

Malignant and Pre-Malignant Manifestations of Xeroderma Pigmentosum in Ghanaians

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Abstract

Introduction: Xeroderma pigmentosum is an autosomal recessive disease with sun sensitivity, photophobia, early onset of freckling, and subsequent neoplastic changes on sun-exposed surfaces. There is cellular hypersensitivity to UV radiation and to certain chemicals in association with abnormal DNA repair. Patients with defective DNA nucleotide excision repair (NER) have defects in one of seven NER genes; xeroderma pigmentosum variants have normal NER and a defect in a polymerase gene. **Study design:** This is a case presentation of five patients with the features of xeroderma pigmentosum, aged 48, 26, 15, 14 and 8 years. The first and last patients were males. Each of the first four patients presented with areas of hyper- and hypo-pigmentation over sun exposed body surfaces. Each of them had a minimum of two cutaneous malignancies, distributed on the upper chest, face or scalp. The fifth patient had skin atrophy, with mottled hyperpigmentation and hypopigmentation but had no malignant lesions. **Result:** The first, second and fourth patients had their lesions surgically excised and the defects were skin grafted. The third patient was treated with radiotherapy. All the lesions were confirmed histologically as squamous cell carcinoma. No recurrence has been observed. **Conclusion:** Xeroderma pigmentosum in Ghanaians presents with squamous cell carcinoma involving the head, neck and upper trunk. A minimum period of exposure to UV radiation, not precisely known, is required for the development of the lesions. Education on sun avoidance and protective clothing is necessary to prevent morbidity and mortality.

Keywords

Xeroderma, Sun Sensitivity, Hypopigmentation, Macules, Freckling

1. Introduction

Xeroderma pigmentosum (XP) occurs with an estimated frequency of 1:1,000,000 in the United States. It is more common in Japan, the Middle East and North Africa. Cases have been reported worldwide in all races including Whites, Asians, Blacks, and Native Americans. Consanguinity is common. There is no significant difference between the sexes [1].

XP is a rare disorder transmitted in an autosomal recessive manner, which is characterized by photosensitivity, pigmentary changes, premature skin ageing and malignant tumour development [2]. These manifestations are

due to a cellular hypersensitivity to ultraviolet (UV) radiation resulting from a defect in DNA repair [3].

The disease which passes through three stages first appears after six months of age characterized by diffuse erythema, scaling and freckle-like areas of increased pigmentation over areas exposed to the sun, appearing initially on the face. With progression of the disease the skin changes appear on the lower legs, neck and trunk [4]. The second stage is characterized by poikiloderma, consisting of skin atrophy, telangiectasia, mottled hyperpigmentation and hypopigmentation. The third stage is heralded by the appearance of numerous malignancies, including squamous cell carcinoma (SCC), malignant melanoma (MM), basal cell carcinoma (BCC) and fibrosarcoma. These are more prevalent on sun exposed areas of the body and may occur as early as 4 years of age [4].

Diagnosis of XP in Ghana is mainly clinical, based on the typical skin and pigmentary changes (usually multiple hypopigmented macules in black Africans) and the presence of cutaneous malignancies.

2. Case Presentation

2.1. Case One

KB a 48 year old man presented in January 2007 with two lesions: an ulcer of 12 cm by 8 cm on the right half of the anterior chest wall, involving the breast, elevated, with an indurated base, with keratinous crusts. The surrounding skin of the rest of the trunk, shoulders, neck and face were covered with numerous hypopigmented macules. There was also a cauliflower-like fungating growth, 4cm by 3cm, at the right temporal region of the scalp. The chest lesion had begun as a small ulcer around the nipple about a year and half previously, and had grown progressively to the current size; the scalp lesion was only eight months old at the time of presentation. There were no palpably enlarged cervical or axillary lymph nodes.

