Case Report

Photoprevention with Oral *Polypodium leucotomos* Extract and Treatment with Medium-Depth Chemical Peeling in Xeroderma Pigmentosum: A Case Report

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Abstract

Early diagnosis of xeroderma pigmentosum (XP) is mandatory to establish adequate sun protection, and regular examinations to detect and treat the premalignant and malignant overgrowths as early as possible. Aqueous extract from the leaves of *Polypodium leucotomos* (PLE) attracts attention due to its photopreventive and anticarcinogenic properties; however, more experience is needed in patients with XP. Chemical peelings help to rejuvenate the photodamaged and cancer-prone skin. However, data about their use in patients with XP is scarce. Herein, we discuss our experience with oral PLE extract and medium-depth peeling in a 34-year-old female patient with XP and the treatment outcomes.

Keywords: Actinic keratosis, chemexfoliation, xeroderma pigmentosum, polypodium

Introduction

Xeroderma pigmentosum (XP) is an autosomal recessively inherited disorder characterized by increased susceptibility to photosensitivity and skin cancer formation due to defects in nucleotide excision repair genes that repair ultraviolet-damaged DNA.[1] The prevalence of XP is about 1/1000000 in the United States of America; however, it is higher in populations with more frequent parental consanguinity.[2]

Patients with XP experience various premalignant and malignant skin tumors and pigmentary changes, including multiple freckles, lentigines, actinic keratosis, melanoma, non-melanoma skin cancers, and sunburns from an early age. In addition, patients are at risk of ultraviolet-related ocular injury, progressive neurological degeneration, and worsening of skin disorders over time.[1]

Currently, there is no curative treatment for XP. Early diagnosis of XP is mandatory to establish adequate sun protection and regular examinations to detect and treat premalignant and malignant overgrowths as early as possible. Managing ultraviolet-damaged skin, actinic keratosis, field cancerization, dyspigmentation, and poikilodermatous changes is mandatory to prevent skin cancer. Chemoprevention and treatment with oral retinoids, topical imiquimod, and topical 5-fluorouracil, as well as physical modalities including various skin resurfacing options, (e.g., dermabrasion, chemical peelings, carbon dioxide or erbium-YAG laser), are frequently performed for XP patients.[1] However, even if the most appropriate and effective treatment is applied, the need to comply with the treatment and come for regular follow-up visits throughout the lifespan may be challenging for XP patients.

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Case Report

A 34-year-old woman with known XP since the age of 6 presented to the outpatient clinic with recurrent crusted lesions and brown spots on her face. She had a homozygous p.Ala656Val missense mutation in the *ERCC2* gene. She had no ocular or neurological findings and reported frequent sunburns, particularly during the summer months of childhood. The patient's parents had a third-degree consanguineous marriage, and two out of her three siblings had the same disease. During childhood, the patient only used moisturizer and sunscreen irregularly. Due to health insurance issues, she could not attend regular check-ups, use the recommended treatments, or be checked for internal malignancies, which may be associated with the ERCC2 mutation. She did not have any malignant skin tumors and had a history of actinic keratosis. On dermatological examination, erythematous, scaly papules were present on the dorsum of the nose and bilateral malar regions, along with widespread lentigines and generalized freckling on the face (Figures 1a, 2a, 3a).

Since the patient was not adherent to previously prescribed topical fluorouracil cream, due to local side effects such as irritation, erythema, and burning sensation, 3% diclofenac gel was recommended for use on the whole face. The patient regularly took 240 mg/d oral *Polypodium leucotomos* (PLE) (Heliocaps capsules with Fernblock®) for 6 months, from May 2024 to October 2024; however, she had not been diligent in using topical treatment and sunscreen, she did not accept additional interventions for actinic keratosis. During 6 months of follow-up, the patient preferred regular oral PLE since its use provided almost no sunburns and discomfort compared to the summer days in the previous year when engaged in outdoor activities. The actinic keratosis area and severity index score changed from 1.8 to 2.0 after 6 months, and no malignant tumors nor additional clinically relevant actinic keratosis were detected (Figures 1b, 2b, 3b).

