Xeroderma pigmentosum: a review and case series

Dr. Fawzia M. A. BUTT, BDS, FDSRCS, MDS-OMS, Consultant Oral and Maxillofacial Surgeon, Lecturer1, Dr. Jeremiah R. MOSHI, DDS, MDS-OMS, Lecturer2, Dr. Sira OWIBINGIRE, DDS, M Dent (Oral Surg), Lecturer2, Associate Prof. Mark L. CHINDIA, BDS, MSc, FFDRCSI, Consultant Oral and Maxillofacial Surgeon3
1 Department of Human Anatomy, University of Nairobi, Kenya; 2 Department of Oral surgery and Pathology, Muhimbili University of Health and Allied Sciences, Dar-es-salaam, Tanzania; 3 Department of Oral Maxillofacial Surgery and Pathology, Faculty of Dental Sciences, University of Nairobi, Kenya

SUMMARY. Xeroderma pigmentosum (XP) is a condition inherited as an autosomal recessive trait and is characterized by photosensitivity, pigmenay changes, premature skin ageing and malignant tumour development resulting from the defect in DNA repair. The management of complications of XP, especially orofacial tumours entails an enormous surgical challenge to the clinicians. We present five cases of XP. © 2010 European Association for Cranio-Maxillo-Facial Surgery

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INTRODUCTION

Xeroderma pigmentosa (XP) was described in Vienna by a Hungarian professor of dermatology Moriz Kaposi in 1870 (Hebra and Kaposi, 1874). The disorder was first called “xeroderma or parchment skin” and in 1882, the term “pigmentosum” was added to emphasize the striking pigmentary abnormality (Kaposi, 1883). Neisse (1883) described two siblings who had XP with progressive neurological degeneration beginning in the second decade. In 1932 two Italian physicians, Carlos Desanctis and Aldo Cacchione described three brothers with cutaneous features of XP with progressive neurological degeneration beginning at 2 years of age associated with dwarfism and immature sexual development, the so called DeSanctis-Cacchione syndrome (Reed et al., 1977). The first description of XP in a black African was published in Loewenthal and Trowell (1938). In an American black the first description was by King and Hamilton (1940).

XP is a rare disorder transmitted in an autosomal recessive fashion characterized by photosensitivity, pigmentary changes, premature skin ageing and neoplasm development (Cleaver, 1968). While XP may be rare the nature of the intrinsic defect in the affected individuals is of great interest especially when it occurs in siblings. In this series we present five cases of XP, four familial and one sporadic.

CASE SERIES

Two XP cases of brothers aged 17 (case 1) and 20 years (case 2) were referred for the evaluation and management of oral conditions. While the 17-year-old had the typical cutaneous scaly hyperpigmentation and a benign ulceration of the lower lip, the brother exhibited severe mental retardation, kyphoscoliosis and metachronous conjunctival and anterior tongue carcinomas (Fig. 1). The eye lesions had been managed prior to this presentation.

After comprehensive examination case 1 was kept under close observation for the lip ulceration while case 2 had lower lip vermilionectomy and excision of an anterior tongue carcinoma performed. This patient had had excision of a post-nasal space carcinoma performed 3 months earlier. Two months after excision of the tongue lesion, the patient presented with another tumour in the right conjunctiva which was promptly removed. During a 1-year follow-up period the patient remained tumour-free.

Two other XP siblings a brother aged 11 years (first-born) and a sister aged 2½ years (fourth-born) were diagnosed with skin and oral lesions (Fig. 2). The brother had a painful swelling in his lower lip and tongue which had been present for 3 months and was progressively increasing in size accompanied with intermittent bleeding. The lesion was approximately 1 cm in diameter, appeared granulomatous and haemorrhagic. Full body examination showed generalized patchy pigmentation of the skin which was dry and scaly and was more pronounced in areas exposed to the sun. His eyes were sensitive to sunlight necessitating use of dark glasses since he was 6 years old. He later developed dense corneal scars with occlusion of the pupil which led to poor vision at the time of presentation. Histopathological examination of the incisional biopsy of the lip and tongue lesions confirmed an ulcerated poorly differentiated squamous cell carcinoma (SCC) while that of the skin revealed albinism xeroderma. The younger sibling had skin rash-like lesions which began at the age of 9 months and were more pronounced over the face and upper limbs but were asymptomatic. Ophthalmological examination
confirmed her photophobia. In addition she also had mild conjunctival injection and corneal haziness, but the pupil was normal. Histopathological examination of a skin biopsy confirmed XP. The brother later succumbed to the complications of SCC as it metastasized to the cervical nodes and lungs 6 months later. The sister was reviewed for 2 years during which her vision deteriorated, the skin lesions enlarged becoming more dry and scaly. Thereafter, she was lost to follow-up.

