XERODERMA PIGMENTOSUM: Difficulty with Management of a case in Tropical Africa

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ABSTRACT

OBJECTIVE: Elucidating the pathogenesis and management of xeroderma pigmentosum (XP), a rare genetic disorder due to molecular defects in nucleotide excision repair genes, resulting in ultraviolet-induced lesions. It occurs in all races. There are eight groups; XP-A to XP-G and XP-V variants corresponding to the eight affected genes.

CASE REPORT: We present a fourteen-year-old boy from Southwestern Nigeria who was diagnosed with XP. He had multiple cutaneous macules in sun-exposed areas, significant corneal scarring of the left eye but neurodegenerative features were absent. He also had a nodular swelling on the right side of his lower lip histologically diagnosed as a well-differentiated squamous cell carcinoma.

CONCLUSION: A diagnosis of XP should be considered in a child with multiple skin macules especially at sun exposed sites, ocular scarring, mucocutaneous malignancies or neurodegeneration at an early age. Testing for defective DNA repair genes confirms or excludes the diagnosis. Meticulous photo protection reduces risk of cutaneous malignancies and this poses a great challenge to effective management of patients in tropical Africa.

KEY WORDS: Xeroderma pigmentosum, DNA repair genes, skin macules, squamous cell carcinoma

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INTRODUCTION

Xeroderma Pigmentosum (XP) is a rare autosomal recessive neuro-cutaneous disorder of deficient nucleotide excision repair (NER) leading to defective repair of DNA damaged by ultraviolet radiation.[1] Hebra and Kaposi first described XP in 1874 [1] and De Sanctis later described a more severe form termed De Sanctis- Cacchione syndrome that was associated with neurological degeneration.[2]

In Western Europe, XP has been estimated at 2.3 per million live births, while in the United States the reported incidence is 1: 250,000. [1,2] Among Indians and Middle Easterners the incidence is quoted as 1:10,000 - 30,000, while among Japanese, an incidence of 1:20,000 – 100,000 has been reported. [1] There was a report of fifteen black South Africans with XP who presented with cutaneous, conjuctival and tongue malignancies.[3]

In Nigeria, three cases of XP affecting children from consanguineous marriages with cutaneous and ocular involvements, two of which were malignant.[4]

XP has equal gender predilection and is strongly correlated to parental consanguinity. [4] There are eight described clinical variants corresponding to the eight affected genes (Types A to G and XP-V), with the commonest type being Type A, the classical form.[2]

The purpose of this report is to elucidate the pathogenesis and management of xeroderma pigmentosum (XP), a rare genetic disorder due to molecular defects in nucleotide excision repair genes, resulting in ultraviolet-induced lesions

CASE REPORT

A 14-year-old boy diagnosed with XP in 2012 was referred from the Dermatology unit to the Dental Centre of the University College Hospital, Ibadan on account of multiple oral ulcers. Twenty days after birth, he developed redness of the eyes and maculo-papular facial lesions. At age ten, he had a malignant corneal lesion excised. There was no positive familial history of XP.

Clinical examination revealed dryness of the skin with multiple macules on the trunk, neck and face. Multiple painful tongue ulcers covered with white slough were observed. An exophytic lower lip swelling measuring approximately 4.5 by 2cm (Figures 1a &b) was excised and biopsy reported a well-differentiated squamous cell carcinoma (Figures 2a &b).

Cervical lymph nodes were enlarged and firm in consistency. Both sclera were red and the patient exhibited photophobia. Systemic assessment revealed no other abnormalities. Immediate dental interventions included debridement of intraoral wounds and oral toileting using dilute hydrogen peroxide under local anaesthesia with maintenance on tetracycline and chlorhexidene mouth rinse. Antibiotics (Caps Amoxyl 500mg & Tabs Flagyl 200mg 8-hourly for five days), analgesic (Tabs Paracetamol 1000mg 8-hourly for three days) and multivitamins (Tabs Supradyne one tablet thrice daily & syrup Astymin 10mls daily for two weeks) were prescribed to control pain and infection as well as to optimize the patient's immune status.

Chest x-ray and abdomino-pelvic ultrasound revealed no underlying pathology. Biochemical (electrolyte & urea, creatinine) and hematological (full blood count) investigations had their values within normal limits. The radio-oncology unit commenced chemotherapeutic agents (Cisplatin and 5-FlouroUracil) after basic investigations of baseline haematological values which were within normal limits as an adjunct to the surgical excision of the lower lip malignancy.

We lost the patient due to hemodynamic instability following the first course of chemotherapy given. Patient was said to have been dehydrated and weak after several episodes of vomiting, yellowish discoloration of the sclera and later loss of communication by the patient.