The two lesions were widely excised under general anaesthesia. The defects were repaired with split thickness skin grafts. The scalp lesion healed after one month; the chest wall wound healed after three months. The histology report confirmed SCC for the two lesions. The chest wall lesion was described as more invasive. No recurrence of the lesions has been observed after six years follow up. He has been advised to avoid excessive exposure to sunlight.

2.2. Case Two

BA a 26 year old woman was referred from a regional hospital to Komfo Anokye Teaching Hospital in November 2013, on account of two ulcers on the scalp which had not been healing for two years. She had multiple scaly itchy hypo and hyper-pigmented lesions distributed over the trunk, face, scalp and limbs. The first ulcer was located on the right frontal region of the scalp, about 6 cm by 4 cm with everted edges; the second ulcer was 5 cm by 3 cm on the left parietal scalp also with everted edges (**Figure 1**). After completing a course of chemotherapy, the lesions were excised with 2 cm margins and the defects were skin grafted. The lesions were confirmed on histology to be SCC.



Figure 1. SCC on scalp of XP patient.

2.3. Case Three

CA a 15 year old girl reported to the plastic surgical clinic of Komfo Anokye Teaching Hospital in August 2009 because of a growth on the nose which was gradually getting bigger and more unsightly. Examination revealed an ulcerated nodular growth on the nose, between the nasal tip and the bridge. There were two darkly-pigmented un-ulcerated smaller satellite nodules on the right side of the nose, and a third hyperpigmented nodule on the left cheek. There were multiple scaly lesions on the face, with areas of hyper- and hypo-pigmentation, involving the neck, arms, and trunk (**Figure 2**).

An incision biopsy of the ulcerated lesion confirmed acantholytic SCC. She was treated with radiotherapy and the tumours regressed. She is being followed up six monthly for any recurrence or evidence of malignant change in the other facial lesions.

2.4. Case Four

JK a 14 year old girl presented in June 2012 with two growths on the scalp. These had developed over eight months, enlarging progressively and discharging serosanguinous offensive fluid. Examination revealed two cauliflower-like pale exophytic growths located on the left parietal and occipital regions of the scalp. The sizes of the lesions were 4 cm by 2 cm and 6 cm by 5 cm at the parietal and occipital regions respectively. She also had multiple hypopigmented macules distributed on the face, scalp, neck, chest, arms and trunk.

The lesions were excised with 2 cm margins and the defects repaired with split thickness skin grafts. The wounds healed after six weeks. The lesions were confirmed as SCC. The patient has been followed up for one year, and there has been no sign of recurrence. She has been counselled against excessive sun exposure, and to report any suspicious skin lesions for investigation.

2.5. Case Five

During a surgical outreach programme to Northern Ghana in December 2014 AZ, an 8 year old boy presented with dry scaly skin with multiple hypo and hyper-pigmented macules on the trunk and shoulders, and the posterior aspect of the neck. The patient had not developed any ulcers on any part of the body (**Figure 3**). The patient's main concern was itching of the lesions which became worst during the dry months of November and December. A moisturizing cream made up of vaseline and aloe vera was prescribed for the management of the skin lesions. The parents were advised on the importance of sun avoidance, wearing of protective clothing and the use of sunscreens.

3. Discussion

All the five patients presented with the typical skin manifestations of xeroderma pigmentosum: premature skin ageing, mottled hyper and hypopigmented macules. All but the last patient had a minimum of two malignant ulcers



Figure 2. Nodular growths on nose and cheeks of XP patient.



Figure 3. (a) XP patient with skin lesions at back of trunk; (b) XP patient with skin lesions on right shoulder.

involving the upper half of the body—head, neck and upper chest, with a predilection for the scalp. These are the areas that are commonly exposed to sunlight. Hair cover does not appear to protect against the development of these lesions which are found on hair bearing scalp. The absence of SCC on the skin of the 8 year old boy implies that this patient has probably not been exposed to the UV light long enough for him to develop the disease. This emphasizes the significance of a minimum period of exposure to the carcinogenic agent (UV light) required to develop the SCC even in those genetically predisposed.