For a better and rapid clearance of pre-existing lesions, the patient accepted to have a medium-depth chemical peeling with a solution containing 15% trichloroacetic acid (TCA) and 3% phenol (Easy TCA Pain Control®, Skintech PharmaGroup, Spain). A 2.7 mL solution was applied to the whole face in 3 layers in small circular movements using cotton buds. The deep dermal application was applied to the hyperkeratotic areas of actinic keratosis. When a uniform white frosting with an erythematous background appeared as a marker of medium-depth peeling, a post-peel cream with antioxidant and moisturizing properties was applied to the skin. After about 2 weeks of rough desquamation, actinic keratosis was cleared, and remarkable clearance of small, light brown mottled pigmentations, freckles, and small lentigines was observed (Figures 1c, 2c, 3c). There were no side effects such as postinflammatory hypo/hyperpigmentation, scarring, or postpeel erythema. Twice daily use of topical diclofenac gel was recommended 2 weeks after the peeling session. She was warned about the importance of regular follow-ups and sun protection. Although the patient was called for monthly follow-ups, she did not come due to socioeconomic problems. The patient in this manuscript has given written informed consent to the publication of their case details and clinical photographs.

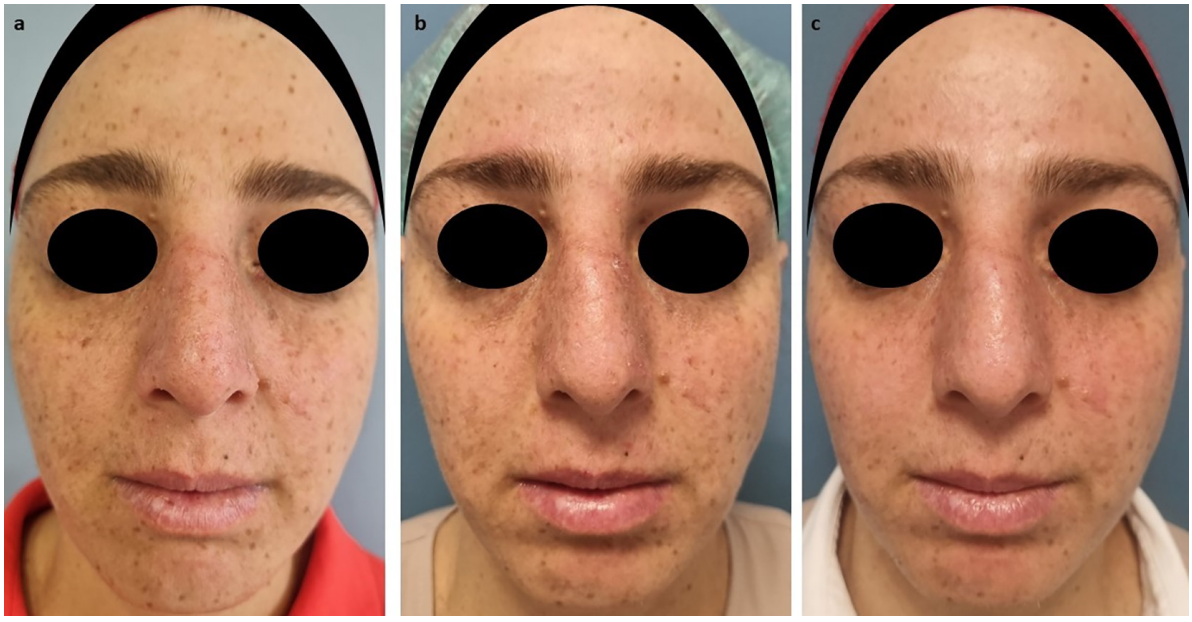

Figure 1. Frontal view of the patient, (a) Before oral PLE supplement and 3% diclofenac gel; (b) After 6 months; (c) Total clearance of actinic keratosis after single session of medium-depth peeling with 15% TCA + 3% phenol solution
PLE: Polypodium leucotomos, TCA: Trichloroacetic acid