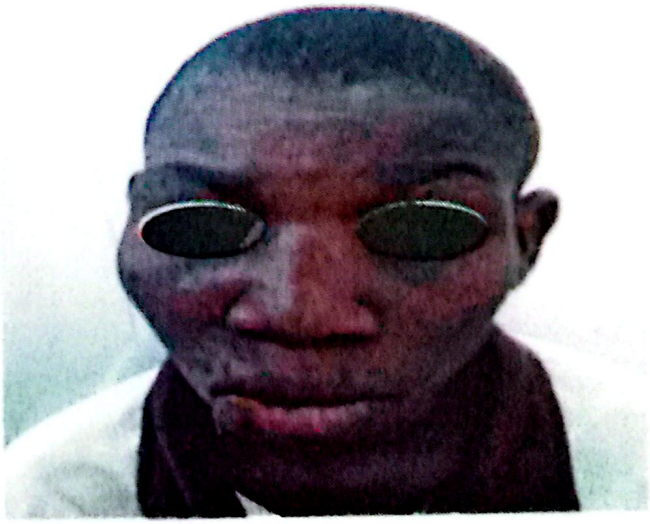

Figure 1a: Lower lip nodular mass

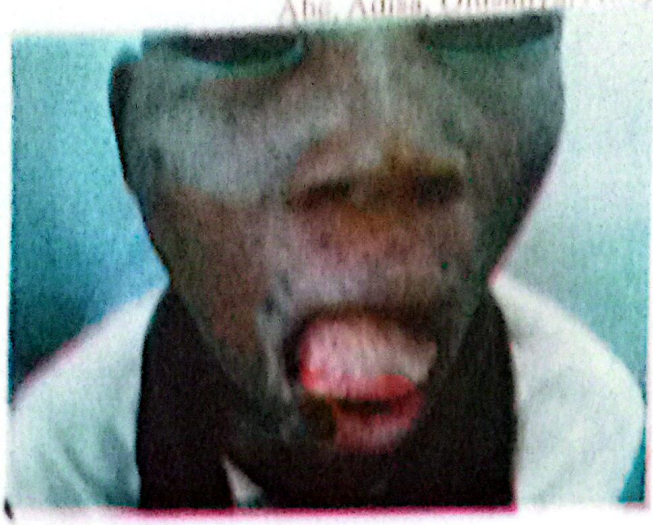

Figure 1b: Multiple tongue ulceration

Figures 2a and b: Well differentiated squamous cell carcinoma consisting of Islands of malignant squamous epithelial cells forming keratin pearls within fibrous connective tissue stroma.

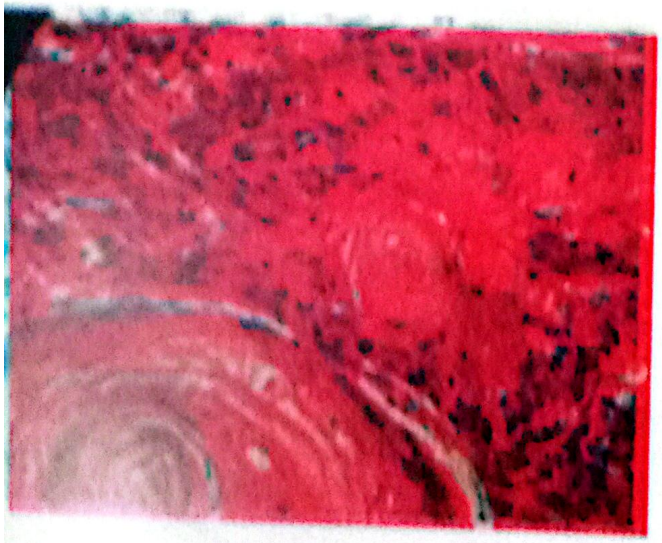

Figure 2b (H&E x400)

DISCUSSION

Xeroderma Pigmentosum (XP) is an autosomal recessive disorder due to mutations in the genes encoding for proteins integral to NER, a pathway that repairs many types of DNA damage including those produced by UV radiation.[1] Anyone of eight different XP genes (XP-A to XP-G and XP-V) can cause impaired NER, [3] with additional functions concerned with other DNA repair pathways and or cellular DNA damage responses. This was attributed to clinical heterogeneity among the different genetic types, with implications for promotion of carcinogenesis in XP patients. [4] However, this patient's diagnosis was based on clinical manifestation without genetic typing, due to lack of equipment and finance to perform testing for defective DNA repair genes in this Centre.

The diagnostic test of choice involves culturing fibroblasts from a skin biopsy (unexposed site), followed by ultraviolet radiation exposure and subsequent measurement of unscheduled DNA synthesis (UDS). A reduced level of UDS confirms the diagnosis of XP. [1] Unavailability of these highly specialized diagnostic facilities and also expensive costs of testing are a challenge to diagnosis in sub-Saharan Africa.

Patients with XP require a multidisciplinary team approach for their care. [4] Although this patient had treatment from several specialists including oral pathologists, oral surgeons, ophthalmologists, dermatologists and radio-oncologist, most of the treatments were made possible through supportive financial contribution as this parent was indigent and had no medical insurance.

The skin lesions appear spider web-like vessels with eventual progression to actinic keratoses and squamous cell carcinomas, which have been similarly documented at a teaching hospital in Northern Nigeria. [4] Malignant involvement of many organs by this defective gene makes it a syndrome. Meticulous photo-protection is essential which our patient was encouraged to do by wearing dark sunglass, broad woven hats and a photo protective cream (SPF 21) was prescribed. Nonetheless, strict adherence to these instructions of photo-protection by the patient could not be ascertained.

In conclusion, a diagnosis of XP should be considered in a patient with multiple skin macules especially on sun exposed sites, ocular scarring, mucocutaneous malignancies and or neurodegeneration at an early age. Testing for defective DNA repair genes confirms or excludes the diagnosis. This case presentation suggests that in tropical Africa, diagnosis and management of XP is challenging with regard to genetic testing and photo-protection.

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