CASE REPORT

ROLE OF ISOTRETINION IN CANCER PREVENTION AND MANAGEMENT IN MALIGNANCIES ASSOCIATED WITH XERODERMA PIGMENTOSUM

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We report a case of 15 year old female patient of xeroderma pigmentosum with large squamous cell carcinoma on the left side of cheek. She received combination chemotherapy with isotretinoin for a period of 4 months and showed complete clinical remission of tumour. The role of isotretinoin in cancer prevention and management of malignancies associated in xeroderma pigmentosum is also reviewed through literature.

Keywords: Xeroderma pigmentosum, isotretinion, malignancies
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INTRODUCTION

Xeroderma pigmentosum (XP) is a very rare skin disorder. This is caused by a cellular hypersensitivity to ultraviolet (UV) light as a result of a defect in the DNA repair system.[1] This results in cutaneous malignancies in the first decade of life. Affected individuals have an increased sensitivity to sunlight, resulting in a markedly increased risk of squamous cell carcinoma (SCCA), basal cell carcinoma (BCC) and melanomas.

The clinical features, as the name implies, are dryness of skin and pigmentation. This appears first on face and hands, often after exposure to sunlight, and later may extend to the extremities and trunk. The early changes of erythema and inflammatory oedema are followed by scaliness and the appearance of atrophic areas. Later keratoses develop, which may be followed by malignant growths.[2]

There is no cure for XP. The DNA damage is cumulative and irreversible.[3] The disease is often fatal before the age of 20 years. Survival beyond middle age is sometimes possible in mild cases with adequate treatment.[4] Management is limited to avoidance of exposure to damaging UV radiation by staying indoor with sunlight blocked out. The patient should adapt to a life style to minimize UV exposure by wearing protective clothing, sunscreens, sunglasses and long hair styles in order to reduce the incidence of cutaneous malignant changes.

In medical literature the oral retinoids have been shown to decrease the incidence of skin cancer.[5] The retinoids are natural and synthetic derivatives of vitamin A (retinol).[6] Experimental animal models, cellular models, epidemiological data and clinical trials provide a strong rationale for the use of retinoid in cancer therapy and prevention.[7] Basic scientific studies have highlighted key regulators of the retinoid signalling pathway. Retinoid signal cellular effects through nuclear retinoid receptors and their co-regulators, as recently reviewed.[7,8] This leads to ligand dependent transcriptional activation of target genes that signal retinoid growth and differentiation effects. These ultimately lead to changes in gene expression that mediate biological effects.[9]

The routine use of oral retinoid in XP associated malignancies has never been tested in clinical trials. Literature review shows one case report that utilized the oral retinoid along with chemotherapy in SCCA with good results.[10]

CASE REPORT

A 15 year old female with XP presented to our tumor clinic with a history of ulcerated lesions on the left side of face for 10 months that had progressively increased in size in the last two months. On local examination she had all the features of XP with rough and dry skin and hyper-pigmentations more pronounced on the face and hands. There was a large 10×7 cm ulcero-proliferative lesion on the left side of the face extending from left infraorbital ridge above to the angle of mouth below with purulent discharge, haemorrhage and everted margins (Figure-1 and 2). There was no significant cervical lymphadenopathy.

Systemic examination including neurological functions was essentially normal. Haemogram and serum biochemistry was within normal limits. Chest radiography and ultrasonography of abdomen were normal. Biopsy of the lesion revealed well differentiated squamous cell carcinoma (SCCA). CT scan done to know the extent of disease and it shows soft tissue mass overlying left maxilla with erosion and infiltration into the maxillary antrum and erosion of inferior and lateral orbital wall. (Figure-3)

The patient was offered chemotherapy with oral retinoid as surgical excision was not feasible due to extensive disease and poor general condition of the patient. The first line chemotherapy, i.e., Cisplatin 75 mg/m2 and 5-FU 1000 mg/m2 (24hour infusion) on D-1 along with isotretinoin (1 mg/kg/day) started at 3 weekly intervals to a total of 5 cycles.

The patient tolerated 5 cycles of combination chemotherapy as per schedule without any major or minor toxicities. After completion of 5 cycles complete clinical response was achieved (Figure-4.). The patient was on radiation therapy to consolidate the response of chemotherapy and expected to complete with a total dose of 600 cGys.

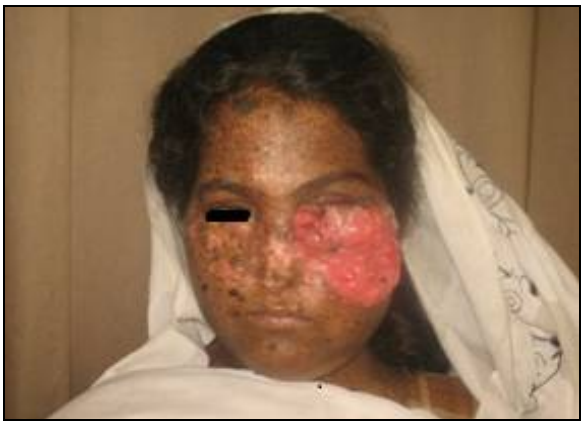

Figure-1: Frontal view showing ulcero-proliferative lesion involving cheek.

