Xeroderma Pigmentosum

Xeroderma pigmentosum (XP) is a skin disorder that is caused by defective nuclear excision repair genes, which causes pyrimidine dimers to accumulate. XP is inherited in an autosomal recessive fashion with patients being susceptible to UVA and UVB sunlight rays. Patients with XP may present with several clinical features including actinic keratosis (AK), neurodegeneration, photosensitivity, corneal ulcers, and hyperpigmented lentigines. XP also carries an increased risk of skin cancer (basal cell carcinoma and malignant melanoma in particular).

PLAY PICMONIC

Pathophysiology

Defective Nucleotide Excision Repair

Scared-exorcist with Evil Nuclear-toad and Falling Repair-hammer

In nucleotide excision repair, damaged bases are cut out within a string of nucleotides and replaced with DNA as directed by the undamaged template strand. Patients with XP are unable to repair DNA pyrimidine dimers caused by UV exposure.

Pyrimidine Dimer Accumulation

Pyramid-dimes

Pyrimidine dimers are photolesions caused by UV radiation in sunlight. This radiation forms covalent links between adjacent pyrimidine bases on the same strand of DNA. These dimers distort the shape of DNA and prevent the accurate copying of DNA. Pyrimidine dimers are usually removed by nucleotide excision repair, but since this mechanism is defective in patients with XP, these dimers accumulate and can lead to mutations and cell death.

Autosomal Recessive

Recessive-chocolate

XP is a disease that is inherited in an autosomal recessive pattern. In an autosomal recessive disorder you inherit two mutated genes, one from each parent. These disorders are usually passed on by two carriers. With each pregnancy, two carriers have a 25 percent chance of having an unaffected child with two normal genes, a 50 percent chance of having an unaffected child who is also a carrier, and a 25 percent chance of having an affected child with two recessive genes.

Susceptible to UVA and UVB Rays

UV-sunlight grabbing an A-apple from B-bee

Patients are susceptible to ultraviolet rays A and B due to having a defective nucleotide excision repair system, which means that the damage caused to the DNA by these UV rays cannot be repaired.

Presentation

Actinic Keratosis

Acting Carrot-toes

XP patients develop actinic keratosis. Actinic keratosis is a premalignant skin condition, which is also called solar or senile keratosis. The lesions from this skin disorder are caused by sun exposure and present as small, rough, erythemetous patches of skin. These lesions are precursors to skin cancer.

Neurodegeneration

Degenerating-nerve

UV radiation does not reach the brain because of shielding from the scalp and bones of the skull. It has been hypothesized that oxidative DNA damage generated through metabolism or other sources might produce DNA damage that is not repaired in the non-dividing cells of the nervous system leading to progressive neuronal death. About 30 percent of people with XP develop progressive neurological abnormalities. These abnormalities can include hearing loss, poor coordination, difficulty walking, movement problems, and seizures.

Photosensitivity

Photo-camera causing Sensitive-tears from Vampire

The defective nucleotide excision repair in patients with XP results in damage to multiple cell types. In skin cells, extreme light sensitivity will be seen. Because of this, many affected children develop a severe sunburn after spending just a few minutes in the sun. The sunburn causes redness and blistering that can last for weeks.

Corneal Ulcers

Corn-eyes in Ulcer-volcano

The eyes of patients with XP may be painfully sensitive to UV rays from the sun. If the eyes are not protected from the sun, the cornea may become cloudy and develop ulcers. In addition to an increased risk of eye cancer, XP is associated with noncancerous growths on the eye. Many of these eye abnormalities can impair vision.

Hyperpigmented Lentigines

Hiker-pig with Hyperpigmentation and Lion-tiger

Due to the lack of DNA repair caused by UV radiation, the skin will begin to damage and by age 2, almost all children with XP develop freckling of the skin and macular, well-circumscribed hyperpigmented lesions referred to as hyperpigmented lentigines in sun-exposed areas (such as the face, arms, and lips).

Considerations

Increased Risk of Skin Cancer

Up-arrow-risk on Skin-suit and Tumor-guy

Without sun protection, about half of children with XP develop skin cancer by age 10. Most people with xeroderma pigmentosum develop multiple skin cancers during their lifetime including basal cell carcinoma and malignant melanoma.