

Case Report

Epidermodysplasia verruciformis: a rare genodermatosis with risk of malignant transformation

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Abstract Epidermodysplasia verruciformis is a rare, lifelong, autosomal recessive hereditary disorder affecting the skin and is characterized by chronic infection with human papillomavirus. We report a case of young boy who presented with widespread pityriasis versicolor-like lesions and was mistreated as fungal infection for some time. A brief review of the condition is also given below.

Key words

Epidermodysplasia verruciformis, human papillomavirus, verruca plana.

Introduction

Epidermodysplasia verruciformis (EV) is a rare disorder characterized by widespread flat skin lesions resembling common plane warts. The disease is universal and affects all races and no sexual preference is noted. Findings are limited to the skin and rarely occur on the mucosa. Primary skin lesions are polymorphic, mostly warty, lichenoid, flat-topped papules. Flat macules and reddish brown plaques with slightly scaly surfaces and irregular borders are also noted. These lesions may resemble pityriasis versicolor. Papules on the knees, the elbows, and the trunk may coalesce into large plaques. Almost half of patients are inherited, usually with an autosomal recessive pattern. An X-linked inheritance

has also been reported.^{1,2} Skin lesions may transform into malignant carcinomas, usually after the age of 30. Individuals with EV have a specific impaired cellular immunity to EV-associated HPVs that makes them susceptible to widespread viral infection³. Carcinogenic cofactors, such as ultraviolet B and x-ray irradiation, are likely involved in the progression from benign warts to malignancy. Failure of programmed cell death to eliminate cells with DNA damage may play an important role in malignant transformation of squamous epithelium. A decrease in UV-induced DNA repair synthesis coupled with an oncogenic viral infection further enhances the disposition for somatic mutations and malignant transformation in patients with EV. EV-associated HPVs can be divided into two groups. One group has high oncogenic potential (types 5, 8, and 47). More than 90% of EV-associated skin cancers contain these viruses. The other group has low oncogenic potential (types 14, 20, 21, and 25), usually detected in benign skin lesions³⁻⁵. The diagnosis of EV should

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be suspected in the clinical setting of numerous verrucous lesions or when lesions are recalcitrant to appropriate therapy. Biopsy is performed for early detection of premalignant and malignant lesions and for the identification of EV-associated HPVs.^{4,5} The keratin layer is loose with a basket weave-like appearance. The most characteristic findings is the presence of clear cells in the granular and spinous layers with occasional enlarged, hyperchromatic, atypical nuclei. The nucleoplasm is clear, and keratohyaline granules of various sizes and shapes are present. In premalignant tumors, the normal keratinocyte maturation is preserved. In contrast, in the malignant lesions, the normal surface maturation of keratinocytes is lost. The premalignant lesions display features similar to actinic keratoses with prominent atypical, dyskeratotic cells. The cytopathic effects of viral warts are often missing.^{1,2} No definitive therapy for EV is available. Experimental therapies include intralesional administration of interferons and retinoids and these have resulted in only a partial or transitory effect.^{1,2} Role of cimetidine has also been controversial.⁶ Surgical and electrosurgical removal and cryotherapy are used in the treatment of benign and premalignant lesions. Surgery is also indicated for treatment of malignant lesions. For localized multiple malignant lesions, autotransplantation of skin from uninvolved skin has been reported with success^{1,2}. In advanced HPV-related carcinomas, an experimental therapy involves treatment with a combination of 13-cis retinoic acid and interferon alpha or cholecalciferol analogues.⁷ UVB and UVA exposure as well as x-ray irradiation should be avoided.²