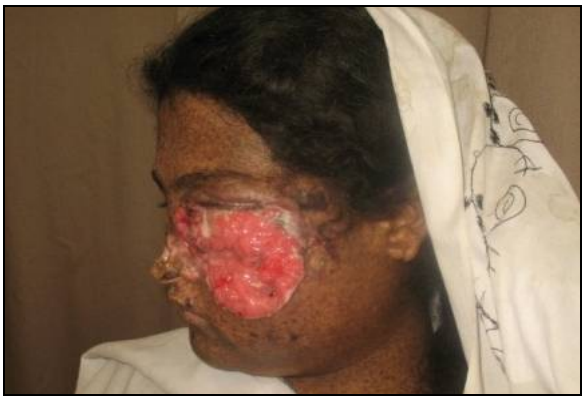

Figure-2: Lateral view showing involvement of inferior and lateral wall of Left Eye.

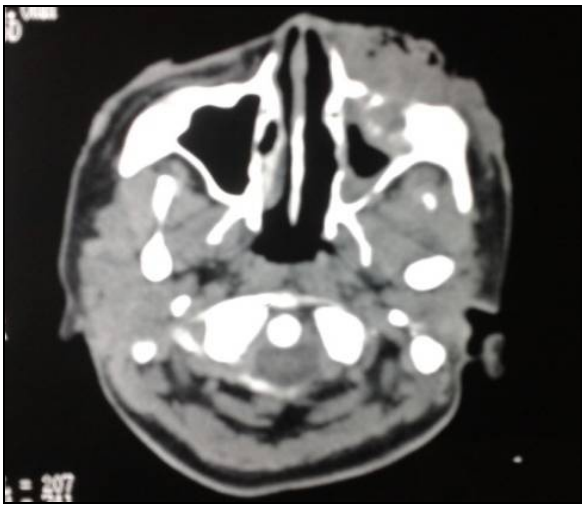

Figure-3: CT image showing involvement of left maxillary antrum and erosion of anterior wall.

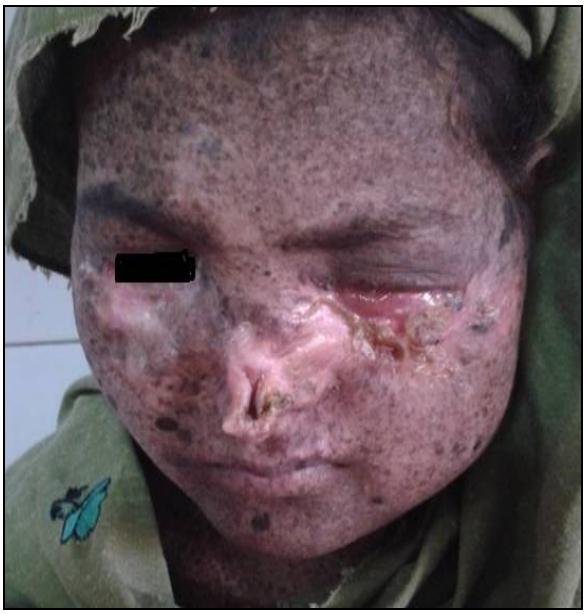

Figure-4: Response of chemotherapy after completion of 5 cycles.

DISCUSSION

The incidence of XP is approximately 1 in 250,000 populations. Xeroderma pigmentosum occurs worldwide and affects people of all races. The risks of cutaneous malignancies in XP are much higher than in general population. Below 20 years of age there is 1000 fold increased risk of cutaneous basal cell or squamous cell carcinoma or malignant melanoma.[3] The mean age for skin cancer is 8 years in patients with XP compared to 60 years in the healthy population.

As multiple cutaneous neoplasms develop in persons with XP at a young age, early diagnosis and management could be life-saving. The use of oral retinoid for skin cancer prevention has been studied and found effective in clinical trials but no definite recommendations are available in the management of cutaneous malignancies

We utilized oral retinoid concurrently with conventional chemotherapy and found excellent results, i.e., complete clinical remission of tumor in short period of time. The same result was also published in one case report utilizing the same treatment strategy.[10] On the basis of these results we recommend the routine utilization of oral retinoid in XP associated malignancies especially in squamous cell carcinomas. The clinical benefits of oral retinoids in others cutaneous malignancies like BCC or melanoma have to be proven.

CONCLUSION

The use of chemotherapy for the treatment of squamous cell carcinoma in XP could be an effective tool where other modalities have limited role. This

response can be further enhanced by the routine uses of oral retinoid in XP patient especially those subjected to chemotherapy.

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