

Overview of Xeroderma Pigmentosum Mutations, Prognosis, and Treatment

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Short Communication

Xeroderma Pigmentosum (XP) is a rare disorder, first described by Hebra and Kaposi [1]. Cleaver provided a clear understanding of XP as it played a central role in DNA mutation in cancer [2].

This rare disorder is an autosomal recessive skin disorder where cells are unable to repair the damage caused by UV radiation. This leads to early skin changes, sunburns, dry skin and increased development of skin tumors and damage to the eyes brought on by UV light. Although rare, XP is present throughout the world in majority of ethnicities. Current statistics indicate that there are approximately 100 diagnosed cases in the UK. Furthermore, 1 in 1 million incidences are reported in the US. In addition, high rates have been reported in certain areas such as Japan and the Middle East.

Mutations in nucleotide excision repair brought on by UV damage, lead to XP. Several types of this disorder have been characterized by XPA-XPG, with an 8th type known as xeroderma pigmentosum variant (XPV), formerly known as Pigmented Xerodermoid [3].

Individuals with XP initially present with photosensitivity, skin changes and high incidence of skin cancer at a very young age. Skin changes in these patients are first seen in areas with great exposure to light, such as the face. Skin characteristics include, marked freckles on sun-exposed areas seen in children, typically before the age of two; photosensitivity-acute sun sensitivity in the form of a sunburn, first seen in infancy; xerosis (dry skin); poikiloderma-irregular patches of hyperpigmentation and hypopigmentation, telangiectasia and atrophy; skin cancers developing at an early age (4 or 5 years old)-seen in the form of solar keratosis (pre-malignant), squamous cell carcinoma, basal cell carcinoma and malignant melanoma [4].

Along with symptoms present on the skin, XP has some effects on the eyes, which include, photophobia; conjunctival inflammation and keratitis-which can lead to corneal opacification (becoming opaque) and vascularization; tumors of conjunctiva and eyelids (benign or malignant); eyelids may be pigmented, loss of lashes may occur or atrophy which can lead to ectropion (eyelids protruding outward) or entropion (eyelids protruding inward) [5]. In addition to skin and eye complications, neurological symptoms are presented in 20 to 30% of patients with XP [6]. These include, acquired microcephaly, diminished or absent deep tendon stretch reflexes, progressive sensorineural hearing loss, and progressive cognitive impairment. Other possible features include: hyporeflexia, sensorineural deafness, spasticity, poor co-ordination and seizures.

Prognosis of XP varies based on the severity of the genetic disorder, avoidance of UV light as well as monitoring possible dangers and difficulties in relation to screening for the disorder. In the past, prognosis was a reduced life expectancy as a result of skin cancers or

neurological complications [7]. However according to recent research, normal lifespan is possible for patients without neurological problems who are cautious about exposure to UV and protecting the skin.

In terms of treatment for XP, there is no specific treatment to date. Management techniques are available and encouraged for patients suffering from this disorder. Protection from UV light greatly improves prognosis and reduces skin changes and cancers, achieved by: avoiding outdoor activities during the day; covering the body and skin with long opaque clothes, sunhats and UV protective sunglasses. Furthermore, some indoor lighting emits UV and these lights need to be changed or covered to avoid emission of UV [8]. In addition to management techniques, surveillance and monitoring by a dermatologist and ophthalmologist is recommended. Drug treatments are available for dealing with symptoms and this includes vitamin D supplements (for lack of exposure to sunlight) [9], emollients for dry skin, artificial tears for dry eyes, high-dose oral isotretinoin for preventing new neoplasms, T4N5 lotion which contains a bacterial enzyme T4-endonuclease V, which repairs some DNA defects [10]. In addition to drug treatments, genetic counselling as well as support and counselling for patients and families are available, in terms of managing and coping with the disorder.

To sum it all up, XP is a rare disorder caused by inherited defects in UV damage nucleotide excision repair pathway, occurring in children as young as 2 years of age. Treatment for this disorder is still not available but patients have to take precautions and learn to manage and cope with the disorder.

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