Bartonella henselae Infection May Occasionally Distract Immune Control of Latent Human Herpesviruses

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To the Editor:

We read with interest the September 2023 *Cutis* article by Swink et al,[1] "Cat Scratch Disease Presenting With Concurrent Pityriasis Rosea in a 10-Year-Old Girl." The authors documented the possibility of *Bartonella henselae* infection as another causative agent for pityriasis rosea (PR) even though the association of PR with human herpesvirus (HHV) 6 and HHV-7 infection is based on several consistent observations and not on occasional findings. The association of PR with endogenous systemic reactivation of HHV-6 and HHV-7 has been identified with different investigations and laboratory techniques. Using polymerase chain reaction, real-time calibrated quantitative polymerase chain reaction, in situ hybridization, immunohistochemistry, and electron microscopy, HHV-6 and HHV-7 have been detected in plasma (a marker of active viral replication), peripheral blood mononuclear cells, and skin lesions from patients with PR.[2] In addition, HHV-6 and HHV-7 messenger RNA expression and their specific antigens have been detected in PR skin lesions and herpesvirus virions in various stages of morphogenesis as well as in the supernatant of co-cultured peripheral blood mononuclear cells of patients with PR.[2,3] Lastly, the increased levels of several particular cytokines and chemokines in the sera of patients with PR support a viral role in its pathogenesis.[4]

Bartonella henselae is a gram-negative intracellular facultative bacterium that is commonly implicated in causing zoonotic infections worldwide. The incidence of cat-scratch disease (CSD) was reported to be 6.4 cases per 100,000 population in adults and 9.4 cases per 100,000 population in children aged 5 to 9 years globally.[5] Approximately 24,000 cases of CSD are reported in the United States every year.[6] Therefore, considering these data, if *B henselae* was a causative agent for PR, the eruption would be observed frequently in many patients with CSD, which is not the case. On the contrary, it is possible that *B henselae* infection may have reactivated HHV-6 and/or HHV-7 infection. It is well established that *B henselae* causes a robust cell-mediated immune response by activating natural killer and helper T cells (T_H1) and enhancement of cytotoxic T lymphocytes.[7] It could be assumed that by strongly stimulating the immune response and polarizing it to a specific antigen cell response, *B henselae* infection may temporarily distract the T cell-mediated control of the latent infections, such as HHV-6 and HHV-7, which may reactivate and cause PR.

It is important to point out that a case of concomitant *B henselae* and Epstein-Barr virus infection has been described.[8] Even in that case, the *B henselae* infection may have reactivated Epstein-Barr virus as well as HHV-6 and HHV-7 in the case described by Swink et al.[1] Epstein-Barr virus reactivation has been detected in one case[8] through

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The authors report no conflict of interest.

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Cutis. 2024 February;113(2):E26-E27. doi:10.12788/cutis.0976

serologic testing—IgM, IgG, Epstein-Barr virus nuclear antigen IgG, and heterophile antibodies—as there were no dermatologic manifestations that may be related to Epstein-Barr virus reactivation from latency.[9]

In conclusion, a viral or bacterial infection such as Epstein-Barr virus or *B henselae* may have a transactivating function allowing another (latent) virus such as HHV-6 or HHV-7 to reactivate. Indeed, it has been described that SARS-CoV-2 may act as a transactivator agent triggering HHV-6/HHV-7 reactivation, thereby indirectly causing PR clinical manifestation.[10]

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