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A Case of Epidermodysplasia Verruciformis Treated with Systemic Acitretin

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Abstract
Epidermodysplasia verruciformis (EV) is a rarely seen, genetically transmitted dermatosis characterized by the tendency to human papillomavirus infections (HPV). Although its etiopathogenesis is not exactly known, dysfunction in cell-mediated immunity is thought to be a very important factor in the development of the disease. Verruca plana, which starts in childhood, and reddish-brown papules and plaques mimicking pityriasis versicolor are seen in EV cases. There are no specific races or geographical differences in the incidence of the disease. On histopathological examination, hiperkeratosis, acanthosis, and intense vacuolization similar to those in classic verruca vulgaris can be seen. Especially in the sun-exposed areas, malignancies may develop. Therefore, early diagnosis and treatment of the disease is significant for the prevention of premalignant and malignant lesions. Some medications such as interferon, retinoic acid, topical imiquimod can be used in the treatment. Here, we present a 14-year-old epidermodysplasia verruciformis case having partially positive response to acitretin treatment
Key Words: Epidermodysplasia Verruciformis (EV); Human Papillomavirus (HPV); Acitretin.

Sistemik Asitretin İle Tedavi Edilen Bir Epidermodisplazya Verrüsiformis Olgusu

Özet
Epidermodisplazya verrüsiformis (EV) persistan human papilloma virüs (HPV) enfeksiyonlarına eğilim ile karakterize, genetik geçişli, nadir görülen bir dermatozdur. Etyopatogenezi tam olarak bilinmemekle birlikte hücre aracılı immünitedeki disfonksiyonun hastalığın oluşmasında çok önemli bir faktör olduğu düşünülmektedir. Çocukluk çağında başlayan, verruka plana ve pitriyasis versikoloru taklit eden kırmızı-kahverengi papül ve plaklar görülür. Hastalığın insidansında belirgin bir ırk ve coğrafi farklılık yoktur. Histopatolojik incelemede klasik verrukalardakine benzer hiperkeratoz, akantoz, yoğun vakuolizasyon görülür. Özellikle güneş gören alanlarda, malignite gelişebilmektedir. Bu nedenle hastalığın erken tanınıp, tedavi edilmesi premalign ve malign lezyonların önlenmesi açısından önemlidir. Tedavide interferon, retinoik asid, topikal imiquimod gibi ilaçlar kullanılabilmektedir. Biz de sistemik asitretin tedavisine kısmen iyi yanıt veren 14 yaşında bir epidermodisplazya verrüsiformis olgusu sunuyoruz.
Anahtar Kelimeler: Epidermodisplazya Verrüsiformis (EV); Human Papilloma Virüs (HPV); Asitretin.

CASE REPORT

Characterised by its tendency towards persistent human papilloma virus (HPV) infections, epidermodysplasia verruciformis (EV) is a rare inherited dermatosis. EV lesions are expected to develop malignancies. Therefore, early diagnosis and treatment are important to control premalignant and malignant lesions (1-3).

INTRODUCTION

A 14-year-old male patient was admitted to our clinic with light-coloured fluffy lesions scattered over his face, trunk and limbs. The patient stated that the lesions started on his face and then spread around the whole body over a period of five years despite topical treatments. We also learnt that his sister also developed similar lesions. The dermatological examination showed widely scattered, warty, verrucous, hyperpigmented papular lesions spread around the face, trunk and extremities. These papules merged around the abdomen and face to form plaques (Figure 1).

We could not detect any remarkable pathological findings in the complete blood count, routine biochemical tests, chest X-ray, or abdominal ultrasound. The histopathological examination of the biopsy from the lesions revealed orthokeratosis in the epidermis as well as acanthosis, spongiosis, many irregular vacuolated keratinocytes, stratum granulosum, pyknotic nuclei in the upper layers, and keratohyalin granules (Figure 2). In the light of the clinical and histopathological findings, the patient was diagnosed with EV. Because the lesions were spread around the whole body and resistant, we initiated a 0.5mg/kg systemic acitretin therapy. During

the treatment, we did not observe any serious side effects. Within 6 months of the treatment, we observed notable recession in the lesions on the face though we failed to observed the same for the lesions around the trunk and limbs.

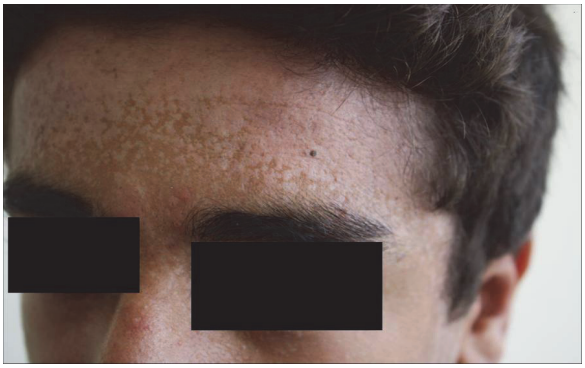

Figure 1. Hyperpigmented verrucous papules and plaques on the forehead of our patient.

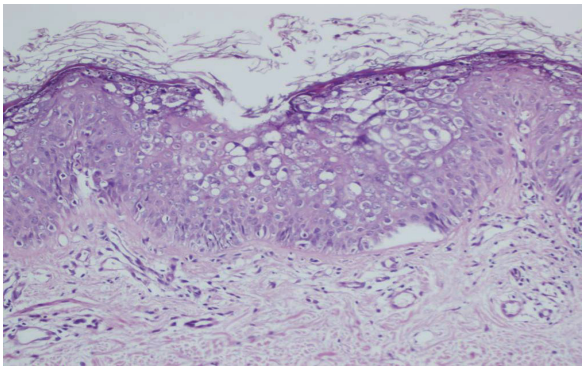

Figure 2. Orthokeratosis, acanthosis, spongiosis, vacuolated keratinocytes, and keratohyalin granules in the epidermis (H&Ex10).

