Report

Xeroderma pigmentosum in black South Africans

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Abstract

Background Xeroderma pigmentosum occurs in all races. There is little information on its clinical picture, frequency, and types of malignant lesions in individuals of African negroid extraction.

Methods Fifteen black South African patients, aged from 10 months to 21 years, with xeroderma pigmentosum were prospectively studied. Detailed dermatologic, ophthalmologic, and neurologic examinations were carried out in all patients. Cutaneous, conjunctival, and lingual malignant lesions were histologically assessed. Complementation studies were not performed.

Results Twelve patients had cutaneous malignancies, predominantly squamous carcinomas, usually several at one time. Carcinomas of the tip of the tongue occurred in five patients and conjunctival carcinomas in four. Cutaneous and mucosal carcinomas developed at an earlier age than in the series from other parts of the world. Three patients had extensive skin involvement characteristic of xeroderma pigmentosum, but did not develop malignancies. They most likely belong to a complementation group(s) with higher rates of unscheduled deoxyribonucleic acid (DNA) synthesis.

Conclusions Xeroderma pigmentosum in South African black people is characterized by the very early development of cutaneous, ocular, and tongue squamous cell carcinomas and usually has a rapid and devastating course.

Xeroderma pigmentosum (XP) is a rare autosomal recessive disease characterized by severe photosensitivity and defective deoxyribonucleic acid (DNA) repair. Patients with this condition have cutaneous and ocular changes, including neoplasias. One-fifth have, in addition, progressive neurologic impairment. XP has been reported in individuals of various ethnic groups with the largest series from the Middle East and Japan. Reports on XP in individuals of African ancestry in sub-Saharan Africa are very scanty. The largest group of six black South African patients was reported by Harris and Keet[1] almost 40 years ago. The purpose of this paper is to report on the clinical findings of 15 black South African patients with XP seen prospectively in the last 11 years.

Patients and methods

Fifteen black South African patients with XP were seen in the period July 1986 to November 1997 in the Department of Dermatology, University of Pretoria. The study included an examination of the skin, eyes, and oral mucosa with a detailed counting of lesions clinically suggestive of malignancies. Such lesions were removed and sections processed for standard histopathologic assessment. In addition, each patient had neurologic and ophthalmologic examinations. Complementation studies were not performed due to their unavailability.

Results

The ages of the patients when seen for the first time varied from 10 months to 21 years. Eleven were then not older than 5 years. Only six were seen more than once and only four were followed for more than 3 years. The patients lived in poverty in remote parts of the country and compliance was very poor. Nine patients were boys and six girls. There were two sets of brothers among the patients, otherwise the occurrence of the condition in the rest of the families and parental consanguinity were denied.

Twelve patients had cutaneous malignancies, predominantly squamous cell carcinomas (SCCs) and solar keratoses. They usually had several SCCs at one time (Figs 1 and 2). Almost all SCCs were on the head and face. All twelve patients developed cutaneous SCCs before reaching the age of 6 years. Metastases to the cervical lymph nodes were observed in two patients. Basal cell carcinomas were detected

only twice, one on the face and one on the upper arm. No malignant melanoma was seen.

Five patients had SCC of the tip of the tongue (Fig. 3). The age of the patients when tongue carcinoma was detected varied from 6 to 9 years. Four had SCCs of the conjunctivae (Fig. 4). The age at detection of eye tumors varied from 18 months to 3 years. Three had carcinomas of the lip. Nine patients had cutaneous and mucosal cancers.

In three patients, no cutaneous or mucosal neoplasms were detected. They all had prominent skin changes: dyschromia, freckling, xerosis (Fig. 5). Their histories revealed that these changes developed later than in those patients with malignant lesions. These three, all boys, were also the oldest when

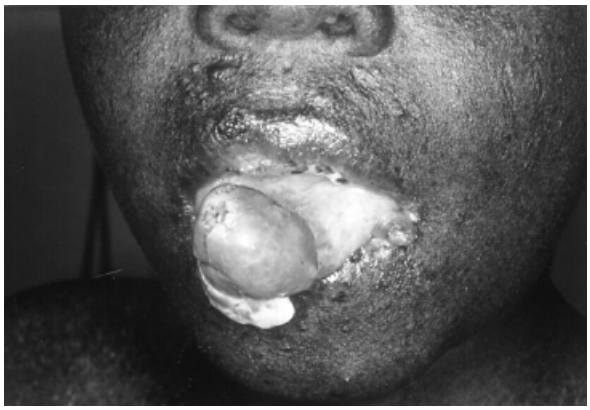

Figure 3 Squamous cell carcinoma of the tip of the tongue in a 7-year-old African girl with xeroderma pigmentosum

