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Epstein-Barr Virus-Positive Primary Cutaneous Diffuse Large B-Cell Lymphoma in an Immunocompetent Patient

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Dear Editor:

Epstein-Barr virus (EBV) is known to induce a number of malignancies, including diffuse large B-cell lymphoma (DLBCL) in immunosuppressed patients. Recently, however, age-related immune impairment was recognized as a predisposing factor in the development of EBV-driven lymphoproliferative processes in elderly patients[1]. Herein, we present a case of EBV-positive primary cutaneous DLBCL in an immunocompetent patient.

A 66-year-old woman presented with a 6-month history of multiple erythematous macules and patches on her trunk and both extremities (Fig. 1). There was no specific past history except for hypertension. A skin biopsy was performed and histological examination of the specimen

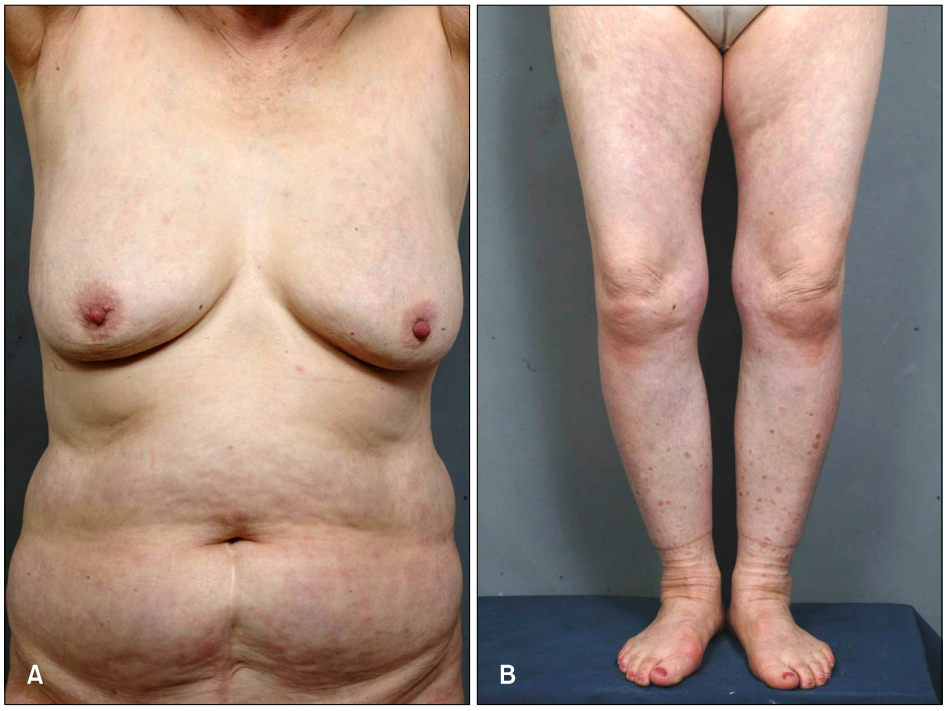

Fig. 1. Multiple erythematous macules and patches were observed on her trunk (A) and both extremities (B).

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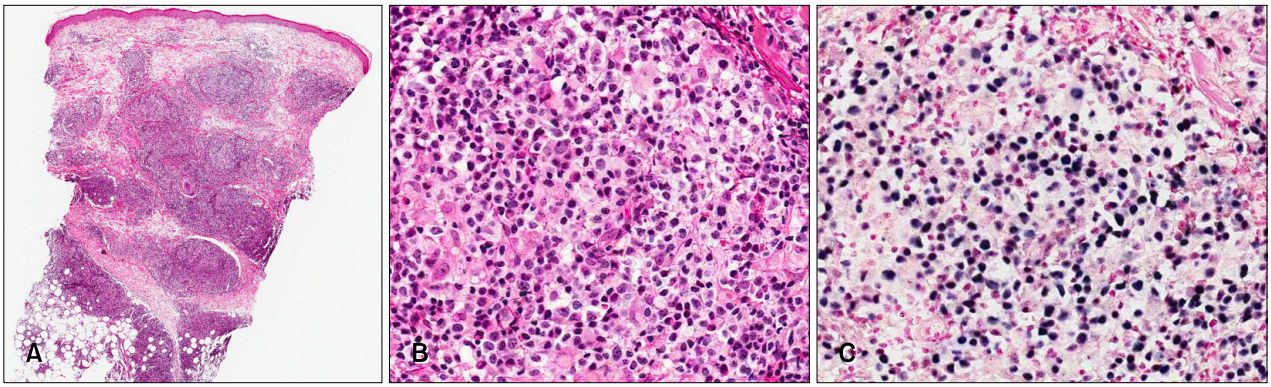

Fig. 2. (A, B) Skin biopsy revealed multifocal and nodular infiltrates of atypical medium- and large-sized mononuclear cells with enlarged nuclei showing one or more prominent nucleoli (H&E; A: ×40, B: ×400). (C) *In situ* hybridization for Epstein-Barr virus-encoded RNA was positive in the majority of tumor cells (×200).

revealed multifocal and nodular infiltrates of atypical medium- and large-sized mononuclear cells with enlarged nuclei showing one or more prominent nucleoli (Fig. 2A, B). Immunohistochemical examination revealed that the tumor cells were positive for CD20, bcl-2 and latent membrane protein 1 (LMP1), but negative for CD3, CD5, CD10, CD30, and bcl-6. *In situ* hybridization for EBV-encoded RNA (EBER) was positive in the majority of tumor cells (Fig. 2C). Bone marrow biopsy revealed no lymphomatous involvement. Based on these findings, the patient was diagnosed with EBV-positive primary cutaneous DLBCL. She was treated with combination chemotherapy (R-CHOP) and reached complete remission. After a year, however, the disease recurred. She was treated with radiotherapy, but the disease progressed.