DISCUSSION

EV, which is characterised by red, brownish, or sometimes hypo-pigmented plaques that are similar to verruca plana and pityriasis versicolor and accompany common and persistent HPV infections, is a rare type of dermatosis. EV can also be defined as a cutaneous immunity disorder characterised by tendency to HPV infections (2, 3). The majority of cases are sporadic whereas 25% of cases have been reported to contain autosomal recessive inheritance (1). Lesions occur at early ages with no significant differences in terms of race and region (1, 2).

Although its etiopathogenesis is unknown, it is thought that cellular immunity dysfunction plays a role in the formation of the disease (2). The HPV infection persistence in EV is thought to be caused by immune system's failure to assign HPV-containing keratinocytes as a result of an unknown immunogenetical defect and deficiency (4-6). EV involves many specific HPVs though only HPV-5 and HPV-8 have been reported to be associated with carcinoma development (2). 30-70% of EV patients develop skin cancers on sun-exposed areas (2).

Dysplastic and malignant changes are seen most frequently in areas exposed to ultraviolet radiation. Malignancies are more of actinic keratoses, Bowen's disease, and, though rarely, of squamous cell carcinoma. Metastasis is barely observed (1, 7). The verruca plana and pityriasis versicolor-like, slightly scaly, hypo- or hyper-pigmented lesions settled on and around the hands, arms, and face are the most common clinical forms of the disease as we have observed in our patient.In some rare cases, seborrheic keratosis-like lesions may also occur (2, 8).

Histopathological examination shows hyperkeratosis and acanthosis very similar to those seen in classic warts but the vacuolisation of keratinocytes is much more intense and may affect the three-fourth of the upper Malpighian layer. There are also remarkable cells formations with central pyknotic nuclei in the upper epidermis (9). In our case, we have also come across similar findings in the pathological examination of our patient, which were eventually confirmed by histopathologically.

There are reports of successful treatment options involving systemic retinoids, interferon alpha, topical imiquimod, and tacalcitol. For malignant and premalignant lesions, fluorouracil and photodynamic therapies can accompany sunscreens (9). The role of acitretin therapy in EV is not clear. It has been suggested that vitamin D in acitretin keratinocytes, which is used in acrokeratosis verruciformis cases, prevents the differentiation of keratinocytes through specific nuclear receptors and is effective in treating such patients (1, 10). This effect can be explained by a similar mechanism in the treatment of EV. Clinical improvement can usually be observed during the treatment whereas histopathological findings of viral infection continue. Relapse is common when the drug is discontinued. The effect of acitretin on dysplastic and malignant changes has not yet been proven (9). However our patient responded well to the moderate-dose treatment with systemic acitretin.

EV is a chronic dermatosis that is difficult to treat. Because of its predisposition to premalignant and malignant lesion development, early diagnosis, follow-up, and treatment of EV are each very significant. Cases with warts or pityriasis versicolor that are resistant to treatment in childhood should be considered for EV and the diagnosis should be confirmed histopathological evidence. We believe that systemic acitretin is an effective treatment option in EV even for younger patients in their childhood.

REFERENCES

1. Braun falco O, Plewig G, Wolff HH, Wurgdorf WHC. Viral disease. Dermatology. 2. baskı, Berlin, Springer Verlag, 2001;53-120.
2. Lane JE, Bowman PH, Cohen DJ. Epidermodysplasia verruciformis. Southern Medical Journal 2003;26:613-5.

3. Polat M, Taşer E, Kölükfakı Ş, Gür G, Üstün H, Allı N. Epidermodisplazya Verrusiformis: İki Olgu. Yeni Tıp Dergisi 2008;25:51-3.
4. Majewski S, Jablonska S. Epidermodysplasia verruciformis as a model of human papillomavirus-induced genetic cancer of the skin. Arch Dermatol 1995;131:1312-8.
5. Majewski S, Jablonska S. Do epidermodysplasia verruciformis human papillomaviruses contribute to malignant and benign epidermal proliferations? Arch Dermatol 2002;138:649-54.
6. Oliveira WR, Festa Neto C, Rady PL, Tyring SK. Clinical aspects of epidermodysplasia verruciformis. J Eur Acad Dermatol Venereol 2003;17:394-8.
7. Çalka Ö,Bilgili SG, Akdeniz N,Bayram İ. Epidermodisplazya verrüsiformisli iki kardeş olguda erken yaşta skuamöz hücreli karsinom gelişimi.Türkderm 2010;44:92-5.
8. Akgül B, Cooke JC, Storey A. HPV-associated skin disease. J Pathol 2006;208:165-75.
9. Tüzün Y, Gürer MA, Serdaroğlu S, Oğuz O, Aksungur V. Derinin Viral Hastalıkları. Öztürkcan S, editör. Dermatoloji. 3 baskı. İstanbul: Nobel Tıp Kitabevi; 2008. p. 554-650.
10. Güler E, Ferahbaş A, Utaş S, Kontaş O. Asitretin ile tedavi edilen bir Akrokeratozis verrüsiformis olgusu. Türkderm 2009;43:35-7.

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