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CLINICAL IMPROVEMENT OF A PATIENT WITH XERODERMA PIGMENTOSUM AFTER TREATMENT WITH UKRAIN: A CASE REPORT

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Summary: *Xeroderma pigmentosum (XP) is a rare genetic defect of the skin DNA reparation system. The author presents a case report of a patient with XP, successfully treated with Ukrain. Future studies should be performed to define the best therapeutical schedules of Ukrain in the treatment of this disease.*

Introduction

Xeroderma pigmentosum (XP) was first described in 1874 by Hebra and Kaposi (1). In 1882, Kaposi coined the term for the condition, referring to its characteristic dry, pigmented skin. XP is a rare disorder transmitted in an autosomal recessive manner. The prevalence in Europe and the United States is approximately one case per 250,000 population, and in Japan, one case per 40,000 population. There are fewer than 1,000 known cases of XP worldwide. Cases of XP are reported in all races with equal distribution between males and females (2).

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The disease manifests at age one or two years. Patients with XP have a severe sensitivity to all sources of ultraviolet (UV) radiation, especially sunlight, and they develop serious sunburns with onset of poikiloderma in light-exposed skin. The range of symptoms is wide: blindness and deafness, blistering or freckling on minimal sun exposure, developmental disabilities, dwarfism and hypergonadism, increased skin and eye cancers, and mental retardation (3). Squamous cell carcinomas, basal cell carcinomas and malignant melanomas can appear in childhood. The majority of patients die before reaching adulthood because of metastases.

XP is based on a genetic defect in the DNA repair system. This defect is in nucleotide excision repair (NER), leading to deficient repair of DNA damaged by UV radiation (4). Seven XP repair genes, XP-A through XP-G, have been identified. These genes play key

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roles in global genome (GG)-NER and transition-coupled (TC)-NER. Both forms of NER include a damage-sensing phase, performed in GG-NER by the product of the XP-C gene complexed to another factor. In addition, the XP-A gene product has been reported to have an affinity for damaged DNA. Therefore, it is likely that XP-A also plays a role in the damage-sensing phase (5).

Genetically, XP is divided into seven complementation groups (XP-A to XP-G) corresponding to defects in the corresponding gene products of XP-A to XP-G genes and the XP variants (XP-V). These entities occur with different frequencies (*e.g.,* XP-A is relatively common and XP-E is fairly rare), and they differ with respect to disease severity (*e.g.,* XP-G is severe and XP-F is mild) and clinical features. Group XP-C is the most common form in Europe and North America, while group XP-A is the most common form found in Japan (6).

Diagnostically, assignment to the specific complementation group is made according to the fusioning of XP fibroblasts (5, 7). Differential diagnosis must distinguish XP from other so-called DNA-repair-deficiency syndromes, such as Cockayne syndrome and trichothiodystrophy (1).

In addition to the defects in the repair genes, UV-B radiation also has immunosuppressive effects that may be involved in the pathogenesis of XP. Although typical symptoms of immune deficiency, such as multiple infections, are not usually observed in patients with XP, several immunologic abnormalities have been described in the skin of patients with XP. Clinical studies of the skin of patients with XP indicate prominent depletion of Langerhans' cells induced by UV radiation. Various other defects in cell-mediated immunity have been reported in XP. These defects include impaired cutaneous responses to recall antigens, decreased circulating T-helper cells-to-suppressor cells ratio, impaired lymphocyte proliferative responses to mitogen, impaired production of interferon in lymphocytes, and reduced natural killer cell activity (8).

In XP, DNA damage is cumulative and irreversible, and treatment is limited to avoidance of exposure to UV radiation by staying indoors with sunlight blocked out and the use of protective clothing, sunscreens, and eyeglasses (9). There is no cure for XP and each advance in treatment should be discussed. We present a case of XP successfully treated with Ukrain (NSC 631570).

Case report

The patient, born in 1985, was diagnosed with XP at an early age. The short summary of clinical course below shows the progression of disease and total failure of palliative treatment.