The basic defect in XP is in the nucleotide excision repair (NER) leading to deficient repair of DNA damaged by UV radiation. The process consists of the removal and the replacement of damaged DNA with new DNA. Two types of NER exist: global genome (GG-NER) and transcription coupled (TC-NER). Seven XP repair genes, XPA through XPG, play key roles in GG-NER and TC-NER. Both forms of NER include a damage-sensing phase. Following detection of DNA damage, an open complex is formed. The resulting gap is filled in with new DNA by the action of polymerases [5].

The “classical” XP patients carry mutations in one of the seven XP genes indicated [3]. An XP variant has been described in which the defect is not in the NER but in post-replication repair; in this variant, a mutation occurs in DNA polymerase [6]. The continued presence of repair proteins at sites of DNA damage contribute to the pathogenesis of cutaneous cancers [7].

Because of the multiplicity of the tumours, and the risk of metastatic spread, it is essential that physicians recognize the typical diffuse erythema, scaling and freckle-like areas of hyper- and hypo-pigmentation, involving exposed parts of the body, especially the face, which occur in early childhood. Patients can then be protected from developing malignancies by preventing them from excessive exposure to UV radiation in sunlight.

Treatment of XP aims to protect the patient from excessive sunlight exposure and to detect and treat any malignancies. The use of sunscreens and other sun-avoidance methods such as protective clothing, hats, and eye-wear can minimize UV-induced damage in patients with XP [7].

4. Conclusion

Xeroderma pigmentosum in Ghanaians presents with multiple SCC involving the head, neck and upper trunk. A minimum period of exposure to UV radiation, not precisely known, is required for the development of the lesions. Education on sun avoidance and protective clothing is necessary to prevent morbidity and mortality from the disease.

References

- [1] Kraemer, K.H. and Sarasin, A. (2006) Xeroderma Pigmentosum. In: Le Boit, P.E., Burg, G., Weedon, D. and Sarasin, A., Eds., *World Health Organization Classification of Tumours. Pathology and Genetics of Skin Tumours*, IARC Press, Lyon, 282-284.
- [2] Bootsma, D., Kraemer, K.H., Cleaver, J.E. and Hoeijmakers, J.H.J. (2002) Nucleotide Excision Repair Syndromes:

- Xeroderma Pigmentosum, Cockayne Syndrome, and Trichothiodystrophy. In: Vogelstein, B., Kinzler, K.W., Eds., *The Genetic Basis of Human Cancer*, McGraw Hill, New York, 211-237.
- [3] Van Steeg, H. and Kraemer, K.H. (1999) Xeroderma Pigmentosum and the Role of UV Induced DNA Damage in Skin Cancer. *Molecular Medicine Today*, **5**, 86-94. [http://dx.doi.org/10.1016/S1357-4310\(98\)01394-X](http://dx.doi.org/10.1016/S1357-4310(98)01394-X)
- [4] Lehmann, A.R., McGibbon, D. and Stefanini, M. (2011) Xeroderma Pigmentosum. *Orphanet Journal of Rare Diseases*, **1**, 70. <http://dx.doi.org/10.1186/1750-1172-6-70>
- [5] Warrick, E., Garcia, M., Chagnoleau, C., Chevalier, O., Bergoglio, V., Sartori, D., *et al.* (2011) Preclinical Corrective Gene Transfer in Xeroderma Pigmentosum Human Skin Stem Cells. *Mol Ther*, **8**.
- [6] Gratchev, A., Strein, P., Utikal, J. and Sergij, G. (2003) Molecular Genetics of Xeroderma Pigmentosum Variant. *Exp Dermatol*, **12**, 529-536.
- [7] Naylor, M.F. and Farmer, K.C. (1997) The Case for Sunscreens. A Review of Their Use in Preventing Actinic Damage and Neoplasia. *Arch Dermatol*, **133**, 1146-1154. <http://dx.doi.org/10.1001/archderm.1997.03890450096012>