Case Report

Basosquamous Carcinoma in Xeroderma Pigmentosum - A Unusual Case Report

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ABSTRACT

Xeroderma pigmentosum (XP), meaning parchment skin and pigmentary disturbance, is a rare and mostly autosomal recessive genetic disorder. The frequency of this disease in the general population of the U.S.A. is 1:250,000.

We hereby report a case of 3 siblings affected by xeroderma pigmentosum, with one manifesting as unusual skin malignanacy- basosquamous carcinoma. Which has been rarely reported previously.

Introduction -

Xeroderma pigmentosum (XP), meaning parchment skin and pigmentary disturbance, is a rare and mostly autosomal recessive genetic disorder that was originally named by two dermatologists, the Austrian Ferdinand Ritter von Hebra and his Hungarian son-in-law Moritz Kaposi in 1874 and 1883. XP is an autosomal recessive disorder with 100% penetrance and can result from mutation in any one of eight genes. The manifestation of tumors in siblings is very disheartening. Undoubtedly, this entails an enormous surgical problem since the occurrence of deep-seated malignant lesions may not be amenable to adequate ablative intervention. The frequency of this disease in the general population of the U.S.A. is 1:250,000. Notably, it is much higher in Japan and other countries. Frequent reports have emanated from other countries including Europe, Egypt, Israel, Korea, China, India and Pakistan.[1,2]

We hereby report a case of 3 siblings affected by xeroderma pigmentosum, with one manifesting as unusual skin malignanacy-basosquamous carcinoma. Which has been rarely reported previously.

Case report -

A 15 year old male, 4th order child, born out of non consanguineous marriage, presented to the Gujarat cancer and research institute, with the chief complaints of generalized skin lesions in the sun exposed area since the age of 2 years. Patient also complained of photosensitivity and watery discharge since the age of 2 years, gradually developed nodular lesion over the face, since last one and half months that progressed in the form of multiple nodular and ulcerative lesion. He also had a history of two to three episodes of simple focal seizures since last one and half years.

He denied history of any visual disturbance in the form of floaters, any blurring of vision, & no history suggestive of any mucosal involvement. There was no history of any skin surgery in the past. Hairs and nails were normal&no any skeletal abnormality.

Family history is suggestive of 3 out of 4 siblings affected with xeroderma pigmentosum, eldest son is not affected, 2nd order daughter had xeroderma pigmentosum and had a cauliflower like neck mass, biopsy was suggestive of hyperkeratosis, acanthosis of epidermis of the skin. She died of her ailment.

On examination of the lesion, multiple ulceronodular mass seen on the face, largest one was 4 cm long and 5 cm broad, ulceroproliferative growth, hypopigmented, with irregular border, pearly ulcer, with rolled out margin. Depth of ulcer is upto mucosa, tender, and bleeding. Ulcer is fixed to the surrounding skin and ulcer base is necrotic, fixed to the underlying bone. Multiple keratoacanthomatous lesion seen over chest and trunk.

