Atypical presentations of pityriasis rosea: a reply

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Abstract

Pityriasis rosea (PR) may have atypical presentations with regard to morphology and distribution of the lesions. Recently, several forms of PR considered atypical for the course of the disease have been described. Distinct from the typical PR that resolves within 2-12 weeks, relapsing and persistent PR forms (lasting longer than 12 weeks) have been described in adults and children. Lesions of the oral mucosa in PR may be more common than reported in the literature. Formerly, the occurrence of oral lesions in PR has been considered more frequent in dark-skinned patients compared to light-skinned patients. However, in 12 Caucasian adult patients with persistent PR that have been recently described, oral lesions were very common (75% of cases). Another study on the clinical features and virological parameters of 31 Caucasian children with PR showed that painless oropharyngeal lesions were present in 35%, a rate much higher than those reported in adult dark-skinned (9%) and Caucasian patients (16%) with typical PR.

Keywords: pityriasis rosea, atypical presentation, human herpesvirus 6/7

We read with interest the article by Gupta and Levitt describing three cases of pityriasis rosea (PR) with atypical clinical presentation [1] and we would like to make some observations and report our experience.

Regarding PR etiology, the authors stated that human herpesvirus (HHV)-6 and HHV-7 have been studied as precipitating factors [1] and that their DNA has been found in 17% and 39% respectively of PR plasmas. We would like to remark that other recent studies established a causal role for HHV-6 and HHV-7 endogenous systemic active infection in the pathogenesis of PR. Indeed, HHV-6 and HHV-7 DNA were found not only in plasma but also in PR skin lesions by quantitative real time polymerase chain reaction (PCR). In addition, HHV-6 mRNA expression and specific antigens have been found by immunohistochemistry in PR skin lesions [2-5]. Herpesvirus virions in various stages of morphogenesis were detected by electron microscopy in skin lesions and in the supernatant of co-cultured peripheral blood mononuclear cells (PBMCs) from PR patients [6]. Notably, HHV-6 and HHV-7 plasma viremia, a marker of systemic active infection, was demonstrated in PR patients and related to the presence of systemic symptoms [2, 4]. Investigations about the cytokines and chemokines network in PR provided evidence that circulating CXC3-chemokine fractalkine (CX3CL1), interleukin (IL)-17, interferon (IFN)-γ, vascular endothelial growth factor (VEGF), and CXCL10 are increased in PR patients. These results underscored the active immunological response in PR and this cytokine pattern supported a viral induced disease process in PR pathogenesis [7, 8].

Secondly, we would like to emphasize that not only drugs, as stated by Gupta and Levitt [1], but also many types of vaccinations may induce PR and PR-like eruptions, as recently reported [9]. Regarding post vaccination PR, it has been hypothesized that the vaccine, eliciting a specific immune response against a definite infectious agent, may disrupt the T-cell-mediated control on the latent infections, such as HHV-6/7, which may reactivate. Conversely, PR-like eruptions may occur as a hypersensitivity delayed response to a vaccine, similar to this response with a drug [10]. Another possible mechanism is

molecular mimicry with a viral epitope that could result in a T-cell-mediated skin reaction. In fact, in our experience with drug-induced PR we did not find any signs of HHV-6/7 reactivation, in plasma or in skin, which is quite different from typical PR [9, 10].

We agree with Gupta and Levitt that PR may have atypical presentations with regard to morphology (vesicular lesions) and distribution of the lesions (inverse PR), [1]. However, the authors did not mention the forms of PR that can be considered atypical for the course of the disease. Differently from the typical PR that resolves within 2-12 weeks [1], relapsing [11] and persistent [12] PR forms have recently been reported in adults and children [13]. These atypical forms are probably underestimated [14].

We also agree with Gupta and Levitt [1] that lesions of the oral mucosa in PR may be more common than as reported in the literature. Formerly, the occurrence of oral lesions in PR has been considered more frequent in dark-skinned patients as compared to Caucasians because 9% of Nigerians with PR have been reported to have oral lesions [15]. Vidimos et al., however, found that 16% of Caucasian patients with PR have various types of painless oral lesions [16]. We recently described 12 Caucasian patients (Fitzpatrick phototype II and III) with persistent PR (PPR), and found that oral lesions, resembling Nagayama spots described in primary HHV-6 infection [17], were more common in PPR compared with typical PR (75% versus 16% of cases), [12], a further sign of active HHV-6 infection [12, 18]. Notably, systemic symptoms were also more common in PPR compared with typical PR (92% versus 69% of cases), in accordance with the persistent systemic reactivation of HHV-6 and HHV-7 [12]. Subsequently, we studied the clinical features and virological parameters of 31 light-skinned children (Fitzpatrick phototype II and III) with PR and found painless oropharyngeal lesions (vesicles, petechiae, papules, and strawberry tongue) in 35% [13], a rate much higher than those reported in Nigerians (9%), [15] and Caucasian patients (16%), [16] with typical PR.

Lastly, since PR is a self-limiting disease with symptoms that are typically mild and tolerable, we agree with Gupta et al. [1] that treatment is usually unnecessary. The authors, however, stated that several therapies reported in the literature may be helpful, including systemic antiviral agents when treatment is desired. This is the case with particularly severe forms of PR occurring during pregnancy [19]. These forms are characterized by widespread involvement of the lesions and accompanied with systemic symptoms in which, in absence of an antiviral drug specific for HHV-6/-7, rest and high doses of acyclovir may prevent miscarriage or premature births [20].

