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Cyclosporine-Induced Posterior Reversible Encephalopathy Syndrome in a Patient with Pemphigus Vulgaris

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Dear Editor:

Cyclosporine is an immunosuppressive drug originally isolated from *Tolypocladium inflatum* in 1970[1]. Here, we report a case of cyclosporine-induced posterior reversible encephalopathy syndrome (PRES) in a patient with pemphigus vulgaris. A 41-year-old Korean woman who had no underlying disease except pemphigus vulgaris was admitted to the emergency room owing to a sudden onset of severe headache, nausea, vomiting, and vision loss. A few minutes after admission, she presented with generalized tonic-clonic convulsive movement and became confused. Transient hypertension (160/100 mmHg) accompanied the episode. Laboratory tests showed leukocytosis (17.9×10^9/L) with neutrophilia (92.2%); cerebrospinal fluid was normal. Multiple ill-defined high-signal enhanced lesions were visible in the cortex and subcortical white matter of the bilateral parieto-occipital lesion on a T2-weighted brain magnetic resonance imaging (MRI) (Fig. 1A). Six months earlier, the patient presented with highly crusted vegetating lesions on her lower lip (Fig. 2A) as well as several flaccid blisters and scaly crusted erosions on her trunk (Fig. 2B). Histopathological examination showed suprabasal acantholysis (Fig. 2C), and a direct immunofluorescence study on the perilesional dorsal skin showed intercellular epidermal IgG deposition (Fig. 2D). Therefore, she was diagnosed with pemphigus vulgaris. Initially, the patient received prednisolone 100 mg/day for 2 weeks and tapered for 4 months; this was followed by cyclosporine 200 mg/day (4 mg/kg) for 2 months. We considered acute hypertension and cyclosporine administration as possible causes of the convulsive encephalopathy. Cyclosporine was discontinued immediately, and conservative therapy was administered. The patient showed a complete clinical recovery in 6 weeks, and signal enhancement also decreased on follow-up brain MRI (Fig. 1B). Cyclosporine is rarely reported to cause PRES; its association with cyclosporine was first described by Adams et al.[2] in 1987. PRES is characterized by clinical symptoms including headache, mental confusion, vomiting, visual disturbance, and multiple generalized tonic-clonic seizures; it is associated with characteristic radiological abnormalities in the posterior area of the cerebral white matter[3]. In addition to immunosuppressive or cytotoxic drugs, reported causes of PRES also include acute hypertension, infection, autoimmune disease, eclampsia, and pre-eclampsia[3]. Although the pathophysiology of PRES remains unclear, several mechanisms have been proposed. Cyclosporine has a direct toxic effect on vascular endothelial cells, causing them to release endothelin, prostacyclin, and thromboxane; these may cause microthrombi and also damage the blood-brain barrier[3]. Many PRES cases have been reported in organ and bone marrow transplant recipients receiving high-dose cyclosporine[4]. However, in the present case, the patient had been taking low-dose cyclosporine 4 mg $\cdot$ $kg^{-1}\cdot day^{-1}$ and had no associated risk factors for neurotoxicity. We finally diagnosed the patient with PRES because of her favorable response to cyclosporine discontinuation and the ultimately near-full reversal of encephalopathy. Thus, the possibility of PRES in patients taking

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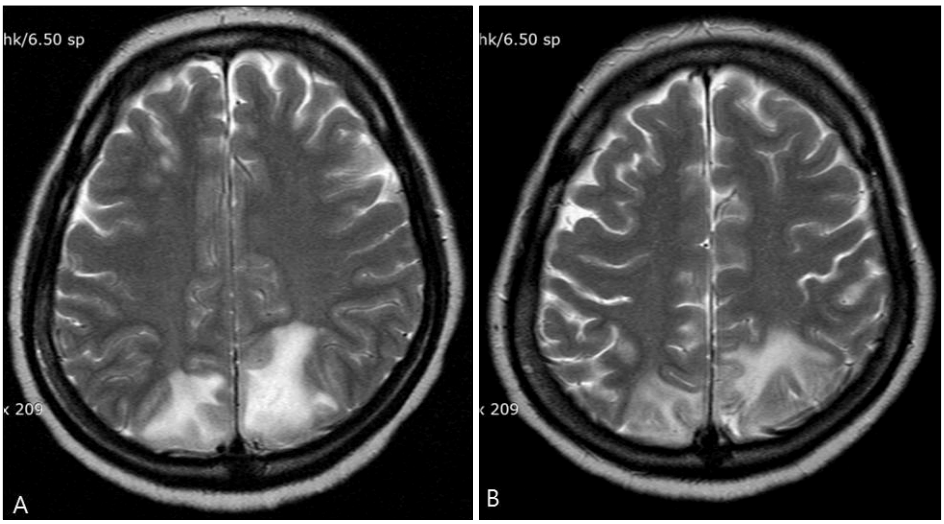

Fig. 1. (A) Axial T2-weighted magnetic resonance imaging (MRI) showing an area of high signal intensity in the bilateral white matter of the posterior parieto-occipital area. (B) Six weeks later, axial T2-weighted MRI showing significant improvement after cyclosporine withdrawal.

