Case Report

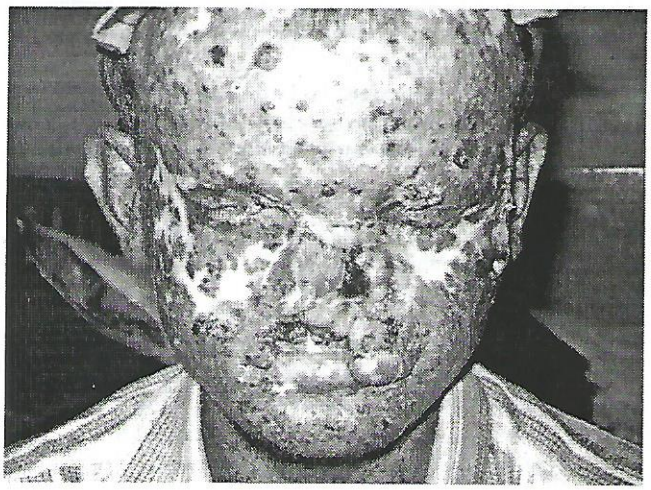
Xeroderma Pigmentosum

M A GHAZI A MAQSOOD Y AKRAM *M A CHEEMA*
Department of Surgery, Mayo Hospital, Lahore
Correspondence to Dr. Muhammad Ahmad Ghazi E-mail: ghazeema@yahoo.com

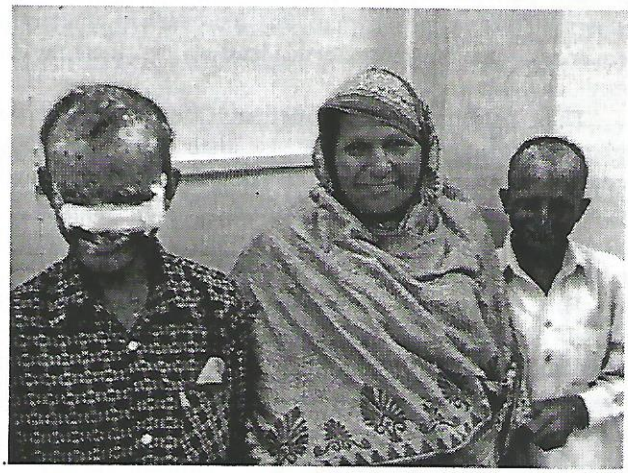
Xeroderma pigmentosum comprises of a heterogeneous group of autosomal recessive hereditary diseases, which are characterized by a number of clinical characteristics and abnormal DNA repair mechanism. These patients are prone to multiple cutaneous malignancies at an early stage in life. We present 2 cases of xeoderma pigmentosum with malignant melanoma and conclude that such cases must be identified at an early stage and properly educated to protect themselves from malignancies.
Key words: Xeroderma pigmentosum, melanoma.

Case report

A 17 year old boy was referred to surgical unit of Mayo hospital by a general practitioner for the treatment of multiple ulcers which he had developed over a period of 4 years on his head, face and tongue. He developed crusting and scaling of skin at the age of 4 years which was progressive .His eye sight started worsening at the age of 7 years and now his vision is reduced to hand movements only. He developed a lesion on his tongue 4 years ago which was biopsed but he did not have its histopathological report .On presentation he had photophobia, crusting, scaling along with multiple areas of keratosis, hyper pigmentation and hypopigmentation all over the body .Whole of the face was disfigured by the gnawing lesions. He had an ulcer involving his nose and philtrum .It had irregular margins and rough surface. Another ulcer was present in the preauricular region with irregular margins and everted edges. An ulcerated growth involving the lateral canthus of left eye and zygoma was present which had red surface, exuberant growth and irregular edges. An ulcer was present on the skull vertex with similar characters. Examination of eyes showed chronic conjunctivitis, blephritis and keratitis. These were managed medically.



Skin biopsy was done from the edges of the ulcers .Fortunately only one ulcer involving the nose, philtrum and upper lip turned out to be malignant melanoma. Rest of the ulcers showed chronic inflammation. The lesion was adequately excised with 1 cm resection of margins around the lesion. On 1 month follow up lesion showed healthy granulation tissue with clear margins. He was advised to avoid sun light exposure .His younger brother 13 years old who also had Xeroderma pigmentosum was properly screened for the cutaneous tumors and advised to avoid ultraviolet rays exposure. Both brothers are on regular follow up in out patient department of surgery at Mayo Hospital, Lahore



Discussion:

Xeroderma pigmentosa is inherited as an autosomal recessive trait. Those affected are extremely sensitive to the ultraviolet portion of sunlight. Ultraviolet light exposure damages DNA (the genetic material within a cell) in skin cells.

Normally, peoples' bodies can repair this damage. However, people with xeroderma pigmentosa cannot repair the damaged DNA and rapidly develop skin atrophy (thinning), splotchy pigmentation, spidery blood vessels in the skin (telangiectasia), oozing from raw skin surfaces and skin cancers. Eye signs may include clouding of

cornea, keratitis, lid tumors and blephritis.Neurological changes are occasionally seen. There may or may not be a family history of Xeroderma pigmentosa but all family members must be examined.