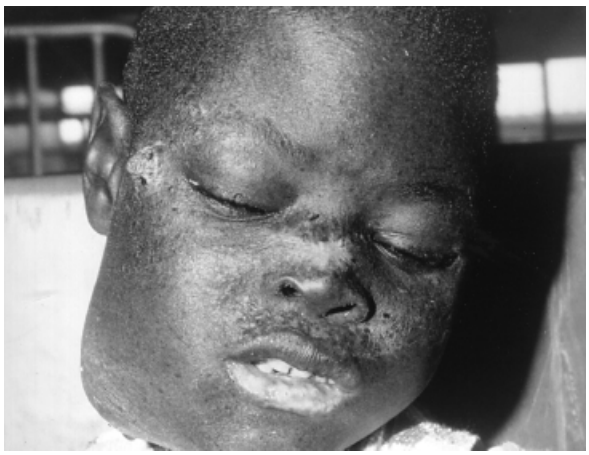

Figure 1 A 4-year-old African boy with xeroderma pigmentosum. Cutaneous squamous cell carcinoma that had already metastasized to cervical lymph nodes

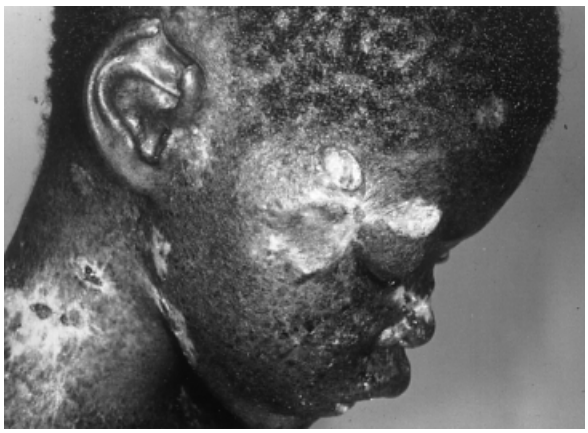

Figure 2 The same boy, now 6 years old. Multiple cutaneous squamous cell carcinomas

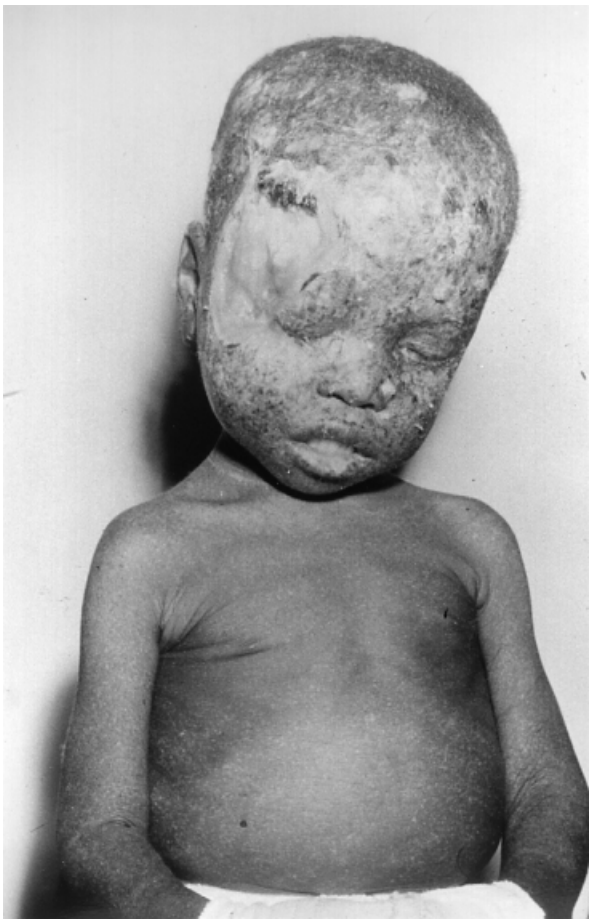

Figure 4 A 3-year-old African child with conjunctival squamous cell carcinoma and several cutaneous squamous cell carcinomas

seen for the first time—aged 12, 17 and 21 years. No neurologic abnormalities were found in the whole group and the intellectual development of the children seemed appropriate for their age and social status.

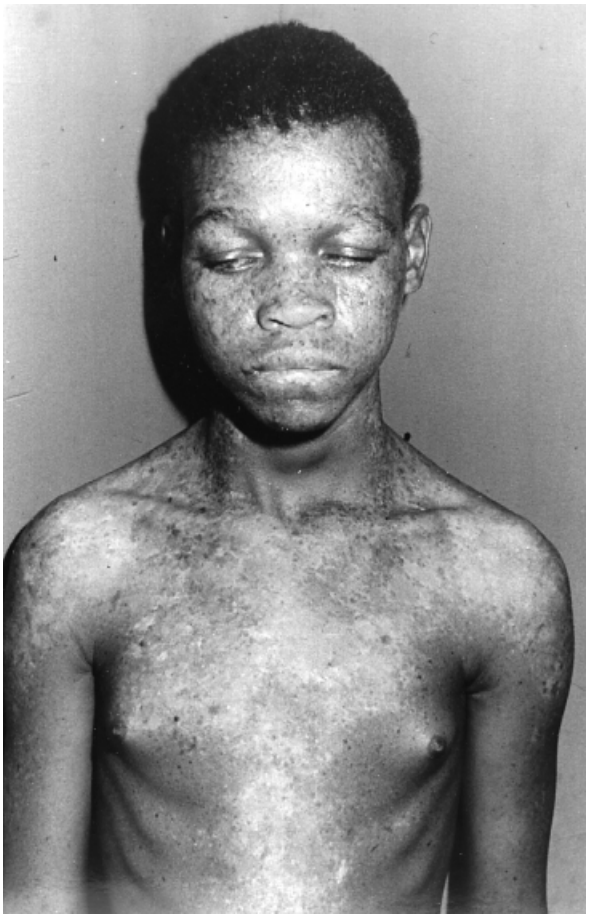

Figure 5 A 17-year-old African boy with xeroderma pigmentosum. Prominent skin changes but no malignancy

