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Letter to the Editor

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Pediatric pityriasis rosea

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To the Editor,

We read with interest the article by Çölgeçen et al. describing 46 cases of pediatric pityriasis rosea (PR) (1) and we would like to make few observations and report our experience.

The authors stated that the cause of PR is not known (1) despite recent studies that established a causal role for systemic active HHV-6 and HHV-7 infection in the pathogenesis of PR. Indeed, HHV-6 and HHV-7 DNAs were found in plasma and lesional skin by real-time polymerase chain reaction (PCR) of patients with PR and HHV-6 mRNA expression and specific antigens by immunohistochemistry in their PR lesions (2–4). Furthermore, herpesvirus virions in various stages of morphogenesis were detected by electron microscopy in skin lesions and in the supernatant of cocultured peripheral blood mononuclear cells (PBMCs) from patients with PR (5). Notably, HHV-6 and HHV-7 plasma viremia, a marker of systemic active infection, was demonstrated in PR patients and was related to the presence of constitutional symptoms (2,4).

We agree with the authors that PR typically resolves within 6–8 weeks (1), but recently relapsing (6) and persistent (7) forms (lasting longer than 12 weeks) of PR have also been reported in adults and children and these forms are probably underestimated.

Çölgeçen et al. stated that few reports of pediatric PR are currently available (1). However, in our series of 640 consecutive PR patients we collected 47 children (7%) under 10 years of age (8). From 31 of them (19 females and 12 males with a mean age of 6.9 years) we obtained informed parental consent to study clinical features and virological parameters, comparing them with adult patients with PR. In disagreement with Çölgeçen et al., who found a higher prevalence of PR in winter (1), we found that pediatric PR (8), like adult PR (9), occurs uniformly throughout the year with no statistically significant differences, unlike other infectious exanthems for which seasonal occurrence has been documented (10). Infections (exanthema subitum, fifth disease, pharyngitis, and tonsillitis) and drug intake (antibiotics) before skin manifestations were recorded respectively in 23% and 6% of our patients, significantly below the figure reported by Çölgeçen et al. (1). Similar to Çölgeçen et al. (1), a herald patch (HP) was found in most of our patients (58%), especially on the trunk; the median time between appearance of HP and secondary eruption was 4 days; and the skin eruption had an average duration of 16 days. Unlike Çölgeçen et al. (1), who did not observe oral lesions, we found in 35% of our patients painless oropharyngeal lesions: vesicles were the most common ones, followed by petechiae, papules, and strawberry tongue. Regarding systemic symptoms, which were not reported in Çölgeçen's series (1), almost half of our patients (48%) complained of systemic symptoms during the course of PR (prodromal or accompanying symptoms especially during the first 7 days from onset): irritability was the commonest one, followed by headache, fatigue, sore throat, and conjunctivitis. Conversely, pruritus, experienced by 74% of the patients in Çölgeçen's series (1), was unremarkable in our patients. Interestingly, 15/46 (33%) patients studied by Çölgeçen et al. took drugs before the appearance of PR (1). However, the authors made no efforts to distinguish between genuine PR and PR-like eruptions (usually drug-induced) according to the criteria previously described (11).

Importantly, comparing the clinical features of children with PR (including the patients of our series and that of Çölgeçen et al.) with those of adult PR patients reported in the literature (9), the occurrence of HP does not differ greatly. By contrast, the mean time lapse between HP and the generalized eruption in children (4 days) is very short compared to adults (about 2 weeks), as well as the exanthem duration, lasting about 2 weeks in children and about 45 days in adults (ranging from 2 weeks to a few months (7)). Oropharyngeal lesions, at least in our series, appear to be commoner in PR children than in adults:

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we reported oral involvement in 35% of children, a rate much higher than those reported in adult dark-skinned (9%) (12) and Caucasian patients (16%) (9). Regarding the occurrence of systemic symptoms, they are frequently reported both in adults (69%) (9) and children with PR (48%) (8).

