A CASE REPORT- EPIDERMODYSPLASIA VERRUCIFORMIS IN AN IMMUNODEFICIENT CHILD

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ABSTRACT

BACKGROUND

Epidermodysplasia verruciformis (EV) is a rare, lifelong, cutaneous, autosomal recessive genetic disorder of the immune system manifested by increased susceptibility to cutaneous Human Papilloma Virus (HPV) infection beginning in the early years of life. EV lesions are frequently described as pityriasis versicolor-like scaly macules, flat warts like papules or verrucous and seborrhoeic keratosis like papules and plaques. Here, we report a case of 14 years old boy who presented to us with multiple hyperkeratotic papules over face and upper extremities since 2 years. Hypopigmented macules over face, neck, upper chest and trunk since 4 months. Patient was treated topically with cryotherapy and systemically with acitretin and immunomodulators for warts and pityriasis versicolor was treated with topical and oral antifungals.

KEYWORDS

Epidermodysplasia Verruciformis, Human Papilloma Virus, Pityriasis Versicolor, Seborrhoeic Keratosis, Cryotherapy, Acitretin.

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BACKGROUND

Epidermodysplasia verruciformis (EV) is a rare, generalised, persistent, inherited disorder that predisposes the patient to widespread HPV infection and cutaneous malignancies.¹ The term "acquired EV" describes a syndrome nearly identical to congenital EV that afflicts immunocompromised patients.²

In EV, there are mutations in the EVER1 or EVER2 genes on the chromosomes 17q25, which due to defect of cell mediated immunity lead to an abnormal susceptibility of the patients to a specific group of HPV genotypes known as EV HPV. Most of these are HPV 5 and 8, more rarely HPV 14, 17, 20 and 47 and all have oncogenic potential.³

EV usually begins in infancy or early childhood, but may appear at any age. The cutaneous lesions are mainly flat warts, reddish-brown scaly macules resembling tinea versicolor or pityriasis rosea.⁴ The lesions mainly occur on sun-exposed area, but may be generalised all over the body. Oral mucosa is spared.

Cutaneous nonmelanoma skin cancers developed in 30% to 50% of the patients within mean of 25 years after the onset of benign skin lesions.⁵ These cancers are mostly Bowen's disease and invasive squamous cell carcinomas, growing slowly on areas exposed to sunlight.

Case Report

A 14 years old boy was admitted in Department of Paediatrics for fever and upper respiratory tract infection. He was referred to our OPD for recurrent Herpes simplex labialis since 1 year. He was treated with antiviral drugs and antibiotics.

The physical examination reveals multiple hyperpigmented keratotic papules over the face and upper extremities since 2 years. Irregular hypopigmented macules were present over face, neck, upper chest and trunk since 4 months. Also, there was presence of multiple fluid filled lesions with crusting near the angle of mouth. There was also presence of recurrent multiple fluid filled lesions near the angle of mouth 4 - 5 episodes per year associate with pain. No clinical signs of squamous cell carcinoma, no history of similar complaints in the family.

A biopsy of a papule was taken from the forearm. Microscopic examination revealed epidermal acanthosis, hyperkeratosis, vacuolation of superficial keratinocytes in the granular layer and mild perivascular infiltrate in the superficial dermis. These findings are consistent with verruca plana.

On laboratory investigation, complete haemogram reveals anaemia and leucopaenia. HIV and HBsAg tests were negative. Patient was treated topically with cryotherapy for once in a week for 1 month. Systemically with acitretin at the dose of 10 mg/day and immunomodulators levamisole 150 mg on two consecutive days in a week for warts. Topical Eberconazole twice a day application and oral Itraconazole 100 mg twice a day for a week for Pityriasis Versicolor. Topical fusidic acid twice a day application and oral acyclovir 400 mg thrice a day for 5 days for herpes labialis.

