Neurology Asia 2020; 25(3) : 415 – 418

A unique leukoencephalopathy accompanied by palmoplantar pustulosis with identical pathological feature of helper T cell accumulation

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Abstract

Palmoplantar pustulosis is a chronic inflammatory skin disease involving the palms and soles where mild accumulation of helper T cells and neutrophils in the dermis histologically are observed. Leukoencephalopathy is a brain disease affecting white matter but is rarely accompanied by skin lesion. Here we report a unique case of leukoencephalopathy accompanied by palmoplantar pustulosis with identical pathological feature of helper T cell accumulation in both the brain and skin, suggesting a possible link in the pathogenesis.

Keywords: Leukoencephalopathy, palmoplantar pustulosis, helper T cell, pathological feature, corticosteroid

INTRODUCTION

Both skin and neuronal system are derived from ectoderm embryologically, and coincidentally involved in sarcoidosis, Bechet disease, tuberous sclerosis complex, malignant tumor, and various kinds of infection. The pathological association between skin and brain lesion was also reported in the autoimmune diseases[1], in which activated skin-T cell migrates into the central nervous system (CNS) and induce inflammation. Palmoplantar pustulosis (PPP) is a chronic inflammatory disorder of the skin, presenting with sterile pustules in palms and soles associated with smoking and aging. Histologically, T cells and neutrophils are observed in the dermis of PPP.[2] Leukoencephalopathy is a disease in white matter of brain caused by various pathological etiologies including lymphoma, infection, and autoimmune diseases. However, there have been no previous report linking leukoencephalopathy to PPP. Here we report the first case of the leukoencephalopathy accompanied by PPP with the pathological feature of helper T cell accumulation observed both in the brain and skin biopsy, suggesting a possible pathological link between the two via helper T cell activity.

CASE REPORT

A 69-year-old woman felt easy fatigue and depression developing gradually over four months. She could not understand her husband's speech or recognize where she was, and was admitted to the nearby hospital due to visual disturbance, headache, and impaired consciousness. She had history of PPP treated with bepotastine besilate, and chronic nontuberculous mycobacterial (NTM) infection treated with clarithromycin and ethambutol. She never smoked cigarette nor take alcohol, and she had no family history of similar illness.

She was 158 cm tall and weighted 45 kg. Blood pressure was 106/71 mmHg with the body temperature of 36.9 °C. Mild pustules of palmoplantar pustulosis were observed in both her palms, fingers, and soles (Figure 1. A-C). Neurological examinations revealed impaired consciousness (confusion, Glasgow coma scale E4V4M6), mild motor aphasia, apraxia, acalculia, agraphia, and left homonymous hemianopsia. There were no other abnormal neurological findings in the motor, sensory, cerebellar or autonomic systems. Serum analyses showed normal white blood cells count (5,290 /μL,

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Date of Submission: 24 March 2020, Date of Acceptance: 1 June 2020

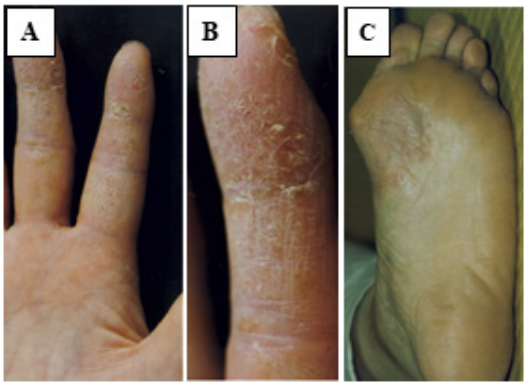

Figure 1. Mild pustules of palmoplantar pustulosis in palm (A), finger (B), and sole (C).

normal 3,300-8,600 /ml) and C-reactive protein (0.02 mg/dl, normal 0.00-0.14 mg/dl) with normal erythrocyte sedimentation rate (8 mm/hr). Angiotensin-converting enzyme (ACE) and tumor markers including soluble Interleukin-2 (sIL-2), carcinoembryonic antigen (CEA), squamous cell carcinoma (SCC), carbohydrate antigen 19-9 (CA19-9), cytokeratin fragment (CYFRA), the PCR test for JC virus were all negative. A cerebral spinal fluid (CSF) study showed normal pressure, slightly elevated cell counts (12 /μl, mononuclear cell 58%) and protein (110 mg/dl, normal 10-40 mg/dl) with normal glucose level (58 mg/dl). The bacterial culture, mycobacterium culture, fungal culture of CSF were negative.

