Herpes Zoster and Multiple Sclerosis

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Multiple sclerosis (MS), a demyelinating disease of the central nervous system, has been considered multifactorial, and viruses may have a role in disease pathogenesis. Evidence suggests that certain viruses may trigger autoimmune neurological processes that lead to MS in genetically susceptible individuals [1, 2].

In this issue of the Journal, Kang et al analyze a database of 349,477 patients who had herpes zoster (experimental group) as a risk factor for MS (study outcome variable) in a region of the world historically considered low risk for MS. The authors compare their data with a randomly selected control group, more than 3 times as large as the initial sample (n = 1,262,200), of participants who did not have herpes zoster. Their results show that the herpes zoster group had a 3.96 times greater risk of developing MS than did the control group (95% confidence interval [CI], 2.22–7.07, P < .001).

This Kang et al study provides clear epidemiological observations suggesting a role for herpes zoster in the development of MS [3]. Previous studies noted that certain herpes viruses may trigger proinflammatory and autoimmune cascades through particles such as the toll-like receptor 4 (TLR-4) [3, 4], and that infectious environmental factors associated with MS may also belong to the herpesviridae family [4, 5].

This study highlights the time elapsed from the event of shingles until the occurrence of MS (approximately 100 d). In addition, evidence suggests that up to 30% of relapses among MS patients are associated with an infectious process [6, 7]. A possible explanation is the reactivation of latent herpes viruses by other infectious agents, and cross-recognition of common viral antigens with antigens found in the myelin sheath, which thereby induces molecular mimicry or superantigens [8–10]. The time lag for the occurrence of MS could be explained by a series of processes required by the immune systems of genetically susceptible individuals. The threshold may also explain, in part, the observation that some patients have higher recurrence rates of MS around certain months of the year [11]. Some viruses of the herpesviridae family cause B cells to express alpha and beta crystal, a small stress protein that is normally absent from lymphoid tissues and has been considered an immunodominant antigen in the central nervous systems of MS patients [12].

Other studies have suggested a role of varicella zoster virus in the genesis of relapse and progression of some patients with chronic-progressive forms of MS [13, 14]. The evidence provided in this study by Kang et al allows us to better understand the role of these viral factors as an MS risk among certain genetically susceptible individuals. These epidemiological findings should be corroborated in other parts of the world to further clarify the role of varicella zoster virus and other herpes viruses in the pathogenesis of multiple sclerosis.

References