In August 1996, the skin of the dorsum of the nose, the upper lip, the front parts of the cheeks and the right interior eyelid was ablated and substitutive dermatoplasty was performed.

In January 1997, the skin of the whole forehead, the superior and interior eyelid, and the nasolabial region was ablated with subsequent substitutive dermatoplasty. Six basaliomas, four squamous cell carcinomas, five precancerous keratosis, two regions of eczema and one nevoid lentigo were also ablated.

In October 1997, squamous cell carcinoma of the left part of the chin and pyogenic granuloma of the right interior eyelid were ablated, and total substitutive dermatoplasty of the right superior and interior eyelid and periorbital region, and implantation of tissue expanders (300 ml) were performed.

In April 1998, skin expander explantation was carried out, and different carcinomas, basaliomas and precancerous lesions in the face region were ablated, followed by substitutive dermatoplasty of the chin and nasolabial region.

In February 1999, a basalioma-like growing squamous cell carcinoma of the right inferior eyelid was resected and followed by plastic cheek reconstruction and conjunctive mobilization; excision of the left cheek, right eyebrow and right supraclavicular region basaliomas was performed, and postoperative skin defects were corrected plastically.

In August 1999, a malignant melanoma (1.20 mm thick; level IV; stage Ib; pT 2) in the region of the right hip was ablated, along with retroauricular (right) and helix (left) squamous cell carcinomas.

In September 1999, squamous cell carcinomas of the concha (the region of the left helix) and the throat, nevoid lentigo of the right hip and basalioma of the right popliteal surface were ablated.

In April 2000, diagnostic curettage of the basalioma and actinic keratosis of the throat took place, along with myxoid dermatofibroma of the right dorsum manus.

In August 2000, multiple basaliomas of the right and left ears, and of the right nostril and right cheek, along with squamous cell carcinoma of the right cheek were resected; an operation was performed to remove Bowen's disease on the right hand and under the costal margin, and a melanoma on the left cheek was excised.

All these diagnostic and therapeutic interventions were performed at different clinics, and consisted only of symptomatic tumor ablation with no attempts made to avoid new cancer lesions.

From September 2001 until the present date, the patient has been receiving Ukrain (Nowicky Pharma, Vienna, Austria) therapy: four ampoules a week intravenously, with topical Ukrain administration (application of 1 mg/ml of the drug solution with lesion bandage. One course of Ukrain lasts 2 months: 160 mg of Ukrain per course, with treatment interrupted for the following 2 months.

Results

Prior to the start of Ukrain treatment, more than 50 operations had been performed with the aim of skin tumor ablation. Since the start of Ukrain treatment, the only operations needed were to excise the following tumors: in July 2002, three little basaliomas and in March 2003 two basaliomas. Prior to Ukrain treatment, six to seven operations were performed. It is noteworthy that no malignant tumor has occurred since the start of Ukrain treatment.

Discussion

XP is usually detected at age one or two years. Individuals with this disease develop multiple cutaneous neoplasms at a young age. Two important causes of mortality are metastatic malignant melanoma and squamous cell carcinoma. Patients younger than 20 years have a 1,000-fold increase in the incidence of nonmelanoma skin cancer and melanoma. The mean skin cancer patient age is eight years in patients with XP, compared to 60 years in the healthy population (3, 10).

As there is no cure for the genetic disorder XP, the main goal of treatment is the prompt and complete removal of skin cancers by skin surgeons.

The treatment goal is to protect the patient from sunlight. Oral retinoids have been shown to decrease the incidence of skin cancer in patients with XP. This therapy is limited by dose-related, irreversible calcification of ligaments and tendons (4, 11). Complete excision of the malignancies associated with XP should be performed. The goals of pharmacotherapy are to reduce morbidity and to prevent complications (12). Fewer than 40% of patients survive beyond age 20 years. Individuals with milder disease may survive beyond middle age. The prominent results of treatment with Ukrain can be explained due to both its direct antineoplastic activity and its indirect immunomodulation. No side effects were observed during the treatment. Future studies should make clear the possible mechanisms of the phenomenon observed.

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