

The Diagnosis of Non Hodgkin Lymphoma in An Epidermodysplasia Verruciformis Patient



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ABSTRACT

Epidermodysplasia verruciformis is a rare, multifactorial disorder. The disease has genetic and immunologic components. Many patients have impaired cell-mediated immunity. Although squamous cell cancers may develop in EV patients, the association with other hematological or solid malignancies and EV is reported in a few studies. In this report, a case of EV with primary mediastinal large B-cell lymphoma is presented.

A 20-year-old man with a five years history of red-brown macular lesions was admitted to our hospital. The skin biopsy revealed epidermodysplasia verruciformis. Persistent cough started during the hospitalization. On the chest X-ray, mediastinal enlargement was determined. Thoracic computed tomography demonstrated a mediastinal mass of 6 cm in diameter. Diffuse, large B-cell lymphoma was diagnosed. The chemotherapy (R-CHOP regiment) and involved field radiotherapy were administered. Complete response was achieved after the combined treatment modality. He is lymphoma-free for 18 months follow-up.

Epidermodysplasia verruciformis is frequently seen in immunosuppressive patients and many accompany infections with type human papilloma virus subtypes such as 5 and 8. These human papilloma virus subtypes that have oncogenic properties may trigger lymphomagenesis. In addition, lymphomas are seen more frequently in immunosuppressive patients than healthy persons. We conclude that there may be a predisposition to lymphoma development in epidermodysplasia verruciformis patients.

Key words: *Epidermodysplasia verruciformis, non-Hodgkin's lymphoma, human papilloma virus, immunosuppression.*

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INTRODUCTION

Epidermodysplasia verruciformis (EV) is a rare, autosomal recessive disease characterized by the inability to terminate Human Papilloma Virus (HPV) infection and later development of multiple squamous cell carcinomas (1,2). HPV 5 and 8 are two of EV-type HPVs and are found in cutaneous lesions (4).

The disease is widely prevalent among young children. Although common lesions are wart-like papules, the lesions may vary from macules similar to those of pityriasis versicolor to darkly pigmented, exophytic, and hyperkeratotic papules and usually occur on the face, neck, hand and feet (1).

Ninety percent of the patients have defects in cell-mediated immunity (3). Whether this impairment is primary or secondary to chronic HPV infection is still inconclusive, however, the humoral immunity remains unaffected.

In approximately one-third of the patients, EV undergoes malignant transformation (4). Although EV frequently relates to squamous cell carcinomas, the association of EV with other cancer types is not fully described. In this report, a case of EV with primary mediastinal large B-cell lymphoma is presented.

CASE REPORT

A 20-year-old man with a five years history of red-brown macular lesions was admitted to our hospital (Figure 1). EV was diagnosed through skin biopsy (Figure 2). The persistent cough started during hospi-



Figure 1. The eruptions of epidermodysplasia verruciformis. The red-brown macular lesions in neck region.

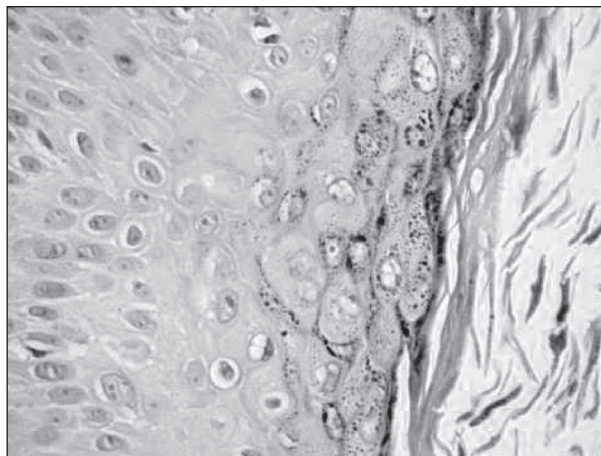


Figure 2. The microscopic appearance of skin biopsy. Viral sitopatic effect and prominent granular layer in the epidermis showing hyperkeratosis and acanthosis (HE, X100).

talization. Enlarged mediastinal structures were seen on the chest X-ray. Thoracic computed tomography (CT) demonstrated a mass of 6 cm in diameter in the anterior-superior mediastinal area. Diffuse, large B-cell lymphoma was diagnosed with CT-guided biopsy. There was neither other nodal nor extra-nodal involvement. The patient was diagnosed as stage IX by Ann Arbor staging.

Six cycles of R-CHOP chemotherapy regimen (Rituximab 375 mg/m² on day 1, cyclophosphamide 750 mg/m² on day 3, doxorubicine 40 mg/m² on day 3, vincristine 1.4 mg/m² (maximally 2 mg) on day 3, and prednisone 100 mg per oral on day 3 to 7) was given. The complete response was achieved with six cycles of chemotherapy. Radiotherapy was delivered to the mediastinum after the completion of chemotherapy. He is lymphoma-free for 18 months follow-up.

DISCUSSION

EV accompanies infection with specific HPV subtypes and is frequently diagnosed in immunosuppressive patients. The profound defect on the cell-mediated immunity is specific to the causative viruses. The immunotolerance, i.e. inability to recognize one's HPVs and reject the viral induced lesions, leads to a life-long disease. Causative HPVs differ from all other cutaneous and genital HPVs, and are referred to as EV-type viruses although they are found in healthy subjects. Among more than 20 known EV-type HPVs,

only a few types have oncogenic potential such as HPV 5 and 8 (4).

In this case report, an EV patient with primary mediastinal large B-cell lymphoma is presented. In a few reports, cases of EV associated with lymphoma were reported (3-5). The association between lymphoma and EV is not well documented. The several aspects of this association may be significant.

The first aspect is whether EV-type HPVs may cause lymphomagenesis. Among few EV-type HPVs, particularly HPV 5 and 8, have oncogenic properties (4). HPVs play roles in cell immortalization, proapoptotic/antiapoptotic pathway, chromosomal destabilization, and activation of telomerase (6). Moreover, the lymphomagenic effects of some HPV subtypes are described (7).

The second is immunosuppressive background. EV occurs in patients with impaired immunity. Lymphomas are also more frequent in immunosuppressive patients (8,9). Particularly innate immunity is important for prevention of HPV infections and HPV often persists due to evasion or inactivation of immune defenses (10). Besides, various immunologic abnormalities such as decreased T-cell mitogenic responses, reduced delayed-types hypersensitivity reaction, and increased natural killer cell activity probably play a role in HPV-induced carcinogenesis (11-13). In view of immunosuppression, the togetherness between lymphoma and EV is not surprising.

Lastly, EV and lymphoma may share the same genetic defects. EV is an autosomal recessive disease (14) and its genetic causes are yet unclear. The genetic alterations are also widely described in lymphomas.

The roles of HPVs in the pathogenesis of lymphomas and genetic aspects of EV need to be evaluated further.

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