

Xeroderma Pigmentosum

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Xeroderma pigmehtosum (XP) is a rare autosomal recessive disorder associated with defective DNA repair which causes photosensitivity. The photosensitivity leads to pigmentary changes, atrophy and later squamous cell carcinoma of the skin(1). So far about 29 cases have been reported from India(2). In this communication we report 7 cases of XP seen over a period of 2 years.

Case Reports

The clinical features are shown in *Table I*, and the representative features shown in *Figs. 1 & 2*. The diagnosis was based on clinical features and histopathologic data.

Discussion

Seven cases of XP seen during a relatively short period of time, possibly indicate a high frequency of this gene in this part of the country. The gene frequency in the general population has been reported to be 1 in 200 million and the frequency of the

disorder, 4 in 1 million(3). Countries like Libya, Egypt, Israel and Japan, with a high degree of consanguinity, have a high incidence of this disease(1). A similar level of consanguinity is seen in South India.

The classical clinical features of XP have been reviewed in recent publications(1-3). All the seven cases reported have had typical features of XP (*Table I*). About 18% of The patients with XP have neurological abnormalities like microcephaly, low intelligence, abnormal motor activity, areflexia, hyperreflexia, ataxia, impaired hearing, abnormal speech and abnormal EEG(2). Three of our cases had microcephaly and one had mild delay in developmental milestones.

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TABLE I—Clinical Features in Patients of Xeroderma Pigmentosa

Features	1	2	3	4	5	6	7
<i>General</i>							
Age of onset (yrs)	3	0.8	0.5	0.5	3	10	0.3
Sex	M	F	F	M	F	F	F
Consanguinity	UN	UN	UN	UN	FC	FC	FC
Family history	Nil						
Stunted growth	+	+	+	+	+	+	+
<i>Skin</i>							
Photosensitivity	+	+	+	+	+	+	+
Hyperpigmentation	+	+	+	+	+	+	+
Scaling	+	+	+	+	-	-	+
Erythema	-	-	+	-	-	-	-
Malignant neoplasms	+	-	-	-	+	-	-
Nature of neoplasms	SCC	-	-	-	SCC	-	-
<i>Ocular</i>							
Photophobia	+	+	+	+	+	+	+
Excess lacrimation	+	+	+	+	+	+	-
Blurring of vision	+	-	-	-	-	-	+
Conjunctival injection	+	+	-	-	+	+	-
Corneal clouding	+	+	-	-	-	-	-
Ocular neoplasm	-	-	-	-	+	-	-
<i>Oral</i>							
Fissuring of lips	+	-	-	+	-	-	-
Hyperpigmentation of lips	-	-	-	-	-	+	-
Whitening of lips	+	-	-	-	-	+	-
<i>Neurological</i>							
Microcephaly	-	-	+	+	-	-	+
Intelligence	N	N	N	N	N	N	-
Neurological deficits	-	-	-	-	-	-	-

M = male; F = female; UN = Uncle niece; FC = First cousin; SCC = Squamous cell carcinoma; N = normal

A syndrome of XP with microcephaly, mental retardation, dwarfism, hypogonadism called Descantis-Cacchione syndrome has been described, including 2 reports in the Indian literature(4,5). XP has to be differentiated from Cockayne syndrome which is a much rarer autosomal recessive disease with cutaneous photosensitivity. These patients are extremely small with large ears, nose and eyes and long arms and legs. They have an appearance of premature aging with grey hair and may be associated with

type II lipoproteinemia. Other characteristic changes include photosensitivity, deafness, optic atrophy, mental deficiency and rarely intracranial calcifications(6).

The malignant potential of XP is the most serious aspect of this condition. Two of our patients, developed squamous cell carcinoma. Recently a 9 year old boy with limbal squamous cell carcinoma has been reported in the Indian literature(7). Rarely, the condition may be associated with other malignancies including leukemia,



Fig. 1. Hyperpigmentation of face, eyelids and secondaries in cervical lymph glands.



Fig. 2. Hyperpigmentation of the face in a 9 yr old girl.

bronchogenic carcinoma, gastric cancer, testicular sarcoma(2). None of our patients, however, had any other malignancy.

The advancement in DNA studies has resulted in classifying XP into 10 subgroups based on complementation analysis as has been shown in *Table II*. Unscheduled DNA synthesis (UDS) refers to the DNA synthesis that has to occur when cells are exposed to the

ultraviolet rays; this capacity for DNA repair on exposure to UV light is reduced to a varying degree in patients with XP(6). Those with very low UDS *e.g.* <5% like in subgroup XP-A have earlier and severe manifestations, on the other hand XP-E with UDS 40-60% have milder manifestations at a later age(3). The nature of malignancy also varies with the type. XP-A are commonly associated with

TABLE-II Complementation Grouping of Xeroderma Pigmentosa

Complementation group	UDS	Skin symptoms	Predominant skin tumors	Neurological symptoms
A	< 5%	Severe, early	SCC	++ (DS-Cacc)
B	10%	Severe, early Cockayne syndrome	-	+
C	10-47%	Severe	SCC, BCC	-
D	25-60%	Moderate	LMM	-
E	40-60%	Mild, late	BCC	-
F	< 10%	Moderate		+
G	< 2%	Moderate		+
H	30%	Cockayne syndrome		+
I	< 15%	Severe		-
Variant	100%	Mild, late	BCC	-

Adapted from reference 3; UDS = Unscheduled DNA synthesis; SCC = Squamous cell carcinoma; BCC = Basal cell carcinoma; LMM = Lentigo malignant melanoma; DS-CACC = Descantis Cacchione syndrome

squamous cell carcinoma, XP-D with lentigo malignant melanoma and XP-E with basal cell carcinoma(3). Although clinical and biochemical features are constant within each complementation group, minor variations may occur.

XP poses a challenge as far as management is concerned. As there is a high risk of subsequent development of malignancy, early diagnosis of the condition is very important. Individuals with the disease should avoid exposure to sun, use protective clothing, sun-screening agents and dark glasses. They should come on a regular follow up to detect and remove pre-cancerous lesions and malignant tumors at an early stage. Tumors have been treated by topical 5-fluorouracil. Surgical procedures like dermabrasion, dermatome shaving and excision with grafting of involved areas has been tried with varying success(2,8). In spite of the various prophylactic measures, the mortality in these patients is high(2), usually secondary to infections or metastasis from malignant growths. However occasionally patients with XP may survive up to the sixth Or seventh decades(9). Prenatal diagnosis is possible by studying UDS in amniotic cells(6).

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