Discussion

Aqueous extract from the leaves of PLE attracts attention due to its photopreventive and anticarcinogenic properties. Research in the last decades has shown that PLE inhibits reactive oxygen species, prevents DNA mutations, and repairs photodamaged DNA products such as cyclopyrimidine dimers when exposed to the ultraviolet to infrared radiation spectrum.[3] PLE was administered to XP patients based on these observations, and promising outcomes were achieved. A prospective study showed that 11 of 18 (61%) patients with XP who were put on oral supplements and topical SPF50+ sunscreen containing PLE did not develop new lesions over 12 months.[4] Treatment of actinic keratosis and field cancerization needs proper management to remove clinical and subclinical damages and overgrowths and appropriate monitoring to reduce the risk of actinic keratosis. Among various targeted and field-directed therapies, oral supplements of PLE are recommended as part of strict photoprevention strategies, especially in patients engaging in outdoor activities.[5] The significant decrease observed in the recurrence of actinic keratosis at 6 months after two sessions of photodynamic therapy combined with PLE supplementation is remarkable for managing field cancerization as a combination therapy.[6]

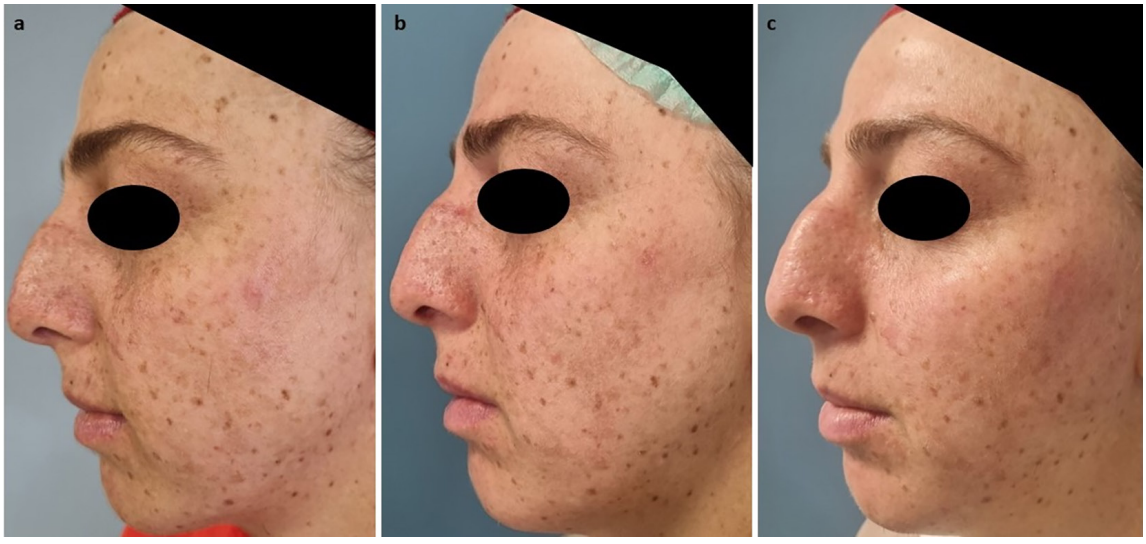

Figure 2. Left profile of the patient, (a) before oral PLE supplement and 3% diclofenac gel; (b) after 6 months; (c) total clearance of actinic keratosis after single session of medium-depth peeling with 15% TCA + 3% phenol solution
PLE: Polypodium leucotomos, TCA: Trichloroacetic acid

