

# A 19 Month Old Male Child with Xeroderma Pigmentosum-A Case Report

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**Abstract:** Background: Xeroderma Pigmentosum (XP) is a rare autosomal recessive genodermatosis characterized by pigmentary abnormalities, solar skin damage and cutaneous malignancies on sun exposed area of skin and eyes. XP occurs in subjects with molecular defects in the genes involved in nucleotide excision repair (NER) of ultraviolet-induced DNA lesions leading to premature skin and ocular ageing consequent upon cellular apoptosis and other UV-induced degenerative changes. If sufficient DNA damage occurs, there will be cellular transformation and the development of malignancies. Both genetic, as well as environmental factor, play an important role in XP. XP has a >1000-fold increased risk of a cutaneous basal cell or squamous cell carcinoma or malignant melanoma. Case history: In this case report, we mentioned about a 19 month old boy who was diagnosed clinically as a case of Xeroderma Pigmentosum and presented with pigmentary skin changes (generalized hypo and hyper pigmented macule), eye problems, developmental delay, acute respiratory infection and failure to thrive. A multidisciplinary team involving the Pediatrician, Dermatologist and Ophthalmologist evaluated, diagnosed and treated the patient. In this case, XP was diagnosed clinically due to lack of all investigation facilities. This genetic premalignant condition is rarely diagnosed at the district level hospitals in Bangladesh. We report this case to upgrade the knowledge of pediatricians working in the rural areas (primary and secondary level health care facilities) regarding the diagnosis, counseling, treatment modalities and appropriate referral for Xeroderma Pigmentosum. Recommended management should be focused on educating the patient and the parents about effective sun protection and early recognition of cancers. Genetic counseling should be offered for families at risk

**Keywords:** Genetic, Premalignant, Xeroderma Pigmentosum

## 1. Introduction

Xeroderma Pigmentosum ('dry pigmented skin') is a hereditary autosomal recessive disorder characterized by mucocutaneous and ocular hypersensitivity to ultraviolet

(UV) radiation with irreparable DNA damage and subsequent malignant changes; and in some subjects also by progressive neurological degeneration [1]. It is estimated to affect about 1 in 1 million people in the United States and Europe. The condition is more common in Japan, North Africa, and the Middle East [2]. XP equally affects males and females.

Incidences in Northern African and Western Asian countries, such as Libya, Tunisia, Morocco, and Pakistan, may be higher due to more frequent consanguineous marriages, however, consanguinity is not felt to account for the entirety of the variations worldwide [3]. XP was first described by Hebra and Kaposi in 1874, which is caused by a defective nucleotide excision repair (NER) system, which produces mainly skin, ocular and neurologic alterations [4]. This abnormality in DNA repair can lead to XP, Trichothiodystrophy (TTD), a combination of XP and Cockayne syndrome (XPCS) or infantile lethal cerebro-oculo-facio-skeletal syndrome [5].

The disease begins around the age of 1–2 years with photosensitivity and burning sensation after nominal sun exposure in 60% of cases causing hyper pigmentation and ichthyosis in sun exposed areas, a 1000-fold increase in the risk of basal cell carcinoma, squamous cell carcinoma and melanoma of skin and eyes [6]. Ocular manifestations are a major component of XP and early descriptions of the disease by Kaposi in the late 19<sup>th</sup> century included xerosis and clouding of the cornea. Ocular findings in XP include photophobia, conjunctivitis, ectropion, exposure keratitis leading to corneal opacification or vascularisation, pterygium, and neoplasia [7]. Neurological symptoms are progressive and may result in severe disability like mental retardation, hearing loss, spasticity, ataxia, polyneuropathy, seizures and epilepsy [8]. The average age at onset of tumors is 8 years according to Kraemer and Lee [9]. Here, we report a case of a 19 month old boy with Xeroderma Pigmentosum who presented with characteristic pigmentary skin changes, eye problems, developmental delay, acute respiratory infection and failure to thrive.

## 2. Case Report

A 19 month old male child of a 1<sup>st</sup> degree consanguineous parents got admitted into 250 Bed Hospital, Moulvibazar, Bangladesh, with the complaints of fever, cough and respiratory distress for 10 days. His mother mentioned that he had repeated attacks of similar respiratory illness since one and half month of age for which he was treated by different pediatricians time to time and also hospitalized several times. At the age of six months, when he was hospitalized second time for the acute respiratory tract infection, his mother noticed a localized hypo pigmented area around the intravenous cannula site of his left hand. The lesion started to spread out and rapidly involved the whole limb and then the lower limbs, abdomen, chest and face sparing the palm and sole. His mother described the skin lesion to be generalized, hypo and hyper pigmented area, non-edematous, non-erythematous, non-tender, not itchy but photosensitive.

There was no history of similar type of skin disorder in his family. Initially the skin lesion was treated by his family Pediatrician, but when the lesion was spreading, they rushed to the Dermatologist as per suggestion of their Pediatrician. The Dermatologist diagnosed him as a case of Xeroderma Pigmentosum clinically. His parents consulted two other

qualified Dermatologists for further confirmation of the initial clinical diagnosis and all opined the same. During the course of this illness, he was also referred to the Ophthalmologist for continued watering of the eyes and photophobia; diagnosed as having nasolacrimal duct obstruction (NLDO) and refractive error and was treated accordingly.



