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RESEARCH ARTICLE

Treatment of Iraqi patient with Gorlin's syndrome and multiple basal cell carcinomas by topical podophyllin solution 25%

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Abstract

Background: Gorlin's syndrome (Basal cell nevus syndrome, nevoid basal cell carcinoma syndrome): is an autosomal dominant disorder characterized by extreme sensitivity to ionizing radiation. Mutation in the PTCH tumor suppressor gene causes Goblin's syndrome, it is follows an autosomal dominant pattern of inheritance. These patients have a higher risk of developing multiple neoplasm, especially basal cell carcinoma (BCC) and medulloblastoma. Podophyllin is an antimitotic and caustic agent.
Objective: to test the effectiveness of topical podophyllin solution (25%) in treatment of Gorlins syndrome with multiple BCCS.

Methodology and results: 30 year-old male often reported a slowly enlarging lesion that does not heal and that bleeds when traumatized. This lesion is seen on the face, scalp, trunk and legs for 8years duration. Patient has a family history of gorlins' syndrome in his family. No history of chronic sun exposure. Improve clinically and histological as BCC, treated with topical podophyllin solution (25%) weekly for six weeks.
Conclusions: 25% topical podophyllin solution is an effective therapy for Gorlins' syndrome with multiple basal cell carcinomas.

INTRODUCTION

Goblin's syndrome (Basal cell nevus syndrome): is an autosomal dominant disorder characterized by extreme sensitivity to ionizing radiation. Mutation in the PTCH tumor suppressor gene causes Goblin's syndrome, it is follows an autosomal dominant pattern of inheritance; mapped the chromosomal locus for the disorder to 9q22.3. These patients have a higher risk of developing multiple neoplasm, especially basal cell carcinoma (BCC) and medulloblastoma. Although affected subjects have normal-appearing skin early in life, they may develop hundreds of BCCs in a generalized distribution over the course of their lifetime.
Additional cutaneous finding in this disorder may include palmoplantar pitting and epidermal inclusion cysts. Incidence of Goblins' syndrome is estimated to be 1 in 56,000 in the general population and may vary by region. A diagnosis of Goblins' syndrome should be considered in any patient who presents with BCC at early age (<30 years), especially if the tumors occur in skin with minimal sun exposure [(1)].
Other common features include odontogenic jaw cyst, skeletal anomalies, such as bifid ribs and tall stature, intracranial calcification and various craniofacial defects, such as cleft palate and coarse facies. Patients with Goblins' syndrome are susceptible to developing other forms of malignant and benign internal tumors, such as meningioma, rhabdomyosarcoma, and ovarian tumors [(2)].

Inactivating mutations in human homolog of the Drosophila patched gene, were detected in Goblins' syndrome patients and implicated in BCC tumorigenesis [3].The irradiation used to treat the BCC can cause further damage and carcinogenesis.

Podophyllin:

Podophyllum resin, also known as Podophyllin, is an antimitotic and caustic agent. Natural sources of Podophyllum are the dried resin extracted from the roots and rhizomes of *Podophyllum peltatum*(known as American mandrake, May apple, Ducks' foot, Indian apple) or a related Indian species, p.hexandrum; active constituents are lignans including podophyllotoxin (20%), alpha-peltatin (10%), and beta-peltatin (5%) [4-6]. Podophyllum resin(Podophyllin) is the powdered mixture of resins extracted from Podophyllum by percolate with alcohol and subsequent precipitation from the concentrated percolate upon addition to acidified water. Podophyllum is indicated for the treatment of condyloma acuminatum (venereal warts). [4-9]

Mechanism of action:

Podophyllum resin's major active constituent, podophyllotoxin, is a lipid-soluble compound that easily crosses cell membranes**;**

- Potent cytotoxic agents that inhibit cell mitosis and deoxyribonucleic acid (DNA) synthesis**.**
- It blocks oxidation enzymes in tricarboxylic acid cycle, so it will interfere with nutrition of the cells.
- And it is also inhibits mitochondrial activity and reduction of cytochrome oxidase activity. [5,6,10,11]

Methodology and results:

30 year-old male often reported a slowly enlarging lesion that does not heal and that bleeds when traumatized. This lesion is seen on the face, scalp, trunk and legs. Patient has a family history of gorlins' syndrome in his family (his brother). No history of chronic sun exposure.