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Fig. 1

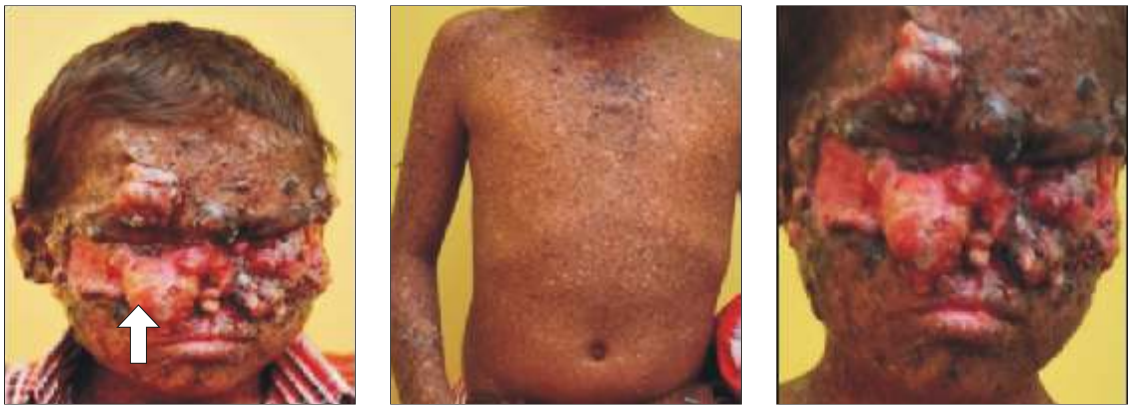

Fig. 2

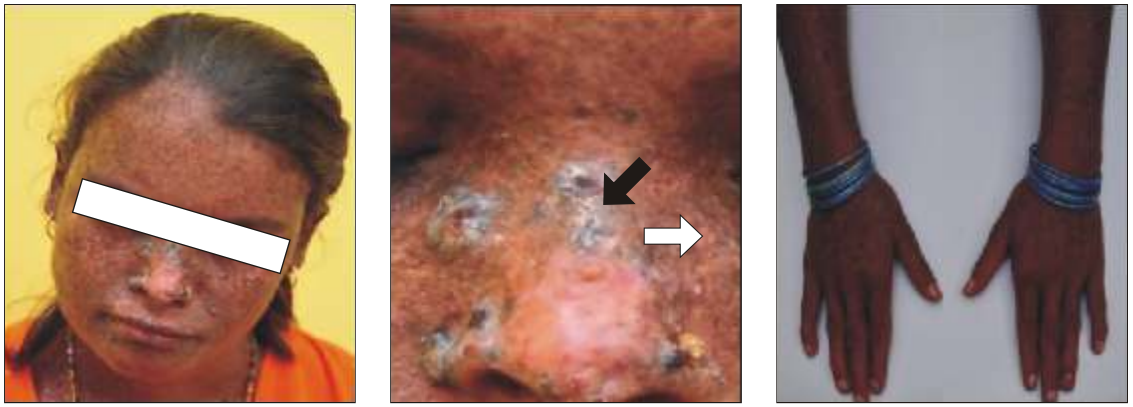

Fig.1 : Proband showing the lesion on right side of face, with multiple nodular, ephilides, and keratoacanthomatous lesion. Basosquamous carcinoma (white arrow) showing rolled out margin,and hypopigmentation.

3rd child is a daughter with xeroderma pigmentosum with freckles all over the face and one ulcerative lesion above the nasal ala. She developed the lesions since the age of 2 years, she also gradually developed photosensitivity. Her neurological examination is normal.

Fig 2 : Elder Sister of proband (3rd child) : fig showing ulcerative lesion at the inner canthus and above the nasal ala, with necrotic base (white arrow), and rolled out margin (black arrow)

Biopsy of the lesion was suggestive of basosquamous carcinoma. Slides showed islands of cells with peripheral basaloid cells and central squamous differentiation. 40x HE view shows, Island of cells with peripheral palisading of basaloid cells. The cells in the central zone showing transition to squamous differentiation. The cells are large with abundant eosinophilic cytoplasm and nuclei showing prominent nucleoli.

Discussion -

No consistent routine laboratory abnormalities are present in XP. There is no specific histology of Xeroderma pigmentosum.[3] While babies are normal at birth, in the first years of life, diffuse erythema, scaling and pronounced freckle-like pigmentation develop. The incidence of tumors is about 1000-fold increased as compared with the normal population. The mean patient age of developing skin cancer is 8 years in XP patients and for the onset of actinic damage around 1-2 years of age.[4]

