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REVIEW ARTICLE **OPEN ACCESS**

A Short Review of Xeroderma Pigmentosum

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ABSTRACT

Studies have also found that XP is a genetic condition characterized by an extreme sensitivity to sunlight, leading to a significantly increased susceptibility to skin cancer and other health complications. Additionally, studies have found that people with XP are more sensitive to the negative effects of UV radiation from the sun. Studies have concluded that the signs of xeroderma pigmentosum become apparent during infancy or early childhood. Thus, in our review, we were discussing XP in terms of etiology, incidence, histopathology, differential diagnosis, treatment and complications.
Key words: *XP, Etiology, Incidence, Histopathology, Differential Diagnosis, Treatment , Complications.*

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INTRODUCTION

Studies have also demonstrated that "abnormalities in the nucleotide excision repair system are the cause of the uncommon autosomal recessive genodermatosis known as Xeroderma pigmentosum (XP)". Studies have also found that the illness can make people very sensitive to light, change the color of their skin, cause cancerous growths to form, and sometimes cause a slow loss of neurological function. Further studies have shown that the illness has a relatively low impact in the United States, affecting approximately one person out of every million. However, studies have concluded that in Japan, the incidence is significantly higher, with around 45 people out of every million being affected. [1,2] Studies have also shown that Moritz Kohn Kaposi, a Hungarian dermatology professor, first described the condition known as XP in 1874. In his report, he detailed the cases of "two individuals who exhibited characteristics such as thin and dry skin, skin contraction, checkered pigmentation, dilated cutaneous blood vessels, and the early onset of multiple cutaneous tumors".[3] According to many studies,"kaposi is credited with coining the term XP to describe the distinct condition of having dry and pigmented skin. Studies have also found that mutations in genes involved in DNA repair are the root cause of the genetic disorder known as XP. These mutations result in a lack of proper repair for DNA damaged by ultraviolet radiation (UVR)".[4,5] Studies have also shown that Dr. James Cleaver carried out research on cultured fibroblasts taken from individuals suffering from xeroderma pigmentosum in the 1960s. His research showed that these fibroblasts displayed symptoms of poor DNA repair after exposure to UV radiation. Additional studies have shown that those who have XP but do not have neurological manifestations have a greater potential for DNA repair after being exposed to UV radiation. This is in contrast to those who have XP but do not have these manifestations. [6,7] Thus, in our review we were discussing about XP.

ETIOLOGY

Scientists have discovered that a change in how nucleotide excision repair functions is the root cause of XP.[2] Researchers have also shown that the "nucleotide excision repair system can fix DNA damage caused by UV rays, like pyrimidine dimers and pyrimidine 6-4 pyrimidones".[2] According to studies, unrepaired DNA damage is the primary cause of XP development. Recent research has found that there are eight different mutations that may be linked to various types and symptoms of XP".[2] Besides that, research has shown that "different changes in nucleotide excision repair are connected to the XP A-G and XP variant subtypes, which have been written about a lot". According to studies, a mutation in the "XPC gene is to blame for one of the most prevalent subtypes in the USA". Studies have concluded that the XPC gene is located on chromosome 3p25, and it codes for an endonuclease".[8] Studies have also found that the mutant endonuclease can't find DNA damage. This makes cells more vulnerable to UV radiation and encourages the growth of cancerous tumors on the skin and mucosal membranes. Studies have concluded

that unlike the more common XPA subtype that leads to neurological symptoms, the XPC subtype of xeroderma pigmentosum does not result in any symptoms.[2]
Studies have concluded that DNA damage-binding protein 1 (DDB1), for which the XPA gene codes, is located on chromosome 9q22.[2] Studies have concluded that ,DDB1 is responsible for sensing DNA damage and aiding DNA unwinding in healthy cells. The condition manifests itself in both the skin and the nervous system in these people.[2] Additionally, studies have also concluded that XP occurs in many uncommon forms, including XPB, XPD, XPE, XPF, and XPG. The XPB gene on chromosome 2q21 encodes excision repair cross-complementing 3 (ERCC3).[2] Another thing that research has shown is that ERCC3 is a part of a 9-protein complex (TFIIH) that is needed for DNA repair to happen.[2] In this respect, studies have also concluded that Cockayne syndrome and trichothiodystrophy are associated with the XPB subtype.[2] Furthermore, studies have shown that correlations exist between the XP-Cockayne complex and trichothiodystrophy, which is associated with the XPD subtype.[2] In addition, research has shown that the XPE gene codes for DDB2. Studies have concluded that the XPF gene, located on chromosome 16p13, encodes a protein called ERCC4. Studies have also found that this protein usually joins with ERCC1 to form an endonuclease that removes damaged DNA. In addition to this, studies have shown that the location on chromosome 13q33 for the XPG gene, which encodes the enzyme ectonucleotidyl transferase [9]