Discussion

Cell fusion studies have demonstrated heterogeneity of the molecular defect in XP and have resulted in the delineation of several complementation groups that have different rates of unscheduled DNA synthesis.[2] Patients with the variant form have normal excision repair and defective post-replication repair. Table 1 shows the rates of unscheduled DNA synthesis, geographic distribution, neurologic involvement, and gene cloning status in XP complementation groups.

Only 21 case of XP have been reported to my knowledge in individuals of African ancestry living in sub-Saharan Africa (Table 2), and in none of them were complementation studies performed. Reports on XP in Afro-Americans are also few in number.[10–13] Afro-American patients in whom comple-

Table 2 Xeroderma pigmentosum in sub-Saharan Africa

Country	Year of publication	Number of cases	Reference
Uganda	1938	3	Loewenthal and Trowell[3]
South Africa	1952	1	Cohen *et al.*[4]
South Africa	1956	1	Targowsky and Loewenthal[5]
South Africa	1958	3	Rose[6]
South Africa	1960	6	Harris and Keet[1]
Senegal	1983	1	Ndiaye *et al.*[7]
Mauritania	1992	1	Bouzamel *et al.*[8]
Comory Islands	1994	5	Hebert *et al.*[9]

Table 3 Frequency of cutaneous and mucosal malignancies

	Kraemer *et al.*[14]	Present series
Cutaneous malignancies	45%	80%
Eye cancer	11%	27%
Tongue cancer	1.6%	33%

Table 1 Complementation groups

Complementation group	UDS (% of normal)	Geography	Neurologic involvement	Gene
XP-A	<2%	Japan, Egypt, Maghreb, Europe, USA	Severe neurologic symptoms (De Sanctis–Cacchione syndrome)	9q34
XP-B	3–7%	USA, Europe, Egypt, Japan	XP–Cockayne syndrome complex	2q21
XP-C	10–20%	Europe, USA, Egypt, Japan	None	3p25
XP-D	25–50%	Europe, USA, Japan	Neurologic symptoms in some patients XP–Cockayne syndrome complex	19q13.2
XP-E	40–50%	Europe, Japan	None	—
XP-F	10–20%	Japan, Europe	None	15
XP-G	<2%, 25%	Europe, Japan	Variable neurologic involvement	13q32–33
XP-variant	100%	Japan, Europe, USA, Egypt	None	—

UDS, unscheduled DNA synthesis.

mentation studies were performed belonged to complementation group C.[12,13]

Table 3 shows the frequency of cutaneous and mucosal malignancies in the study of Kraemer *et al.*,[14] comprising 830 cases published in the medical literature from 1874 to 1982, and in the present series. SCCs were the predominant type of cutaneous malignancy in the present series. Also, the review of the previous sub-Saharan publications did not disclose malignancies other than cutaneous SCC. No malignant melanoma was observed in 15 patients in the present series, while this tumor constituted about 5% of the cutaneous malignancies in the world review of Kraemer *et al.*[14] All patients in the present series who developed cutaneous SCC did so before reaching the age of 6 years, which differs from Kraemer *et al.*[14] where the median age for the first skin neoplasm was 8 years.

One-third of the patients in the present series had SCC of the tip of the tongue. All five were under 10 years of age. Development of carcinoma of the tip of the tongue appears to be particularly common in dark-skinned individuals of African and Middle Eastern extraction.[15] Apparently, when complementation studies were performed in XP patients with tongue carcinoma they invariably belonged to group C.[16]

The median age at development of the first ocular neoplasm in the review of Kraemer *et al.*[14] was 11 years. It was much lower in the present group. All four patients developed conjunctival carcinoma in the first 3 years of life and one, in whom the tumor was detected at 18 months, is probably the youngest XP patient developing eye carcinoma. Photophobia, corneal abnormalities, and impairment of vision were observed to a variable degree in all patients. Three boys who did not develop cutaneous or mucosal malignancies either belonged to a complementation group(s) with a fairly high rate of unscheduled DNA synthesis or to XP-variant.

The level of unscheduled DNA synthesis seems to determine the age of onset of the cutaneous malignancies in patients with XP. Also, there appears to be a correlation between the degree of cellular hypersensitivity to killing *in vitro* and the severity of neurologic abnormalities.[17] Therefore, the determination of the excision repair level in South African patients may be of prognostic significance.

Conclusions

XP in South African black people is characterized by a very early development of cutaneous, ocular, and tongue SCCs and has, in the majority of cases, a rapid and devastating course.

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