Fig. 3

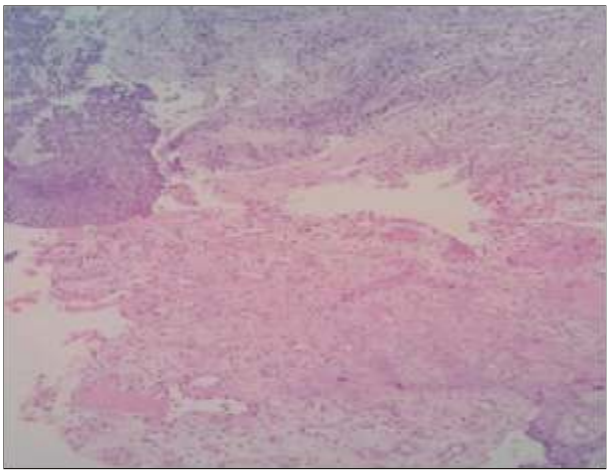

Fig. 3 : Basosquamous carcinoma (10X-HE) - squamous cells are seen singly as well as in small nests along with numerous keratin pearls. Also seen is the island of cells with peripheral basaloid cells and central cells with squamous differentiation (upper left)

Fig. 4

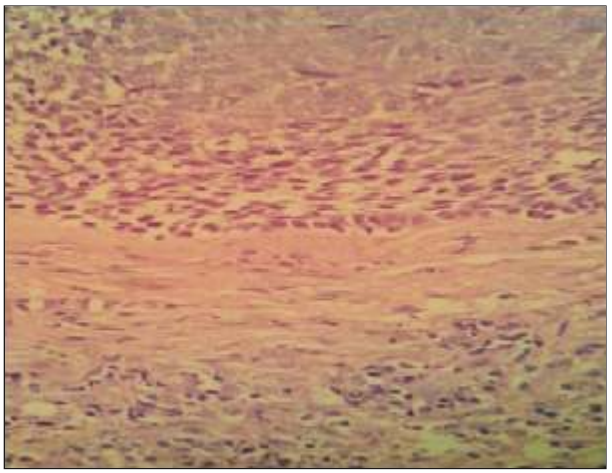

Fig. 4 : Basosquamous carcinoma (40X-HE) - Island of cells with peripheral palisading of basaloid cells. The cells in the central zone showing transition to squamous differentiation. The cells are large with abundant eosinophilic cytoplasm and nuclei showing prominent nucleoli.

Clinical hallmarks of xeroderma pigmentosum

- Severe photosensitivity (painful sunburns in early childhood)
- Poikiloderma
- Dryness (xerosis)
- Premature skin aging
- Malignant tumors (squamous cell cancers, basal cell cancers and melanoma), most often on face, head and neck

Complementation groups were defined and assumed to represent mutations in different genes.The number of complementation groups in XP eventually settled down to 8, A through G and V.3

Characteristics of xeroderma pigmentosum complementation groups

Complementation group	Frequency (%)	Skin cancer	Neurological involvement	Ophthalmological involvement	Gene defect
A	30	+	+++	+	XPA
B	0.5	+	+	+	XPB/ERCC3
C	27	+	-	+	XPC
D	15	+	+++	+	XPD/ERCC2
E	1	+	-	+	DDB2/XPE/p48
F	2	+	-	+	XPF/ERCC4
G	1	+	+	+	XPG/ERCC5
Variant	23.5	+	-	+	XPV/hRAD30

Differential diagnosis : Xeroderma pigmentosum is differentiated from Cockayne syndrome by the absence of cataract and skeletal dysplasia.

Differential diagnoses	
Cockayne syndrome	Hydroa vacciniforme
Trichothiodystrophy	LEOPARD syndrome
Epithelids	Hartnup disease
ubacute cutaneous lupus erythematosus	Rothmund Thomson syndrome
Basal cell nevus syndrome	Progeria
Erythropoetic porphyria	Bloom syndrome

Unfortunately our patient lost follow up, while on treatment for this disease.

Non melanomatous skin cancers in Xeroderma pigmentosum -

The hypersensitivity of DNA repair deficient xeroderma pigmentosum (XP) patients to solar irradiation results in the development of high levels of squamous and basal cell carcinomas as well as malignant melanomas in early childhood. A predisposition to skin cancers is the cardinal feature of xeroderma pigmentosum (XP) and is the grave phenotypic consequence of the failure of crucial cellular pathways required to maintain genome integrity[4].