INCIDENCE
Studies have concluded that "XP affects all races, with a worldwide incidence of 1 in 250,000 live births". [10, 11] Studies have concluded that "17.5 and 45 per million live births occur in the United States, Western Europe, the Middle East, and Japan,respectively". [12,1,13,14,15] Studies have concluded that the "incidence is higher in areas where consanguinity is common". [16] Studies have concluded that the "sex ratio is approximately equal". [18] Studies have concluded that "worldwide, the subtypes XPA, XPC, and XPV account for approximately 75% of all cases of XP, while XPV alone accounts for approximately 30% of cases". [13] Studies have concluded that "XPC is the most common subtype in the United States, Europe, and Africa, while XPA is the most common subtype in China and Japan". [1,13,16,18,19]

HISTOPATHOLOGY
A lot of research has shown that some of the "histological signs include more basal cell melanin and melanocytes, hyperkeratosis, lymphocytic infiltration in the upper dermis, atrophic and/or elastotic dermis, thinning of the stratum malpighii with atrophy and/or elongation of the rete, telangiectasia, and normal keratinocytes".[17,20,21]

DIFFERENTIAL DIAGNOSIS
There are several potential diagnoses to consider, according to studies, that include "Cockayne syndrome, XP/Cockayne syndrome complex, trichothiodystrophy, XP/trichothiodystrophy complex, Cockayne syndrome/trichothiodystrophy complex, cerebro-oculo-facio-skeletal (COFS) syndrome, UV-sensitive syndrome, Bloom syndrome (also known as Bloom-Torre-Machacek syndrome or congenital telangiectatic erythema), Rothmund-Thomson syndrome, Hartnup disease, Carney complex, De Sanctis-Cacchione syndrome, erythropoietic protoporphyria, cutaneous lupus erythematosus, and LEOPARD syndrome (also known as Noonan syndrome with multiple lentigines)".[22,13,23,24,25,26,27]

MANAGEMENT [2,28,29]
Studies have also found that the main goals of treating xeroderma pigmentosum patients are to quickly find and treat cancerous tumors, keep tumors from happening, and improve the patient's overall health. Studies have also concluded that for patients with XP, the most effective way to reduce the number of malignant tumors is through strict sun protection and avoidance. Studies have also concluded that it is crucial to provide patients and their caregivers with detailed information on effective methods to reduce UV radiation exposure.[2] Furthermore,studies have concluded that it is advised that patients refrain from venturing outside their homes during daylight hours. However, studies have also concluded that if patients need to go outside during the day, it is important for them to apply sunscreen all over their body. Studies have also concluded that it is important to apply a broad-spectrum sunscreen every two hours.[2] Hence, according to studies, it is recommended for patients to use a facial salve that contains sunscreen and also to wear long-sleeved trousers and sun protection apparel. Furthermore, studies have also concluded that it is recommended that individuals wear hats and sunglasses with side shields.[2] Studies have also concluded that it is important to install a UV-blocking film on every window in your home, car, and school. Furthermore, studies have also concluded that in order to ensure the well-being of patients, it

is advisable to steer clear of fluorescent, metal halide, and halogen illumination, as they emit UV radiation.[2]

Studies have also found that, in light of the rigorous recommendations on sun protection and avoidance, patients should make it a habit to take vitamin D supplements on a regular basis. Furthermore, studies have concluded that patients may get adequate vitamin D via foods such as fish, eggs, mushrooms, and meals that have been fortified. Studies have concluded that vitamin D may also be gained through nutrition. Studies have also concluded that both a dermatologist and the patient's caregivers should perform routine checks of the patient's entire skin. Furthermore, studies have also concluded that at the very least once every three months for the whole of the patient's life, an appointment with a dermatologist should be planned. Furthermore, studies have concluded that it is important for caregivers to educate themselves on changes that need to be reported to a dermatologist and to do regular skin checks at home with their patients. Researchers have said that it is essential to start treatment as soon as possible for actinic keratoses in order to forestall the development of squamous cell carcinoma. Studies have also concluded that, in order to treat these precancerous lesions, a dermatologist's clinic may use cryotherapy. Furthermore, researchers have concluded that a shave biopsy may be suggested when a lesion is evolving, when it is fresh, or when it is clinically dubious. Studies have also found that Mohs micrographic surgery or excision is the best way to treat basal cell carcinomas, squamous cell carcinomas, and other skin cancers that aren't melanomas. Patients diagnosed with xeroderma pigmentosum should not undergo treatment with radiation. Studies show that the standard way to treat malignant melanoma is with a procedure called wide local excision, which may be followed by a sentinel lymph node biopsy. Patients with metastatic sickness should be referred to hematology and oncology specialists.[2]