Brain magnetic resonance imaging (MRI) showed high intensity lesions in right temporal lobe and left occipital lobe on fluid-attenuated inversion recovery (FLAIR) images and most of the lesions were limited to white matter of the brain (Figure 2. D, arrowheads), where Gadolinium (Gd) -enhanced T1-weighted MRI showed enhancement (Figure 2. E, arrowheads).

On admission Day 11, surgical open biopsy was performed for the right uncus. Pathological study found mild gliosis in brain parenchyma with diffuse accumulation of mononuclear cells suggesting lymphocytes, without neutrophils and eosinophils accumulation. There were no typical findings including viral inclusions or bizarre astrocytes. Immunohistological examination showed that mononuclear cells were strongly and diffusely positive for cluster of differentiation 3 (CD3, Figure 3. H) and CD4 (Figure 3. I), weakly positive for CD8 (Figure 3. J), CD20 (Figure 3. K), CD68, and negative for Bcl6, Ki-67, PD-1, or TIA1 (data not shown), suggesting that non-neoplastic helper T cell accumulation in the lesion. The next day of the biopsy (Day 12), the administration of prednisolone 40 mg/day was started and tapered to 10 mg/day over 10 days, and off in Day 24. With the prednisolone, the symptoms gradually improved.

On Day 33, she was referred to our hospital for further investigations. We performed skin biopsy of right palms, where mild accumulation of

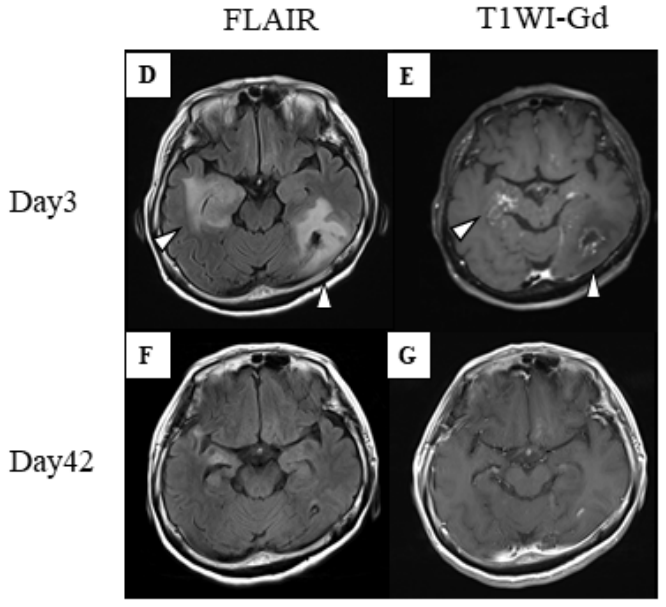

Figure 2. FLAIR and Gd-enhanced T1-weighted imagings of brain MRI, showing high intensity lesions with enhancement in right temporal lobe and left occipital lobe (D and E, arrowheads) on Day 3, which greatly improved on Day 42 (F and G).

mononuclear cells were found in the dermic layer. Immunohistologically, the mononuclear cells were positive for CD3 (Figure 4. L) and CD4 (Figure 4. M), weakly positive for CD8 (Figure 4. N), and negative for CD20 (Figure 4. O) which were similar to the immunohistopathological characters of brain biopsy. On Day 42, brain MRI showed improvement for the lesions in the right temporal and left occipital lobe on FLAIR and GdT1WI (Figure 2. F and G). She was discharged without symptoms on Day 56.

DISCUSSION

The brain biopsy showed accumulation of mononuclear cells with positive CD3 (Figure 3. H) and CD4 (Figure 3. I), and weakly positive for CD8 (Figure 3. J) and CD20 (Figure 3. K) suspected of helper T cells. The accumulations of helper T cells in leukoencephalopathy were reported in T cell lymphoma[3], central nervous system vasculitis[4], and viral infection[5]; but the present case showed no symptomatic or pathological features of these diseases. A previous report revealed that the biopsies were not useful for diagnosis in 40 % of the cases with brain lesion of unknown etiology[6] as in the present case, so that we need to add further examination including skin biopsy of the PPP lesion.

