

**Commentary on: "Pityriasis Rosea Recurrence is Much Higher than Previously Known: A Prospective Study"**

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We read with great interest the paper by Yüksel (1) about recurrent pityriasis rosea (PR). We would like to share our experience and make some observations (2). We agree with the author that the rate of recurrence of PR is probably greater than that reported in the literature. In our updated series of approximately 700 patients with PR, we found a recurrence rate of 4.3%, in line with those of other authors (2–4). However, the prevalence of recurrent PR is probably underestimated, due to the occurrence of atypical PR forms and the number of patients who are misdiagnosed by non-dermatologists, who attend a different specialist, or are not concerned with the lower severity of the eruption. The author claims that the aetiology of PR is still unknown. Indeed, a large body of evidence highlighted a close relationship between PR and human herpesvirus (HHV)-6 and/or -7 endogenous reactivation (5–11). In fact, the association of PR with HHV-7 infection is based on several and consistent investigations using the most modern biological techniques, and not on occasional findings. Several studies have identified HHV-6 and HHV-7 DNA by PCR and calibrated quantitative real-time PCR in plasma, peripheral blood mononuclear cells (PBMCs) and lesional skin of patients with PR. Furthermore, cytopathic effects specific for herpesviruses and virions resembling herpesviruses were detected in co-cultured mononuclear cells from patients with PR. HHV-6 viral messenger RNA (mRNA) expression by *in situ* hybridization and specific HHV-6 and HHV-7 antigens by immunohistochemical staining, involved in the late stages of the infection, were found in PR skin lesions. Neutralizing antibodies and high-avidity IgG antibodies against HHV-6 and HHV-7 have been demonstrated in patients with PR, indicating a viral endogenous reactivation. Importantly, the detection of cell-free viral DNA in plasma, mRNA and antigens in skin lesions and cytopathic effects in culture are considered as markers of active viral replication. A recent study provided evidence that circulating interleukin 17, interferon (IFN)- γ , vascular endothelial growth factor (VEGF) and the IFN- γ -induced protein 10 (IP-10) are increased in patients with PR compared with controls, supporting the active immunological response in PR and contributing to a better definition of the skin defence network (5–11). All these data emphasize the role of both viruses in the pathogenesis of PR; in only a few diseases is there so much evidence proving a viral aetiology. Furthermore, the aetiopathogenesis of PR as the consequence of HHV-6 and/or HHV-7 reactivation (the viruses may be reac-

tivated independently or simultaneously) may explain the cases of recurrent PR. Indeed, a parallelism can be established between HHV-6/7 reactivation and other typical reactivating HHVs, such as varicella zoster virus, cytomegalovirus and Epstein-Barr virus. Recurrences of PR would happen in the patients in whom the immune response is not fully in control of viral reactivation, preferably within a limited period of time (5–18 months in our series), time needed to achieve complete control of replicating HHV-6/7 (2). We agree with Yüksel that the mean duration of recurrent PR was shorter than that of primary episodes: the size and number of the lesions were decreased and the related constitutional symptoms less severe. The less severe course of the disease may be explained by the increasing response of the immune system against HHV-6 and HHV-7 reactivation, so that the immune response is at least partially effective and the virus load declines.

We also agree with Yüksel about the presence of a history of atopy in PR patients, with a rate in our series of 19%. However, we must take into account that atopy is common in the general population and its prevalence has grown considerably, ranging from 30% to almost 50% (12). Moreover, we can assume that the frequency of relapses in atopic individuals is due to underlying cell-mediated immunological deficiency, which is crucial for control of the viral infection and replication.

In fact, in atopic patients, Th2 cell predominance leads to production of IL-4, which induces IgE formation and prevents differentiation of IFN- γ -producing Th1 cells (13).

Yüksel did not mention the possible treatment of recurrent PR with acyclovir. This would have been interesting, since we successfully treated several patients with acyclovir 800 mg, 5 times a day for 5 days (14, 15), in order to interrupt the sequence of relapses.

Lastly, controversial opinions remain about a higher seasonal prevalence of PR, but in our experience, PR occurs uniformly all year and no statistically seasonal prevalence could be shown, either in primary episodes or in relapsing disease (5).

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The author of the original article (Mavişe Yüksel) was given the opportunity to comment in response to this Correspondence, but chose not to do so.