On examination 30 year-old patient with coarse facial feature with family history of Gorlins' syndrome has multiple lesions occurs mostly on the face, scalp, trunk, and legs; Appears as waxy papules with central depression, pearly appearance, bleeding, especially when traumatized, rolled (raised) border, telangiectases over the surface, slow growing since 8 years. After Full clinical, radiological and laboratory investigation, Shave or incision biopsies were done for all lesions at the first visit for Histopathological examination, and Serial-section skin biopsies were stained with hematoxylin & eosin. Biopsy showed pigmented basal cell carcinoma.

The patient was fully screened to recording podophyllin side effects through and after treatment by doing the following investigations: liver and, renal function tests, complete blood picture, erythrocyte sedimentation rate, serum electrolytes, fasting blood sugar, serum amylase, general urine examination, Lactic Dehydrogenase (LDH).

Treatment session: treatment sessions are given every week for 6 weeks. The amount used in each session did not exceed 0.5ml. The solution was allowed to dry in approximately 3 minutes and patients were instructed to wash off it after 5hours. And on each visit the size of the lesion was assessed by marking the lesion and measuring its diameter with a ruler and taking a photo in the same place, light exposure and two dimensions, by using SONY® CORP.MODEL NO.DSC-W220. 12.1 MEGA PIXELS

Biopsy and histopathological examination were done for all lesions treated and Serial-sectioned skin biopsies were stained with hematoxylin & eosin: (all lesions showed no residual carcinoma cells after six sessions for six weeks).

Follow up: Number of treatment sessions was determined according to the clinical and histopathological response. Clinical follow up examinations after cure were done every 3 months for up to 18 months, and Patients were also instructed to come back if any suspicious lesion appeared at the site of healing lesion or nearby in order to determine the recurrence rate.

Inflammatory reaction was noted in all treated lesions and this appeared as edema and redness 36-72 hour after application of podophyllin solution with or without pain. This local reaction was more exaggerated after further 3-5 days after podophyllin application as most lesions became ulcerated and some discharge, after that crust formation appearing in all lesions.

Regarding the side effects, no evidence of systemic side effects was found in any of these cases, and this had been confirmed by clinical examination and lab results including blood picture, liver, and renal function tests. Minimal or no scarring was noticed in all lesions.

Discussion:

Most BCC cases are sporadic, but it may also appear in genetic disorders such as Gorlins syndrome and XP. [12]

There are many standard therapeutic modalities used in treatment of BCC including surgical excision, curettage with

electrodessication, cryotherapy, and radiotherapy, Mohs Micrographic Surgery, photodynamic therapy (PDT), laser therapy, intralesional interferon, intralesional zinc sulphate 2%. Moreover topical remedies such as Imiquimod, 5-flurouracil, tazarotene, also have been used. However many side effects were encountered with this medication. The irradiation used to treat the BCC can cause further damage and carcinogenesis. [13]

In **conclusions** 25% topical podophyllin solution is an effective therapy for Gorlins' syndrome with multiple basal cell carcinoma without topical or systemic side effects, with rapid recovery and no relapse during follow up and gave very nice cosmetic appearance.