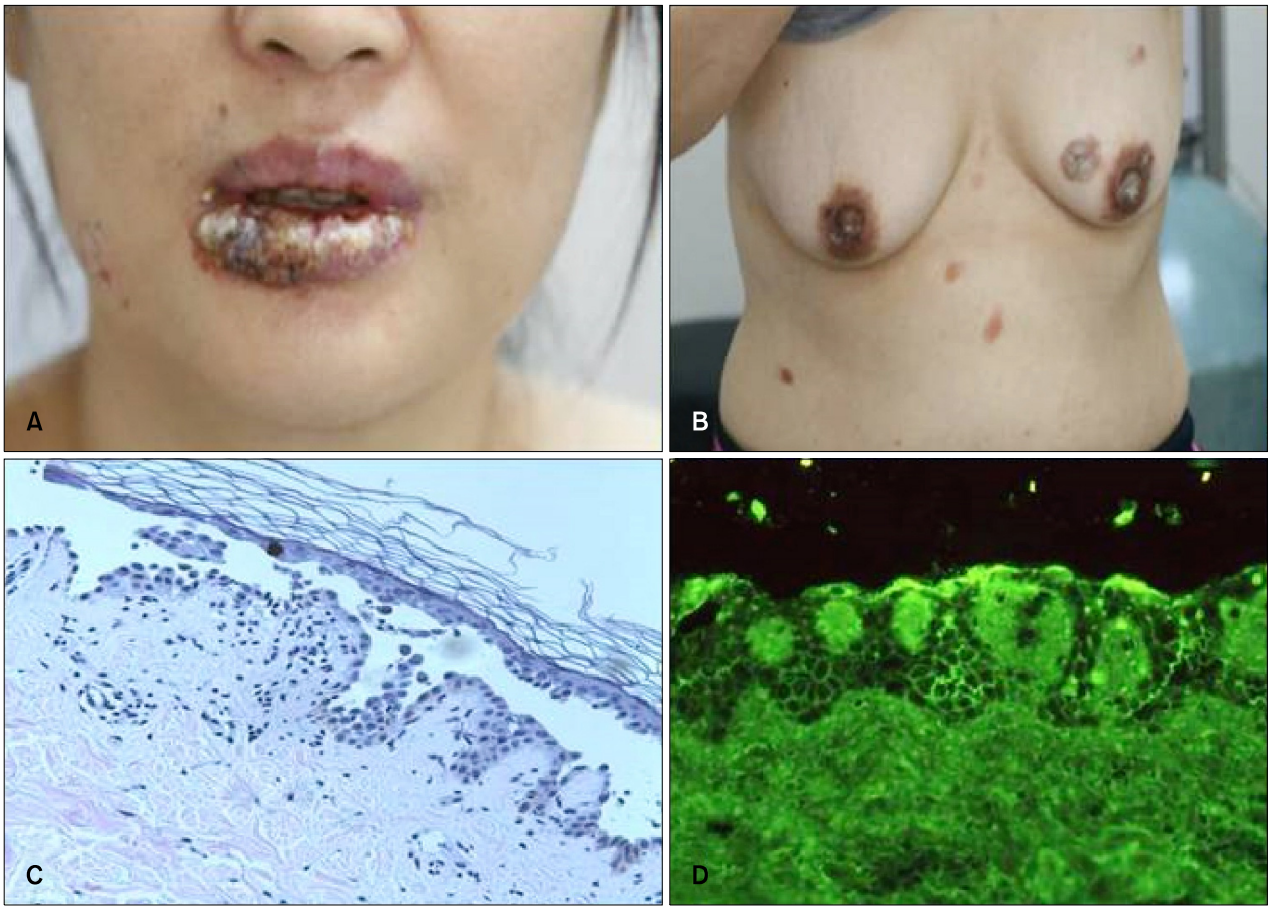

Fig. 2. (A) Highly crusted vegetating lesions on the lower lip. (B) Several flaccid blisters and scaly crusted erosions are distributed on her trunk. (C) Separation of the epidermis above the basal layer and scattered acantholytic cells (H&E, ×200). (D) Direct immunofluorescence study of the perilesional skin shows intercellular deposition of immunoglobulin G (×100).

even low-dose cyclosporine who present with neurologic symptoms should be emphasized. Physicians should rapidly diagnose this disease and withdraw the causative drug(s), because delayed diagnosis could lead to permanent sequelae.

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Synchronous Onset of Symmetrically Associated Extragenital Lichen Sclerosus and Vitiligo on both Breasts and the Vulva

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Dear Editor:

Lichen sclerosus (LS) is a chronic destructive inflammatory disease that affects the epidermis and dermis, particularly the genital and perineal areas[1]. However, cases of coincidental LS and vitiligo are rare reported[2]. Although the exact mechanism of the co-development of LS and vitiligo is unknown, both have been reported to be associated with autoimmune diseases or certain infections[2].

A 66-year-old woman presented with asymptomatic hypopigmented patches symmetrically located on both breasts and the genital area (Fig. 1). These patches first appeared on her left breast 1.5 years ago and on her right breast and genitalia 1 year ago. She was healthy with the exception of being a hepatitis B carrier and had no history of medication. On physical examination, the left breast lesion was a shiny crinkled thin hypopigmented patch; meanwhile, both the right breast and genital lesions were even hypopigmented patches. Wood's lamp test showed the right breast and genital lesions were accentuated while the left breast lesion was not. She was positive for hepatitis B surface antigen (HBsAg) and negative for HBs antibody (HBsAb) and hepatitis C virus (HCV) hepatitis C virus antibody (HCV Ab). The results of other laboratory tests including thyroid function test and antinuclear antibody screening were normal. Punch biopsies were performed on the left breast and genital lesion. Histologic analysis of the left breast lesion showed an effaced epidermis and homogenized edematous papillary dermis. Meanwhile, the genital lesion exhibited an absence of melanin, which was highlighted by Fontana-Masson staining (Fig. 2). Therefore, the left breast lesion was diagnosed as LS, and the right breast and genital lesions were diagnosed as vitiligo. Vitiligo and LS were treated with an excimer laser and a topical steroid, respectively; she has since exhibited gradual improvement.

Both LS and vitiligo have autoimmune etiologies. A study of autoimmunity in 350 women with LS revealed that

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