Original Article

Four Cases of Xeroderma Pigmentosum in a Pakistani Family

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Pak J Ophthalmol 2014, Vol. 30 No. 4

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Xeroderma pigmentosum (XP) is a rare autosomal recessive genetic disorder resulting from the defective repair of DNA, damaged by exposure to ultraviolet radiation. This case series is focused on a Pakistani family with 4 of its members suffering from XP. An 11 year old girl belonging to this family presented to us with substantial loss of vision in right eye, intolerance to light and mild pain for the past 4 years. Her visual acuity was hand movement in the right eye and no perception of light in the left. On examination multiple hypo- and hyper pigmented areas of skin around the eyes were visible. Her signs and symptoms together with positive family history helped us reach the diagnosis of XP.

Xeroderma Pigmentosum (XP), first described by Hebra and Kaposi in 1874,[1] is a rare autosomal recessive genetic disorder. It is characterized by faulty repair of DNA damage induced by ultraviolet radiation. XP occurs worldwide, affecting all age groups, both sexes and all racial groups. The basic deficiency lies in the nucleotide excision repair (NER), a mechanism responsible for recognizing and repairing bulky DNA damage caused by environmental and other exposures, thus resulting in the clinical manifestations. Fibroblasts in normal human skin can repair damage caused by exposure to UV radiation. However, in patients with XP, this ability of fibroblasts is slower or completely absent.[2] XP have many consequences including skin cancer, ocular abnormalities (e.g., conjunctivitis, ectropion and corneal opacities) and neurological anomalies resulting in decreased reflexes, progressive hearing loss and mental retardation.[3] Here, we describe four cases of this disease in a single Pakistani family.

OUR XP FAMILY

An 11 year old girl, resident of Karachi, Pakistan presented to us with complaints of loss of vision in her right eye, intolerance to light and mild pain and ocular irritation for the past 4 years. The symptoms had increased in the last 4 months. Her left vision was completely lost 3 years back. She had a strong family history of XP. Four out of her 7 siblings suffered from it. Two elder siblings, one elder brother and one elder sister, died because of XP – related complications at ages 18 and 9 respectively. Their parents were first cousins. On examination multiple hypo and hyper pigmented areas of skin around the eyes were visible. Similar lesions were observed on the scalp with loss of hair. There was no evidence of systemic malignancy. Her visual acuity in the right eye was hand movement. Her left eye was phthysical with no perception of light. Examination showed right eye madarosis, completely opaque and dry cornea with peripheral corneal vascularization. Based on her signs and symptoms and the associated family history, a clinical diagnosis of xeroderma pigmentosum was confirmed.

DISCUSSION

We reported a single Pakistani family with 4 of 7 siblings affected by severe xeroderma pigmentosum. Two of them died at the age of 9 and 18 years, respectively, while the two survived with unilateral blindness and extreme sensitivity of the skin.

Fig. 1: A picture of the family including the patient and her siblings affected by XP

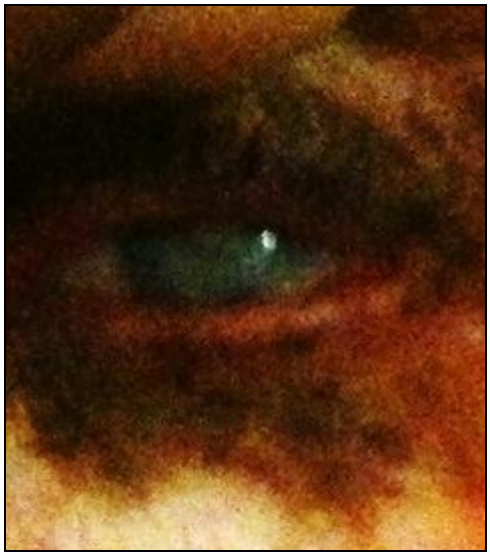

Fig. 2: Picture taken while examining the patients' eye (left or right). Visible pigmentation of skin near the eye

There are multiple manifestations of XP including cutaneous, ocular and neurological - some more prevalent and severe than others. For example, among 36 cases studied by Bhutto and colleagues(18 males and 18 females, age range 2 - 30 years)[4] in the dermatology unit of a tertiary care hospital in Larkana or medical camps in remote areas over a period of seven years, two thirds had severe disease. They also found that 29 (81%) cases had ocular symptoms including photophobia, conjunctivitis, corneal keratitis and lid ulcer. One patient had complete bilateral loss of vision.

Both the family members we examined had unilateral loss of vision and severe ocular damage. It is well-established that ocular changes are more common in the tissues exposed to UV light, such as the eyelids, conjunctiva, cornea, and the lens.[5] Photophobia is often the first symptom to appear followed by pigmentation of eyelids, madarosis, ectropion and lower lid cancer. Conjunctival damage results in xerosis, telangiectasia, chronic congestion, and pigmentry changes whereas involvement of the cornea results in dryness, exposure keratitis, hazyness, band-like nodular keratopathy and scarring and ulceration, resulting in severe visual impairment. Other reasons for visual loss in XP patients could be pterygium, tumour invasion from the limbus, and corneal vascularization.[6]

The diagnosis of XP in this case series was based on clinical findings and positive family history. Unfortunately, diagnostic tests were not available in our setting.

Although there is no cure for XP, an important measure of protection from sunlight is adopted to overcome skin damage. This is carried out by covering windows with UV resistant films and application of sun screen on exposed skin. Since avoiding sunlight may result in Vitamin D deficiency, it is advisable to prescribe Vitamin D supplements. Other protective actions like frequent eye examinations and removal of pre-cancerous lesions are also advised. More importantly the patient is offered psychological support to improve his quality of life. The common problems that need to be addressed here are feelings of isolation and career prospects. There are XP support groups in developed countries such as France, Germany, UK and USA. They offer a wealth of advice and help. Unfortunately, such groups do not exist in our part of the world and need to be established. Moreover, genetic counseling and testing is also an important component of its prevention which is not readily available in Pakistan.

In conclusion, the four cases of XP we reported had devastating ocular consequences.

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