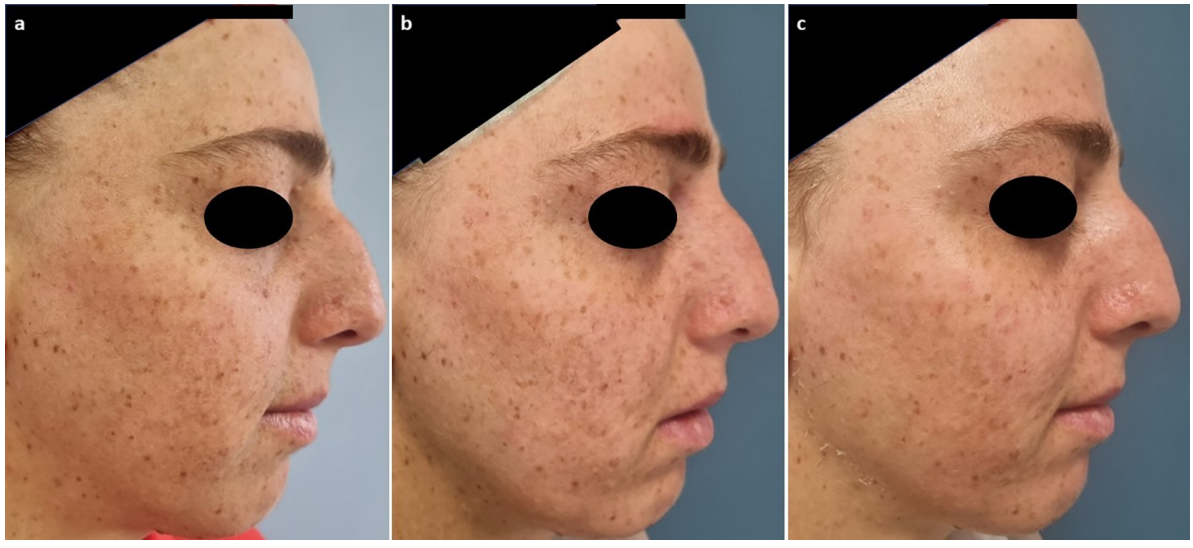

Figure 3. Right profile of the patient, (a) before oral PLE supplement and 3% diclofenac gel; (b) after 6 months; (c) total clearance of actinic keratosis after single session of medium-depth peeling with 15% TCA + 3% phenol solution
PLE: Polypodium leucotomos, TCA: Trichloroacetic acid

In our case, oral PLE provided remarkable photoprotection and comfort in summer. Furthermore, using it as an adjuvant treatment with topical 3% diclofenac gel seems to help prevent new premalignant tumors, although this gel is less effective compared to topical fluorouracil cream.

The treatment of severely photodamaged and cancer-prone skin of patients with XP using resurfacing modalities, including dermabrasion and chemical peelings, has resulted in significant control of new growths of premalignant and malignant tumors within months to years.[7] Full-face medium-depth peels with 35-40% TCA and deep peels with 35% phenol have been reported as effective for the treatment and prevention of new tumors.[7,8] As observed in our patient, a low concentration of phenol (3%) combined with 15% TCA was sufficient to penetrate the dermis when applied in subsequent coats. Deep phenol peels require experience and close monitoring of patients due to potential cardiotoxic effects. Therefore, deep peeling applications using high concentrations of phenol may be an appropriate approach to reserve for patients with medium-depth peeling who have a low treatment success rate. A medium-depth peel with the proper technique may remove the non-clinically detectable subtle lesions and prophylactically clear the photodamaged skin. The procedure is more straightforward, cheaper, and better tolerated than dermabrasion techniques. Furthermore, the combination with other topical agents is reasonable due to their effects on facilitating drug transport.

Oral Polypodium leucotomos extract is a promising adjuvant treatment for the control of field cancerization, especially for patients prone to photocarcinogenesis and potentially non-compliant with treatments such as XP. Since treatments for actinic keratosis and field cancerization may take significantly longer and require compliance, chemical peelings may serve as a relatively shorter and better-tolerated management option, which can be combined with topical agents when needed.

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Ethics

Informed Consent: The patient in this manuscript has given written informed consent to the publication of their case details and clinical photographs.

Footnotes

Authorship Contributions

Surgical and Medical Practices: G.A., Concept: G.A., A.T., Design: G.A., A.T., Data Collection or Processing: G.A., A.T., Analysis or Interpretation: G.A., A.T., Literature Search: G.A., A.T., Writing: G.A., A.T.

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