

Could Increased Vascular Endothelial Growth Factor Induced by Interleukin 17 Be the Cause of Posterior Reversible Encephalopathy Syndrome in Systemic Lupus Erythematosus?

To the Editor:

We read with interest the contribution by Varaprasad, *et al*¹. They studied patients with systemic lupus erythematosus (SLE) and posterior reversible encephalopathy syndrome (PRES) and suggested that PRES occurs in young patients with lupus at the early stage of the disease. However, they did not explain the exact mechanism of the disease. We would like to add the possible pathomechanism in the development of PRES in SLE.

PRES is an uncommon condition that typically shows a characteristic pattern of vasogenic edema in magnetic resonance imaging. The brain biopsies performed in the cases of Horbinski, *et al*² and Kofler, *et al*³ revealed evidence of endothelial activation, T cell trafficking, and vascular endothelial growth factor (VEGF) expression, suggesting that the systemic immune system may be involved with triggering PRES.

According to a study by Carvalho, *et al*⁴, serum levels of VEGF correlated with disease activity in a large number of autoimmune diseases. VEGF is a potent stimulating factor for angiogenesis and vascular permeability that is associated with autoimmune diseases such as rheumatoid arthritis and SLE⁴. Also, Kuryliszyn-Moskal, *et al*⁵ demonstrated that serum concentrations of VEGF in patients with SLE ($p < 0.05$), and in SLE patients with microvascular changes determined by nailfold capillaroscopy ($p < 0.01$), were significantly higher than in healthy control groups, indicating that serum VEGF level might be a useful marker of disease activity and internal organ involvement in patients with SLE.

Significant evidence has implicated interleukin 17 (IL-17), a CD4 T cell-derived proinflammatory and proangiogenic cytokine, in the pathogenesis of SLE^{6,7}. Importantly, Takahashi, *et al*⁸ showed that when VEGF and IL-17 were used together, 100 ng/ml IL-17 clearly promoted 10 ng/ml VEGF-mediated proliferation of human dermal microvascular endothelial cells. The result indicates that IL-17 can enhance VEGF-induced growth of vascular endothelial cells.

Therefore, it is possible that VEGF enhanced by IL-17 may cause vasogenic edema, resulting in the development of PRES in patients with SLE. It would be interesting to measure the levels of VEGF and IL-17 in SLE patients with PRES. Further studies are necessary to elucidate the exact signaling pathways of IL-17 and VEGF in the disease process. The potential therapeutic strategies in SLE and PRES with the anti-VEGF or anti-VEGF receptor should also be further evaluated.

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J Rheumatol 2012;39;4; doi:10.3899/jrheum.111124