An 8-year-old boy presented with a chief complaint of swelling in the lower lip and anterior portion of the tongue for 1 month (Fig. 3). His medical history was unremarkable at birth. At the 2 years of age he developed generalized hyperpigmented skin spots followed by photophobia and lesions in the oral cavity. The skin in the areas exposed to the sun was dry, scaly and atrophic. The lower lip had a pedunculated, nodular and ulcerated swelling measuring 3 cm in the widest diameter which was hemorrhagic. There were two bilaterally placed lesions 1.5 cm from the tip of the tongue, each 1 cm in diameter similar to the appearance of those in the lip. Histopathological examination of the excisional biopsies of the oral lesions revealed a diagnosis of pyogenic granuloma. Ophthalmological examination showed corneal scarring with neovascularization, for which Chlomphenical ointment, artificial tears and the use of photochromatic lenses were prescribed. During a 4-month follow-up period the patient’s skin had improved with no evidence of recurrence of the oral lesions. The salient clinical characteristics among the five XP cases are summarized in the Table 1.

DISCUSSION

XP is characterized by photosensitivity, pigmentary changes, premature skin ageing, photophobia, neoplasia and abnormal DNA repair to UV radiation-induced damage due to defective endonuclease activity. Basal cell carcinoma (BCC) and SCC of the lids and cornea (limbus) occur frequently. Melanomas of the skin are known to occur in XP but are rare in the conjunctiva (Mehta et al., 1996; Saralya et al., 2005). Cleaver suggested that an increase in sunlight-induced cancer was a direct consequence of an increase in mutated cells of the skin of XP (Cleaver, 1968). The XP patients
posses cells that are defective in the excision repair of UV-induced pyrimidine dimers from their DNA. This defect is correlated with hypermutability when XP cells are exposed to ultraviolet radiation. Approximately 80% of patients have ocular complications. These complications may include severe keratosis which could be followed by corneal opacification, and vascularization. Patients with XP may lose their eye lashes and in severe cases may lose the entire eyelids. Neurological symptoms such as microcephaly, progressive sensorineural hearing loss and cognitive impairment can be found in 30% of XP patients (Gartler, 1963; Rook et al., 1968).

XP is classified into eight genetic complementation subgroups from XP-A to XP-G and a variant group XP-V with different gene alterations (Thompson, 1998). Seven (XP-A to XP-G) are involved in nucleotide excision repair and the variant is involved in the replication of damaged DNA on the leading strand (Svoboda et al., 1998). 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 (Kraemer and Slor, 1985; Pawsey et al., 1979; Hasem et al., 1980; Jiang et al., 1981; Fischer et al., 1982; Hwang et al., 1982; Park and Chung, 1982; Bhutto et al., 2005), when he reported 36 cases of XP including sporadic and familial cases in Pakistan, emphasized the tropical nature of the climate. Although skin types need to be considered, Africa has a non-white population with the majority having black pigmentation. Due to the inherent defect the XP affected black patient possesses; they are more prone to malignancy as shown in the present series.

The skin of the affected children may appear normal at birth, then exposure to sunlight results in a dry scaly appearance with multiple areas of hyperpigmentation. The marked tendency to develop malignancy in the orofacial area during childhood and adolescence should be of particular interest. In a generally sunny environment, the primary challenge is how to assist afflicted individuals lead a normal life as much as possible. The manifestation of tumours 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.

CONCLUSION

The follow-up care was geared to closely monitor and educate the patient and their guardians’ about effective sun protection and early recognition of the skin cancer. This case series emphasizes on a multidisplinary approach in the management of patients affected with XP. It also highlights the challenges that present in the management of such patients.

References


Table 1 — Presenting salient features among five XP cases

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Gender</th>
<th>XP-lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sibling group A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>M</td>
<td>Cutaneous manifestations, lower lip ulcer, mental retardation</td>
</tr>
<tr>
<td>20</td>
<td>M</td>
<td>Kyphoscoliosis, conjunctival, tongue and post-nasal space Carcinoma</td>
</tr>
<tr>
<td>Sibling group B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>Lower lip and tongue carcinoma, skin hyperpigmentation</td>
</tr>
<tr>
<td>2.5</td>
<td>F</td>
<td>Photophobia, corneal scarring</td>
</tr>
<tr>
<td>Isolated patient</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>Skin hyperpigmentation, Photophobia, Pyogenic granuloma, Corneal scarring</td>
</tr>
</tbody>
</table>

Fig. 3 — Demonstrates a case of XP with tongue and lower lip granulomatosis lesions and cutaneous hyperpigmentation areas on his hands.


Dr. Fawzia M.A. BUTT, BDS, FDSRCS, MDS-OMS
Consultant Oral and Maxillofacial Surgeon, Lecturer
Department of Human Anatomy
University of Nairobi
P.O. Box 25361-00603
Nairobi, Kenya
Tel.: +254 02 387770
Fax: +254 20 2710712
E-mail: fawzia_butt@yahoo.co.uk (F.M.A.B.), jermiah@muhas.ac.tz (J.R.M.), swibingire@muhas.ac.tz (S.O.), profchindia@yahoo.com (M.L.C.)

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