Primary cutaneous DLBCL is a malignant proliferation of large B cells, presenting primarily in the skin with solitary or clustered erythematous or reddish-brown tumors. Histologically, dense diffuse infiltrates characterized by predominance of large cells with round nuclei are observed. Tumor cells express B-cell markers (CD20, CD79a). Most of the cases are positive for bcl-2 protein and multiple myeloma oncogene-1 (MUM-1), but are negative for CD10. EBV-related primary cutaneous DLBCL in non-immunocompromised patients is extremely rare. So far, only 11 cases have been reported[1]. All of the cases in the literature were of DLBCL except for 1 case. All of the cases of DLBCL occurred in elderly patients (over 55 years), presenting more frequently with multiple lesions at various locations. Many cases of DLBCL required combination chemotherapy, although one case underwent spontaneous remission[1].

Immunohistochemistry and *in situ* hybridization are the most important tests for the diagnosis of EBV-positive DLBCL. The tumor cells are usually positive for CD45 as well as for B-cell markers such as CD20, CD19, CD79a, and PAX-5. The cases are usually negative for germinal center markers, CD10 and bcl-6, and frequently positive for MUM-1. EBV-associated latent antigens such as LMP1 and EBNA-2 are positive in 94% and 28% of cases, respectively. Moreover, up to 50% of cases express CD30 but are negative for CD15. EBER *in situ* hybridization is the most reliable method for the diagnosis of EBV-positive DLBCL. It has the highest diagnostic sensitivity in the diagnosis of EBV-positive DLBCL[2].

So far, the prognosis of the newly recognized subtype of DLBCL remains in doubt, and there is no uniformly accepted treatment due to the small number of reported cases. On the basis of several literatures, EBV-positive DLBCLs seem to have worse response to chemotherapy than EBV-negative DLBCLs[3-5]. However, the response to rituximab-containing regimens has not yet been properly evaluated, and further studies are needed to clarify the role of rituximab and EBV-targeted therapy in EBV-positive DLBCL[2].

The proportion of EBV-related DLBCL cases in the elderly may be higher than that estimated at present. Therefore, we propose that EBV expression should be assessed in primary cutaneous DLBCLs. More information needs to be obtained regarding this new entity and further investigation is necessary.

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Congenital Form of Isolated Benign Primary Cutaneous Plasmacytosis in a Child

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Dear Editor:

Lymphoplasmacytic proliferation in the skin can be seen in various disorders from secondary syphilis to malignancies including cutaneoues involvement of multiple myeloma[1]. Among various conditions, isolated benign primary cutaneous plamacytosis (PCP) is known as a rare entity and is characterized by the infiltration of plasma cells in the dermis without systemic involvement. Isolated benign PCP, a rare disease itself, in childhood or at birth is extremely rare, with only four reported cases in the literature[2,3]. Herein, we present a congenital form of isolated benign PCP. A 1-year-old female visited Ajou University Hospital for a skin rash on her right lower leg noted at birth. The skin rash was a small plaque at birth but became insidiously larger in size. She had been using a topical steroid on the rash before visiting us, but claimed there was no improvement. Physical examination revealed a solitary asymptomatic erythematous plaque on the right calf (Fig. 1). Her general appearance was good, and no enlarged lymph nodes were palpated. She had no previous surgicomedical history or traumatic episodes. Laboratory tests including a complete blood count and serum chemistry were within the references ranges. The result of the venereal disease research laboratory (VDRL) test was negative and serum protein and serum immunoeletrophoresis were within the normal limits. A skin biopsy revealed psoriasiform hyperplasia with dense lymphoplasma cells infiltration in the superficial and deep dermis without atypia (Fig. 2A). Through immunopero-

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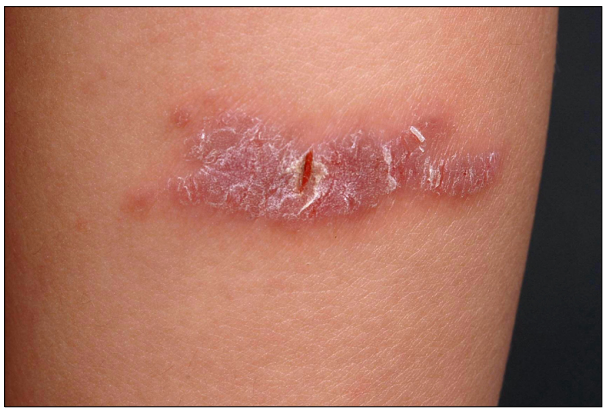

Fig. 1. A solitary asymptomatic erythematous plaque on the right lower leg.