**Figure 1.** Case patient at 19 months of age with generalized hypo & hyper pigmented macule.



**Figure 2.** Pigmentary changes in Xeroderma Pigmentosum.

He was delivered at term by normal vaginal delivery. His antenatal, natal and immediate postnatal histories were uneventful. He was immunized as per the expanded program of immunization (EPI) schedule. Regarding the motor development, his neck control was achieved at 5 months, sitting around 6-7 months and standing at 14-15 months of age. He can't walk till date but his other developmental domains were age appropriate. On examination, he was fretful. Vital signs were within normal limit. There was no lymphadenopathy, cyanosis or clubbing. Ear, nose, throat were normal, no dental caries. Occipitofrontal circumference (OFC) was 47 cm which lies on 25<sup>th</sup> centile in CDC chart (published 30th May, 2000). Anthropometry revealed that his weight was 7.17 kg, length 75 cm, weight for length <-3 standard deviation (SD) and length for age -2.8 SD. Skin survey revealed diffuse hypo and hyper pigmented macules distributed over face, trunk, back and extremities sparing the palm and sole. Hair distribution and nail apparatus was

normal. There was no mucosal involvement, nor any ulceration or growth elsewhere. His eyes were sensitive to sunlight and exposure to light causes watering and redness. Systemic examination revealed no abnormality. During the course of his illness the following investigations were done by different physicians: complete blood count (CBC)- Hb 12.5gm%, TC 16000/cmm, Neutrophil 56%, Lymphocytes 29%, Platelets 4,40,000/cmm; serum IgE- 90 IU/ml. Now, he is being treated and under regular follow up by a multidisciplinary team involving a Pediatrician, Dermatologist and Ophthalmologist.

### 3. Discussion

XP being a diagnostic challenge in most health facilities is also difficult to manage in severe cases. With a mortality rate of 40% before the age of 20, mostly due to melanoma and metastatic squamous cell carcinoma, not many treatment options are available [10]. Seven complementation groups, XPA through XPG, corresponding to defects in the corresponding gene products of XPA through XPG genes, have been described. These entities occur with different frequencies (e.g., XPA is relatively common, whereas XPE is fairly rare), and they differ with respect to disease severity (e.g., XPG is severe, whereas XPF is mild) [10]. Defects in nucleotide excision repair lead to premature sunlight-induced damage including hypo & hyper pigmentation, lentigos, telangectasias, actinic keratoses, and atrophy [11]. Cutaneous symptoms usually present before 2 years of age, and the median age of first skin neoplasm is under 10 years. In our case, skin manifestation was first noticed at the age of six month. These children may present with ocular changes before skin lesions like photophobia, keratitis, atrophy of the skin of the lids, cataract, and eye tumors [12]. In this case, the ocular manifestations were photophobia, refractive error and NLDO.

Over and above its defects in the repair genes, UV-B radiation also has immunosuppressive effects that may be involved in the pathogenesis of Xeroderma Pigmentosum [10]. Although typical symptoms of immune deficiency, such as multiple infections, are not usually observed in patients with Xeroderma Pigmentosum, several immunologic abnormalities have been described in the skin of patients with Xeroderma Pigmentosum. Various other defects in cell-mediated immunity have been reported in Xeroderma Pigmentosum. These include reduced natural killer cell activity, decreased ratio of circulating T-helper cells to suppressor cells, impaired cutaneous responses to recall antigens, impaired lymphocyte proliferative responses to antigens and impaired production of interferon in lymphocytes [10].

Progressive neurologic symptoms are present in about 25% of affected patients [11]. Neurologic abnormalities include cognitive impairment, acquired microcephaly, abnormal motor activity, areflexia, sensorineural hearing loss, and abnormal speech [11]. Studies suggest that neuronal degeneration in XP is a primary process, possibly caused by the inability to repair DNA that has been damaged by oxidative damage from endogenous metabolites [11]. This

patient presented with delayed motor milestone of development.

No consistent routine laboratory abnormalities are present in Xeroderma Pigmentosum cases. The diagnosis of Xeroderma Pigmentosum is usually established by studies performed in specialized laboratories [13]. These include cellular hypersensitivity to UV radiation and chromosomal breakage studies, complementation studies and gene sequencing to identify the specific gene complementation group [13]. Prenatal diagnosis is possible by amniocentesis or chorionic villi sampling [14]. This case was diagnosed clinically due to the lack of facilities for genetic confirmation.

### 4. Conclusion

XP is rarely diagnosed at the district (secondary level) hospitals in Bangladesh. Management of such a case is difficult for doctors working at the sub-district (primary level) or district (secondary level) hospitals. From this point of view, this case is being reported to create awareness about XP among the root level doctors of rural Bangladesh. A broad avoidance of sun exposure is obligatory, including the use of sunscreens with high factor ratings, long-sleeved protective clothing, wide-brimmed hats and UV-absorbing eye glasses when outdoors. It is also advisable to use films with UV filters on window glass and to check the environmental UV level with UV-measuring devices. All sources of UV radiation in the home, school or work environment should be identified and eliminated, if possible [15]. Individuals should be taught to recognize new lesions and monitor for any changes, including size and color, in pre-existing skin lesions for early detection of cancer. Genetic counseling should be offered for families at risk [15].

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