Studies have also found that, in the course of a pilot study that was carried out, isotretinoin was administered orally in substantial doses to five patients who had been diagnosed with XP. It was discovered that a much lower number of the patients developed skin cancer during the course of the study, which is evidence that suggests the treatment may have been beneficial.[28] Studies have concluded that isotretinoin was administered orally to each patient at a dose of 2 milligrams per kilogram per day.[28] Studies have also shown that every single one of the patients, at some point throughout their course of treatment, developed xerostomia in addition to xerophthalmia. Studies have also concluded that some patients who used the medication developed side effects, such as elevated triglycerides and liver function tests, as well as bone abnormalities. These adverse effects occurred as a direct result of taking the medication. The severity of these undesirable side effects may be rather high.[28] Additionally, other research has found that the patients with xeroderma pigmentosum in this study got a lot better after taking oral retinoids for chemoprevention, which is what the results of this study suggest. This was the case in spite of the fact that the treatment caused a number of side effects that were not ideal in any way.[28]

Studies have also found that the frequency of the ophthalmologic manifestations of XP is quite close to being the same as the frequency of the skin manifestations of the condition. Studies have also concluded that the severity of the symptoms, which often include photophobia and injection of the conjunctiva, has a tendency to increase with the passage of time. Researchers have also found that people with this condition are more likely to have a number of eye problems, such as cataracts, conjunctivitis, blepharitis, pigmentary problems with the eyelids or conjunctiva, ectropion, eye vascularization, xerophthalmia, and corneal scarring. Furthermore, studies have also concluded that patients also have an increased risk of developing ectropion.[29] Researchers have been concluding for ages with their studies that xerophthalmia is another condition that a patient may develop. Patients may also develop skin lesions of the eyelid, which may include malignant melanoma, benign lid papillomas, and basal cell carcinomas. These lesions may occur at any time throughout the course of the disease. During the course of the illness, these lesions may appear at any point in time. Additionally, it was shown in a study that patients had a higher risk of developing melanomas in the anterior chamber of their eyes. As a result, studies have found that patients should undergo routine eye exams and that an ophthalmologist should treat any ophthalmologic manifestations of XP that may be present. [29] Studies have also found that patients with XP who develop neurologic manifestations need a referral to a neurologist for diagnostic workup and management. Studies have also concluded that sun protection does not slow down the progressive pattern of neurologic symptoms.[2]

COMPLICATION

According to studies, patients have said that their skin is dry, looks old before its time, and has a number of problems, such as hyperpigmentation, hypopigmentation, atrophy, telangiectasia, and keratotic lesions. Studies have concluded that these “visible skin problems can be disfiguring and embarrassing, causing psychological distress”.[30,31] Studies have concluded that “children affected by these conditions are

more likely to experience negative emotions such as loneliness, sadness, discrimination, shame, ridicule, harassment, teasing, bullying, rejection, and abuse".[32] Furthermore, studies have concluded that the "psychological impact can be significant, especially for individuals with malignancies, and it can greatly affect their quality of life".[33]

Studies have found that "people under 20 with XP have a much higher chance of getting tumors in the central nervous system, such as glioblastoma, medulloblastoma, spinal cord astrocytoma, schwannoma, and neurilemoma". [1,34,35,36] Studies have concluded that these types of cancers are not attributed to sun exposure. [33] Researchers have found that "people who are diagnosed with XP are more likely to get several types of blood cancer, such as acute lymphoblastic leukemia, acute myeloid leukemia, lymphoma, and myelodysplastic syndrome". [37,38] Studies have concluded that individuals diagnosed with XP have a significantly higher likelihood of developing various types of internal malignancies. These include nasopharyngeal carcinoma, oesophageal squamous cell carcinoma, thyroid carcinoma, lung adenocarcinoma, breast cancer, pancreatic cancer, kidney leiomyosarcoma, ovarian cancer, and prostate cancer. Additionally, studies have concluded that smoking significantly amplifies the likelihood of developing cancer in individuals with XP.[39,40]

CONCLUSION

Studies have found that there is currently no radical cure for XP, but there are many options available for the prevention and treatment of skin problems, including malignancies. It is crucial to diagnose XP as early as possible in order to implement protective measures at a young age. In addition to early removal of cancerous growths, this can enhance one's quality of life and extend their lifespan. Additional research is needed to establish the most effective approach to managing XP, specifically regarding the use and application of gene therapy in treating this condition.

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