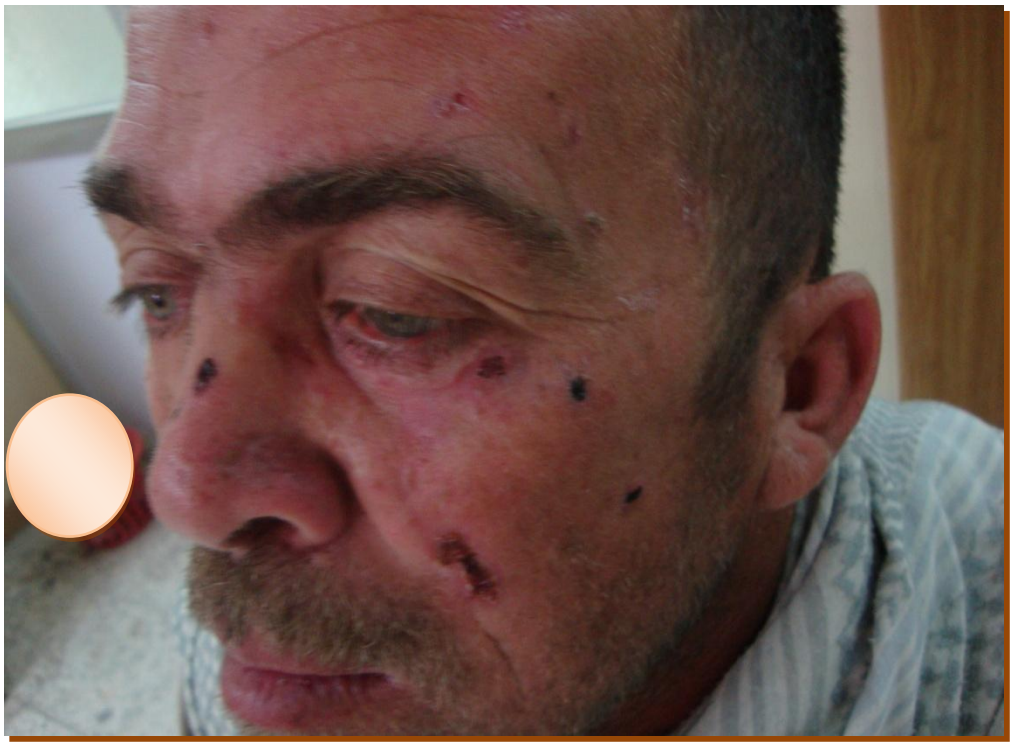

Fig-1: Iraqi patient with Gorlins syndrome with multiple BCCs

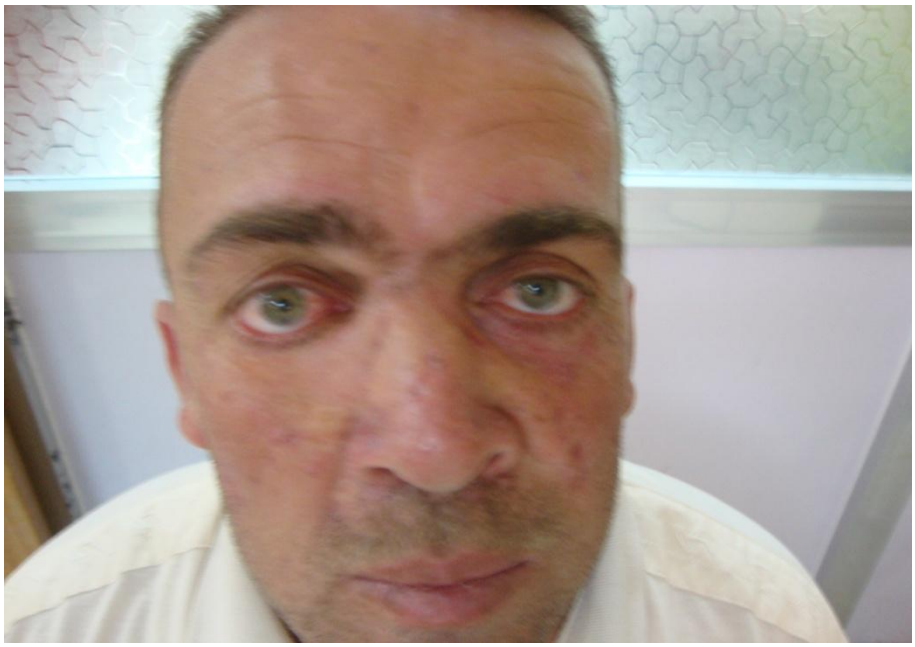

Fig-1: same Iraqi patient with Gorlins syndrome with multiple BCC.
He is treated with topical podophyllin solution for 6 weeks.

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