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A) Multiple Hyperpigmented Keratotic Papules over the Face and Presence of Multiple Fluid Filled Lesions with Crusting Near Angle of Mouth. B) Irregular Hypopigmented Macules were Present over Face, Neck and Upper Chest

DISCUSSION

Epidermodysplasia verruciformis (EV) is a rare, generalised, persistent, inherited disorder that predisposes the patient to widespread HPV infection and cutaneous malignancies.¹ Although, it has an autosomal recessive transmission in most cases, X-linked recessive and autosomal dominant forms also exist.⁶

The disease was first described by Lewandowski and Lutz in 1922 and is characterised by both impaired immunity and viral oncogenesis.⁷ The term "acquired EV" has been used to describe a condition with clinical features similar to EV that occurs in immunocompromised patients, specifically those with HIV or those on immunosuppressive therapy.² In EV, there are mutations in the EVER1 or EVER2 genes on the chromosomes 17q25, which due to defect of cell mediated immunity lead to an abnormal susceptibility of the patients to a specific group of HPV genotypes known as EV HPV. Most of these are HPV 5 and 8, more rarely HPV 14, 17, 20 and 47 and all have oncogenic potential.³

HPV 5 and HPV 8 have been isolated in more than 90% of EV-associated squamous cell carcinomas. Two loci on chromosomes 17q25 and 2p21-p24 are associated with EV in some families. Many HPV types found in EV lesions are non-pathogenic to the general population. EV is universal and affects all races. It typically presents in childhood, but congenital forms are known. Malignant change occur in 20% - 30% cases, more commonly in fourth and fifth decade.

The classic histological finding of epidermodysplasia verruciformis is a verruca plana-type lesion with mild-to-moderate hyperkeratosis, acanthosis and enlarged vacuolated keratinocytes with perinuclear halos and blue-gray cytoplasmic pallor.⁸ Pre-malignant lesions display features similar to actinic keratosis with prominent atypical dyskeratotic cells. Malignant tumours most commonly show squamous and occasionally adnexal differentiation.⁹

EV usually begins in infancy or early childhood, but may appear at any age. The cutaneous lesions are mainly flat warts, reddish-brown scaly macules resembling tinea versicolor or pityriasis rosea.⁴ The lesions mainly occur on sun-exposed area, but may be generalised all over the body. Oral mucosa is spared. EV lesions are remarkably persistent and may remain unchanged for decades. Though impairment of cell immunity is found in EV, patients are not susceptible to other viral and bacterial infections.

Cutaneous nonmelanoma skin cancers developed in 30% to 50% of the patients, within mean of 25 years after the onset of benign skin lesions.⁵ These cancers are mostly Bowen's disease and invasive squamous cell carcinomas, growing slowly on areas exposed to sunlight.

However, nowadays, malignant conversion is seen over shorter periods of time, possibly due to the increase of time to sun exposure, altitude or outdoor occupations.¹⁰ Therefore, malignancies start to appear well before 40 years of age. The lesions appear mainly on sun-exposed areas, frequently on the forehead. This could be explained by the combination of chronic ultraviolet exposure and probable presence of oncogenic EV-HPV in hair follicles. Ultraviolet and x-rays are cocarcinogens. Metastasis in these cases is very rare, if there is no history of radiation therapy.¹¹

Sun exposure can greatly hasten time to malignant transformation. If a patient with EV is living at a high altitude

and/or works outdoor and does not use sunscreen, malignant transformation can be seen earlier in the disease progression. Treatment of EV remains challenging. Patients should be routinely monitored for the development of cutaneous cancers, because of its malignant potential.⁷ Sun avoidance and photoprotection are also recommended. Etretnate 1 mg/kg/day is helpful in some cases, but the lesions recur.¹²

Oral isotretinoin is also effective. Topical imiquimod, calcipotriol and squaric acid dibutyl ester have been found to be effective in individual cases.¹³

Electrocautery and cryotherapy are used in the treatment of benign and premalignant skin lesions. Although more radical than pharmacological treatment, surgical treatment is considered more effective. Complete excision and defect reconstruction with split-thickness or full-thickness skin grafts or local flaps are the preferred approaches.

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