Diagnosis before birth can be made by:

Amniocentesis

Chorionic villous sampling and amniotic cell cultures

Diagnosis after birth includes:

Skin fibroblasts culture

Skin biopsy

Common **complications** include disfigurements and cutaneous malignancies such as basal cell carcinoma, squamous cell carcinoma and malignant melanoma.

Pathophyiology: These individuals posses cells that are defective in the excision repair of UV-induced pyrimidine dimers from their DNA. This defect was correlated with hyper-mutability, when XP cells were exposed to ultra violet radiations (UV). This was the suggested hypothesis of early increase in sunlight-induced cancers.Another hypothesis shows that the crucial effect of sunlight which led to the early appearance of skin cancers was not the excessive induction of mutations but the exacerbation by UV of a defect in immune surveillance which resulted in existing transformed cells being able to grow and express their malignant pheno-type. Cells of a patient with Cockayne syndrome were also hyper-mutable by UV[1] and yet such patients were not known to be prone to skin cancers. This suggests that an increase in mutation frequency does not necessarily lead to an increase in cancer.

Thus light-exposed XP patients are susceptible to higher risk of skin cancer because their defect in DNA repair results in an increased frequency of initiated (mutated) skin cells which are able to grow into tumorous colonies early in life, probably because of failure of the immune system to restrict their growth.

This failure may be two-fold: a constitutive defect (probably in NK cell func-tion) exacerbated by a UV-dependent impair-ment (probably of cell-mediated immunity and possibly also of residual natural killer cell function)[3]..

The (presumed constitutive) immune defect in natural killer cell function present in classic XP patients may also be due to a further independently mutated gene, and this may also exist in individuals independently of the DNA repair defect. Such individuals might also be at some increased risk of skin cancer, but this would probably be expressed as single rather than multiple neoplasms (since the mutation frequency would be normal), and the skin cancers might appear earlier than in no Mutations, once formed, could persist in stem cells for a very long time. Ultraviolet light may also impair immune surveillance. The combination of these two effects would produce a response which causes acute exposures to be more effective than chronic. To avoid early skin cancer the advice must therefore be to avoid high peak exposures. since these should dominate the risk assessment. In contrast, for cancers appearing in later years as the immune system loses it's effectiveness, the total lifetime cumulative exposure would be expected to be rela- tively more important, although the effect of peak exposure might still be most important.

Educating the patient of xeroderma pigmentosum is vital to improve the quality of life and incresed survival by avoiding malignancies. A few useful tips to the patients may include avoiding sunlight exposure by wearing caps and using umbrellas,using sunscreens and specific SPF clothing and sunglasses.Avoiding charboiled (blackened) food items (added to EPA list of known carcinogens). Routine medical examinations i.e. skin examination every 3 to 6 months and eye and neurological examination anually is recommended.

Conclusion:

Although a rare but important clinical entity –xeroderma pigmentosum, is to be diagnosed at earlier stages so that malignancies and early deaths can be avoided.

References:

1. A.R.Nalgirkar, S.S. Borkar, S.A. Nalgirkar, Xeroderma pigmentosum with multiple malignacies Indian Pediatrics 2000;37: 1377-1379
2. Arlett CF. Mutagenesis in repair-deficient human cell strains. In: Progress in Environ-mental Mutagenesis. Ed. Alacevic M. Amsterdam, Elsevier, 1980; pp 161-174
3. Morison WL, Bucana C, Hashem N, Kripke ML, Cleaver JE, German JL. Impaired immune function in patients with xeroderma pigmentosum. Cancer Res 1985; 45: 3929-3931.
4. Mehta C, Gupta CN, Krishnaswamy M. Malignant melanoma of conjunctiva with xeroderma pigmentosa--a case report. Indian J Ophthalmol. 1996 Sep; 44(3):165-6.
5. Tullis GD, Lynde CW, McLean DI, Stewart WD. Multiple melanomas occurring in a patient with xeroderma pigmentosum. : J Am Acad Dermatol. 1984 Aug; 11(2 Pt 2):364-7
6. Masinjila H, Arnbjornsson E. Two children with xeroderma pigmentosum developing two different types of malignancies simultaneously Pediatr Surg Int. 1998 Apr; 13(4):299-300.
7. El-Hayek M, Lestringant GG, Frossard PM. Xeroderma pigmentosum in four siblings with three different types of malignancies simultaneously in one. : J Pediatr Hematol Oncol. 2004 Aug; 26(8):473-5.
8. Aoyagi M, Morishima N, Yoshino Y, Imagawa N, Kiyosawa M, Ito M, Kondou S, Matsubara O. Conjunctival malignant melanoma with xeroderma pigmentosum. : Ophthalmologica. 1993; 206(3):162-7.