CASE REPORTS

EPIDERMODYSPLASIA VERRUCIFORMIS WITH MULTIPLE CUTANEOUS CARCINOMATA TREATED WITH ETRETINATE

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A Chinese lady, fourth in a family of four unaffected brothers and six sisters affected with epidermodysplasia verruciformis was treated with aromatic retinoid (Etretinate) when she developed multiple recurrent squamous as well as basal cell carcinomas. Etretinate was effective in preventing the occurrence of cutaneous malignancies.

Key words : Epidermodysplasia verruciformis, Malignancies, Retinoids.

Epidermodysplasia verruciformis (EV) is a rare disorder of human papilloma virus (HPV), first described by Lewandowsky and Lutz in 1922.[1] It is characterized by generalised flat wart-like lesions seen commonly on the face and hands, and pityriasiform red warts (PRW) found mostly on the trunk and legs resembling pityriasis versicolor-like macules or pigmented and depigmented plaques.[2] Several HPV types such as HPV 3, 5, 8, 9, 12, 14 and 15 have been isolated from EV patients.[3] The lesions start in childhood and persist life-long. It is considered a genodermatosis since 25% of the reported cases were familial with parental consanguinity suggestive of autosomal recessive mode of inheritance.[4,5] X-linked recessive inheritance has also been reported,[6] postulating the existence of two different genetic loci in this disorder which is also associated with reduced cell-mediated immunity.[7] About 20 to 30% of the EV lesions turn malignant[8] to either Bowen's disease, basal cell carcinoma or squamous cell carcinoma. Viral particles have been found in EV lesions[4,9] but never in the advanced malignancy arising from them. By means of molecular hybridization experiments and restrictive enzyme analysis, it has been shown that specific HPV types such as HPV5 have oncogenic potential[2] and that HPV genomes were present in malignancies arising from specific HPV-induced EV lesions.[3] This paper describes a Chinese woman with EV who was treated with etretinate for recurrent and multiple basal cell carcinomas (BCC) and squamous cell carcinomas (SCC).

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Case Report

A 35-year-old, unmarried Chinese lady, fourth in a family with consanguinous marriage was seen in May 1983 with numerous, tiny, warty lesions over the chest, back and both the limbs since the age of 7. She also had pityriasis versicolor-type of macules. Amidst these lesions, there were a few small proliferative growths over the left infraclavicular region and right forearm. Her five other sisters were affected with EV, whereas her three brothers were not. The clinical features of this patient when she was first seen in 1968, profiles of her family members, the mode of inheritance, light microscopy studies and electronmicroscopic demonstration of viral particles had been described elsewhere.[4] She was noted to have BCC and SCC then, and subsequently, she developed similar lesions from 1978 to 1983

which were either curetted, excised or treated with 5% 5-fluorouracil ointment. She developed a SCC below the left axilla which required excision and skin-grafting. In spite of these measures, in 1985 she presented with small but multiple BCCs and SCCs over the skin graft, chest, trunk and back.

Investigations such as full blood picture, urine analysis, blood sugar, liver function tests, serum lipids, urea, calcium and phosphate were within normal limits. She was informed about etretinate and its complications especially that of teratogenicity. After obtaining informed consent, in January 1986 she was started with etretinate (Tigason) 1mg/kg/day. During the first month of etretinate 25 mg twice daily dose, she noticed dryness of the lips and eyes. A few warty lesions as well as cutaneous malignancies appeared to have regressed. On the third month, the dose was reduced to 35 mg daily. Pregnancy test was done monthly before supplying the medicine and she was taught to record her menstrual cycle. On the sixth month of therapy, etretinate was reduced to 25 mg daily and maintained at this dosage till March 1987. During the 15-month period of treatment and later, carcinomas were not found. She is being followed up and EV lesions have not relapsed after withdrawal of the drug.

Comments

The impressive feature of etretinate was that the skin lesions of EV which were predominantly verrucous, not only became much flatter but many regressed and disappeared within a month of starting the treatment. The skin cancers also involuted and there was no further need for surgical intervention since there was no new malignancy. The patient actually demanded continuation of her treatment undeterred by known complications. Serum lipids especially the triglyceride level was not significantly raised. Since EV is a life-long condition, cutaneous malignancies may still recur after a short-course of treatment. Hence, she was maintained with a minimal dose of etretinate as long as 15 months. But, the possibility of teratogenic potential restricted its usage for a longer period.

Isotretinoin has been used with considerable success in keratoacanthoma and SCC,[10] BCC[11] and mycosis fungoides.[12] The anti-neoplastic effect has been utilised for the prevention of malignant transformation in EV,[13] and proliferation of warts in immunocompromised patient.[14] Synthetic retinoids exert their action by promoting epidermal differentiation. Although the mode of action may be more than one, the biochemical pathways involved are not clear. The anti-tumour action is achieved by the steroid-hormone like properties on the nucleus, resulting in suppression of neoplastic phenotype expression. Alternatively, these drugs may enhance gap-junction proliferation enabling better intercellular communication, stimulation of glycoprotein synthesis essential for various cellular functions, immunomodulation and competitive oncogenic interferance.[15]

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