors. Systemic Pathology. The Skin. 1st ed. Churchill Livingstone; 1992:pp827-8.
3. Lambert WC, Kuo HR, Lambert MW. Xeroderma Pigmentosum. Dermatol Clin 1995;13:169-209.
4. Kraemer KH, Lee MM, Andrews AD, Lambert WC. The role of sunlight and DNA repair in melanoma and non-melanoma skin cancer. The Xeroderma Pigmentosum paradigm. Arch Dermatol 1994;130:1018-21.
5. Kraemer KH, Lee MM, Scotto J. Xeroderma Pigmentosum: cutaneous, ocular and neurological abnormalities in 830 published cases. Arch Dermatol 1987;123:241-50.
6. Cleaver JE. Defective repair replication of DNA in XP. Nature 1968;218:652-56.
7. Newsome DA, Kraemer KH, Robbins JH. Repair of DNA in Xeroderma Pigmentosum conjunctiva. Arch Opthalmol 1975;93:660-2.
8. Watson JD. Molecular biology of the gene. 3rd ed. Menlo Park, CA: Benjamin Cummings,1976;pp244-5.
9. Murray RK, Granner DK, Mayer PA, Rodwell VW. DNA organization and replications: In: Harper's biochemistry 25th ed. Norwalk,CA: Applenton and Lange,1988;401-2.
10. Goyal JL, Rao VA, Srinivasan R, Agrawal K. Oculocutaneous manifestations in Xeroderma Pigmentosum. Br J Opthalmo1994;78:295-7.
11. Bhutto AM, Shaikh A, Nonaka S. Incidence of Xeroderma Pigmentosum in Larkana, Pakistan: a 7 year study. Br J Dermatol 2005;152:545-51.
12. Cleaver JE, Carter DM. Xeroderma Pigmentosum variants: influence of temperature on DNA repair. J Invest Dermatol 1973;60:29-32.
13. Tekebe H, Nishigori C, Satoh Y. Genetics and skin cancer of Xeroderma Pigmentosum in Japan. Jpn J Cancer Res (Gann) 1987;78:1135-43.
14. Kato T, Akiba H, Seiji M, Tohda H, Oikawa A. Clinical and biological studies of 26 cases of Xeroderma Pigmentosum in Northeast district of Japan. Arch Dermatol Res 1985;277:1-7.
15. Mohanty P, Mohanty L, Devi BP. Multiple cutaneous malignancies in Xeroderma Pigmentosum. Indian J Dermatol Venereol Leprol 2001;67;96-7.
16. Robbins JH. Xeroderma Pigmentosum: defective DNA repair causes skin cancer and neurodegeneration. JAMA 1988;260:384-8.
17. Cairns J. The origin of human cancers. Nature 1981;289:353-7.
18. Cleaver JE: DNA repair deficiencies. In: Progress in diseases of the skin (Fleischmajer R, ed.) vol 2. Orlando: Grune and Stratton,1984. pp53-67.
19. English JSC, Swerollow AJ. The risk of malignant melanoma,

internal malignancy and mortality in Xeroderma Pigmentosum patients. Br J dermatol 1987;117:457-61.

20. Bradford PT, Goldstein AM, Tamura D et al. Cancer and neurological degeneration in Xeroderma Pigmentosum: long term folloe-up characterizes the role of DNA repair. J Med Genet 2011;48:168-76.

21. Patil MR, Vishwanath V, Arya M, Shenoy BP, Bharmel RN, Torsekar RG. Pilomatricoma in a case of familial Xeroderma Pigmentosum. Indian J Dermatol Venereol Leprol 2007;73:198-9.