Indeed, XP presents a unique model for analysing the effects of unrepaired DNA lesions in skin carcinogenesis. The skin cancer predisposition, observed in XP patients, is due to the mutator gene activity of XP cells which lead to high levels of UV specific modifications of crucial regulatory genes in skin cells leading to cancer. Thus, the high levels of UV specific mutations, seen in oncogenes and tumor

Gene modifications in Xeroderma Pigmentosum skin tumors

Gene	Gene alterations non melanoma skin cancers	Melanoma
Oncogenes		
RAS	53%	#
SMO	30%	nd
SHH	18%	nd
C-MYC	<70%	nd
Ha-RAS	<50%	nd
Tumour suppressor genes		
P53	<90%	>50%
INK4a-ARF	43%	-
PTCH	<90%	-

Specific differences are seen between basal cell carcinomas (BCC) and squamous cell carcinomas (SCC) in XP patients. Higher levels of p53 modifications are found in BCC as well as the sonic hedgehog pathway genes (*). RAS and INK4a-ARF modifications are prevalent in SCC.

The nonmelanoma skin cancers (NMSC), which account for mainly basal cell carcinomas (BCC) and squamous cell carcinomas (SCC) develop as multiple primary tumors in XP patients. NMSC are derived from the basal layer of the epidermis with BCC occurring in the hair-growing epithelium whereas SCC derive from inter-follicular cells. BCC arise de novo as slow growing, locally invasive tumors which metastasize rarely. SCC which develop with a multistep progression, are often derived from precancerous skin lesions, actinic keratoses (AK) and tend to be more aggressive and frequently metastasize.4 sonic hedgehog (SHH) signaling pathway plays a central role in the genesis of BCC, whereas specific pathways involved in the development of SCC and melanoma have not been defined as yet. UV induced mutations have, nevertheless, been found in genes associated with different cellular pathways leading to the activation of proto-oncogenes and modification of tumor suppressor genes in SCC, BCC and melanoma.

HPV and SCCs from young XP patients, are comparable to that found for NMSC from adult immunosuppressed organ transplant patients and raise the question of the importance of HPV infection in skin carcinogenesis. Thus, one wonders whether the immunological defects reported in XP patients play an important role in HPV infection of XP patients and what is the impact of HPV on skin tumour development.

Baso-squamous carcinoma. (BSC) -

BSC is a rare tumor with an incidence of less than 2%. 97% of the tumors were located on the head and neck. Face and ears being the commonest sites.[7] Molecular etiology have been linked to Human papiloma virus in lower animals.[8] Metastases of BSC are known to occur many years after identification of the primary tumor. These tumors are radioresistant. Hence such patients should undergo regular follow-up as long as possible. BSC has biological aggressiveness intermediate between basal cell and squamous cell carcinomas. Authors have described BSC as a wolf in sheep's clothing. A male gender, large size (> 20mm), positive surgical resection margins and lymphatic or perineural invasion are indicators for the aggressiveness of basosquamous carcinoma.The 5-year survival rate is estimated to be 17.5%.[7]

Conclusion -

Basosquamous cell carcinoma (BSC) is a rare cutaneous neoplasm with features of both basal (BCC) and squamous cell carcinoma (SCC) which has a potential for aggressive infiltration and destruction. Treatment of the disorder includes avoidance of Ultra violet radiation, topical application of 5 - fluorouracil to treat actinic keratoses, and regular evaluation by an ophthalmologist, dermatologist, and neurologist. genetic counseling is required in case of consanginous marriage, ours was also a case of 3 out of 4 siblings affected, by xeroderma, born out of nonconsanguinous marriage. Anecdotal reports of such siblings affected have been published.There are very few cases of xeroderma pigmentosum reported in literature from India. Reporting every case might help us to know the incidence and prevalence of XP in India which is yet unknown.

Conflicts of Interest : Nil reported by Author

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