References

1. Gupta N, Levitt J. Unique clinical presentations of pityriasis rosea: aphthous ulcers, vesicles and inverse distribution of lesions. Dermatol Online J. 2017;23 (2):11. [PMID: 28329497].
2. Broccolo F, Drago F, Careddu AM, Foglieni C, Turbino L, Cocuzza CE, Gelmetti C, Lusso P, Rebora AE, Malnati MS. Additional evidence that pityriasis rosea is associated with reactivation of human herpesvirus-6 and -7. J Invest Dermatol. 2005; 124: 1234–1240. [PMID: 15955099].
3. Watanabe T, Kawamura T, Jacob SE, Aquilino EA, Orenstein JM, Black JB, Blauvelt A. Pityriasis rosea is associated with systemic active infection with both human herpesvirus-7 and human herpesvirus-6. J Invest Dermatol. 2002; 119: 793–797. [PMID: 12406322].
4. Drago F, Rebora A. Viral reactivation and skin eruptions. Dermatology. 2003;207:1-2. [PMID: 12845239].
5. Broccolo F, Drago F, Cassina G, Fava A, Fusetti L, Matteoli B, Ceccherini-Nelli L, Sabbadini MG, Lusso P, Parodi A, Malnati MS. Selective reactivation of human herpesvirus 6 in patients with autoimmune connective tissue diseases. J Med Virol. 2013;85:1925-34. doi: 10.1002/jmv.23670. [PMID: 23983182].
6. Drago F, Ranieri E, Malaguti F, Battifoglio ML, Losi E, Rebora A. Human herpesvirus 7 in patients with pityriasis rosea. Electron microscopy investigations and polymerase chain reaction in mononuclear cells, plasma and skin. Dermatology. 1997;195:374-8. [PMID: 9529560].
7. Gangemi S, Cannavò SP, Guarneri F, Merendino RA, Sturniolo GC, Minciullo PL, Di Pasquale G, Valenzise M, Drago F, Rebora A. The CX3C-chemokine fractalkine (CX3CL1) is detectable in serum of patients affected by active pityriasis rosea. J Eur Acad Dermatol Venereol. 2006;20:1366-7. [PMID: 17062081].
8. Drago F, Ciccarese G, Broccolo F, Ghio M, Contini P, Thanasi H, Parodi A. The Role of Cytokines, Chemokines, and Growth Factors in the Pathogenesis of Pityriasis Rosea. Mediators Inflamm. 2015;2015:438963. doi: 10.1155/2015/438963. [PMID: 26451078].
9. Drago F, Ciccarese G, Javor S, Parodi A. Vaccine-induced pityriasis rosea and pityriasis rosea-like eruptions: a review of the literature. J Eur Acad Dermatol Venereol. 2016;30:544-5. doi: 10.1111/jdv.12942. [PMID: 25545307].
10. Drago F, Broccolo F, Agnoletti A, Drago F, Rebora A, Parodi A. Pityriasis rosea and pityriasis rosea-like eruptions. J Am Acad Dermatol. 2014;70:196. doi: 10.1016/j.jaad.2013.08.056. [PMID: 24355268].
11. Drago F, Ciccarese G, Rebora A, Parodi A. Relapsing pityriasis rosea. Dermatology. 2014;229:316-8. doi: 10.1159/000363568. [PMID: 25412725].
12. Drago F, Broccolo F, Ciccarese G, Rebora A, Parodi A. Persistent pityriasis rosea: an unusual form of pityriasis rosea with persistent active HHV-6 and HHV-7 infection. Dermatology. 2015;230:23-6. doi: 10.1159/000368352. [PMID: 25612842].
13. Drago F, Ciccarese G, Broccolo F, Cozzani E, Parodi A. Pityriasis

Rosea in Children: Clinical Features and Laboratory Investigations. Dermatology. 2015;231:9-14. doi: 10.1159/000381285. [PMID: 25997658].

14. Drago F, Ciccarese G, Rebora A, Broccolo F, Parodi A. Pityriasis Rosea: A Comprehensive Classification. Dermatology. 2016;232:431-7. doi: 10.1159/000445375. [PMID: 27096928].
15. Jacyk WK. Pityriasis rosea in Nigerians. Int J Dermatol 1980; 19: 397–399. [PMID: 7419321].
16. Vidimos AT, Camisa C. Tongue and cheek: oral lesions in pityriasis rosea. Cutis. 1992;50:276-80. [PMID: 1424793].
17. Hall CB, Long CE, Schnabel KC, Caserta MT, McIntyre KM, Costanzo MA, Knott A, Dewhurst S, Insel RA, Epstein LG. Human herpesvirus-6 infection in children. A prospective study of complications and reactivation. N Engl J Med 1994; 331: 432–438. [PMID: 8035839].
18. Drago F, Paolino S, Rebora A, Broccolo F, Drago F, Cardo P, Parodi A. The challenge of diagnosing atypical exanthems: a clinico-laboratory study. J Am Acad Dermatol. 2012;67:1282-8. doi: 10.1016/j.jaad.2012.04.014. [PMID: 22627037].
19. Drago F, Broccolo F, Javor S, Drago F, Rebora A, Parodi A. Evidence of human herpesvirus-6 and -7 reactivation in miscarrying women with pityriasis rosea. J Am Acad Dermatol. 2014;71:198-9. doi: 10.1016/j.jaad.2014.02.023. [PMID: 24947696].
20. Drago F, Rebora A. Treatments for pityriasis rosea. Skin Therapy Lett. 2009;14:6-7. [PMID: 19585058].