Case report

A 12-year-old boy presented with multiple small coalescent slightly raised but flat surfaced asymptomatic skin colored to reddish brown lesions over his neck, trunk, face, and upper limbs. Lesions started about 5 years ago as flat brownish spots involving neck, hands and upper trunk but gradually spread to involve, face, lower trunk forearms and feet. These have largely been asymptomatic apart from occasional itching. There was no family history of skin cancer or similar lesions. Consanguineous marriages were common in the family and his parents were first cousins in relation. On examination, numerous flat planar warts were noted on his upper chest, upper back, around neck, hands, forearms and feet (**Figure 1** and **2**). Palms and soles were also affected. Lower trunk, thighs and lower legs were less involved. Lesions were mostly flat surfaced and coalescent (pityriasis versicolor-like) and some of them (on hands and feet) appeared verrucous and discrete. The mucous membranes, hair and nails were not affected. During early 2-3 years, he was frequently mistreated as a case of pityriasis versicolor by some medical practitioners and was given some topical as well as systemic antifungals with no response. Patient otherwise enjoyed good general health with no past history of any significant past illness. Clinical picture suggested the diagnosis of EV. His routine laboratory investigations were within normal limits. Skin biopsy was done to confirm the diagnosis, which revealed hyperkeratosis with a basket weave-like appearance and clear cells were evident in the granular and spinous layers with occasional enlarged, hyperchromatic, atypical nuclei (**Figure 3**).



Figure 1 Polymorphic, discrete and coalescent patches and plaques on face, neck and upper chest along with warty lesions on dorsum of the hands.



Figure 2 Polymorphic, discrete and coalescent maculopapular lesions and plaques on upper back and around neck.

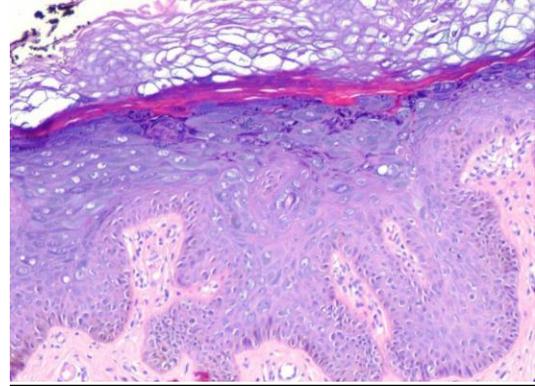


Figure 3 Hyperkeratosis and characteristic presence of multiple clear cells and along with occasional enlarged, hyperchromatic, atypical nucleus in upper layers of epidermis.

On confirmation of diagnosis, he was started acitretin (Cap Neotigason) 25mg one daily and application of tretinoin (Retin-A) cream once daily over facial lesions. Lesions over the face were better after one but no significant improvement was seen otherwise. Dose of oral acitretin was the doubled and he was also advised topical treatment over his neck, hands and forearms.

Discussion

This rare disease usually begins in infancy or early childhood and can present with following three types of lesions; (i) pityriasis versicolor-like, (ii) verruca plana-like and (iii) seborrhoeic keratosis-like, in isolation or in combination.^{1,2,8} The clinical course is protracted. As the disease progresses, some lesions disappear, while new lesions may appear on other areas of the body. A specific defect of cell-mediated immunity manifested by the inhibition of natural cytotoxicity and the proliferation of T lymphocytes against HPV-infected squamous cells in EV skin lesions is a characteristic feature of EV.³ Chronic sun-exposure coupled with immunologic defects in patients with EV is likely to induce mutations of the tumor

suppressor gene protein (p53), leading to the development of malignant skin cancer in adult patients. Skin cancers initially appear on sun-exposed areas, such as the face and the ear lobes. Patients with EV are usually infected with multiple types of HPV. More than 30 HPV types, including types 3, 5a, 5b, 8-10, 12, 14, 15, 17, 19-21, 23-26, 37, 38, and 47, have been identified in EV tumors.^{4,5} EV when presents in the form of skin coloured or brownish discrete or coalascent macules and patches becomes difficult to be differentiated from a ubiquitous fungal infection pityriasis versicolor and may be treated as a fungal infection for a considerable period of time and this actually happened in our case. Few raised lesions (plane warts-like) over dorsum of the hands and upper chest suggested the possibility of EV, which was then confirmed on histopathology. Therefore, if a patient with clinical diagnosis of pityriasis versicolor does not respond to standard antifungal treatment, he should be evaluated for EV as this benign looking disease may transform into skin malignancy at some later stage.^{4,5}

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