PPP is a chronic inflammatory disorder characterized by sterile pustules involving palms and soles of middle-aged women, but the pathogenesis of PPP is incompletely understood.[7] Histological examination of PPP shows mild acanthosis of the epidermis and mild accumulation of helper T cells followed by neutrophils in the upper dermis[2] which were observed in the present case (Figure 4. L-O).

Surprisingly, the pathological character of brain tissue was almost identical to that of skin tissue in the present case (Figure 3. H-K, Figure 4. L-O). A few previous reports of progressive multifocal leukoencephalopathy (PML) secondary to some monoclonal antibody drug therapy for PPP revealed T cell accumulation in the brain.[8,9] However, the present case did not use any monoclonal antibody drug previously nor was she under immunosuppressed status. We speculated that there was potential relationship between the brain and the skin lesion, and some previous papers support our hypothesis by showing relationship between psoriasis skin and central or peripheral nerve damage.[10,11] However, the possibility that the links were by chance cannot be ruled out.

In the present case, we did not find any significant accumulation of neutrophils or eosinophils which can be seen in PPP. The pustule formation was seen only in the early stages but had improved when skin biopsy was performed. The limitation of this report is that the palmar findings may have improved with steroid administration for the treatment of leukoencephalopathy, thus we should have performed the biopsy both in brain and skin over the same period.

We report here a unique case of leukoencephalopathy accompanied by PPP with the pathological feature of helper T cell accumulation observed in both the brain and skin biopsy. The present case suggested an unknown link of leukoencephalopathy and PPP with helper T cell accumulation.

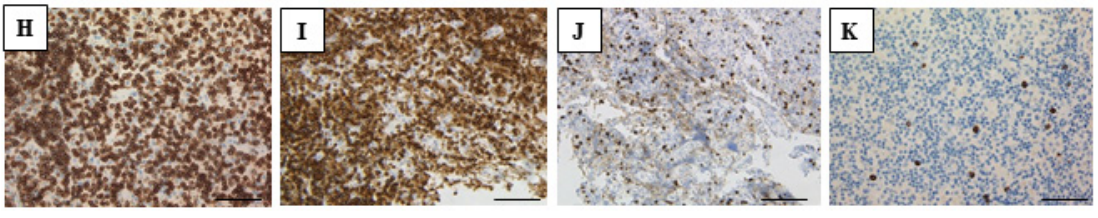

Figure 3. Immunohistological examination of brain tissue showed mononuclear cells being positive for CD3 (H) and CD4 (I), weakly positive for CD8 (J), CD20 (K).

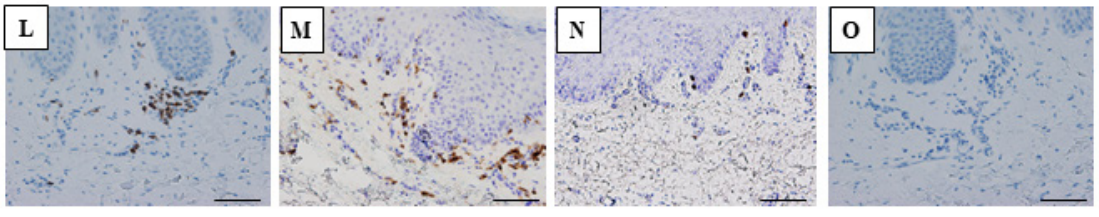

Figure 4. Immunohistological examination of the skin showed an almost identical pathological character to the brain biopsy (Fig. H-K), mononuclear cells being positive for CD3 (L) and CD4 (M), weakly positive for CD8 (N), CD20 (O).

DISCLOSURE

Financial support: This work was partly supported by a Grant-in-Aid for Scientific Research (B) 17H0419611, (C) 15K0931607, 17H0975609, and 17K1082709, and by Grants-in-Aid from the Research Committees (Kaji R, Toba K, and Tsuji S) from the Japan Agency for Medical Research and Development 7211800049, 7211800130, and 7211700121.

Conflict of interest: None

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