Finally, we also compared our children PR patients with adult PR patients from a virological point of view: we collected blood samples at the first visit for specific anti-HHV-6 and anti-HHV-7 serology and for the search for HHV-6 and HHV-7 DNA loads in plasma and PBMCs by calibrated quantitative real-time PCR (cq-PCR). For 12 children we also took blood samples 4–6 weeks after recovery for the same investigations. Unfortunately, in Çölgeçen's series, virological investigations were not performed. Our serological findings in children with PR showed IgG antibody positivity against HHV-6 in 26 of them (84%) and IgM antibodies only in 5 (16%). Serology for HHV-7 revealed IgG antibodies in 19 patients (61%) and IgM antibodies only in 3 cases (10%). In all cases, the presence of high-avidity IgG antibodies allowed us to rule out the possibility of a primary infection, thereby confirming an HHV-6 and/or HHV-7 endogenous systemic reactivation. cq-PCR demonstrated in all patients HHV-6 and/or HHV-7 plasma viremia (8). Compared to adult PR patients (4), both during the acute phase and 4–6 weeks after recovery, children showed a higher average level of plasma viremia for both HHV-6 and HHV-7 (8).

In conclusion, our data point out that PR has different clinical and virological features between adults and children, suggesting that, following HHV-6 and/or HHV-7 systemic reactivation, the pathogenetic mechanisms involved in PR may be at least partially different in children and adults.

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Reply to Letter to the Editor

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To the Editor,

We are most grateful to Drago et al. for their interest in our paper entitled "Pityriasis rosea: a natural history of pediatric cases in the Central Anatolia Region of Turkey" (1). The basic aim of our study was to examine the demographic, clinical, and epidemiological characteristics of pityriasis rosea (PR) in children (1). That is why no virological examination was performed.

While drugs, stress, pregnancy, and various infections have previously been implicated in the etiopathogenesis of PR, there has recently been focus on systemic activation of human herpes virus (HHV)-6 and HHV-7 (2–8).

Drago et al. observed that pediatric PR appeared at similar rates throughout the year (7), while we determined a higher prevalence of PR in children in winter (1). The fall in environmental temperatures may have triggered the disease by suppressing cellular immunity in susceptible individuals.

Drago et al. recorded various infections in 26% of patients before skin manifestations in pediatric PR, and drug use in 6% (7), while 32.6% of our patients had a history of upper respiratory tract infection and 32.6% a history of drug use (1). These levels were close to those reported in Gündüz et al.'s study from Turkey (9).

PR-like eruption is defined as a medication-induced cutaneous rash whose clinical characteristics are remarkably similar to those of genuine PR, and that often cannot easily be distinguished from it. However, it is exceedingly important to do so, since typical PR may occur during treatment, but independently of it. Various differentiating criteria have recently been suggested. Clinical, histopathological, and virological investigations will certainly be useful in such differentiation (8,10). However, even if virological investigations prove to be useful in this area, they are nevertheless difficult to implement in practice. Diagnosis of PR was based on history and physical examination in the majority of our cases. However, in atypical cases, skin biopsy performed by a dermatologist was used in order to differentiate between PR and other exanthemas. Patients with indefinite diagnoses were considered for enrollment (1).

Pruritus has been reported in 25% of adult PR patients and in 69%–90% of children. The incidence of pruritus in our study was 74% (9,11,12). The incidence was higher than the general figure reported for adults, but similar to previous studies involving pediatric populations (1,9,11,12).

Drago et al. observed oral involvement in 35% of children with PR (7), while Amer et al. determined no oral lesions in children of Afro-American origin (11). We also observed no oral lesions in our patients (1). This suggests that socioeconomic status and genetic factors may be involved in the course of PR.

In conclusion, PR exhibits a similar course in children and adults in Turkey. We observed a higher incidence of disease during the rainy and snowy months. Upper respiratory tract infection was determined prior to rash in 32.6% of our subjects. The high prevalence of pruritus also constituted a significant finding, but this quickly resolved. Further studies involving larger patient numbers are now needed to compare PR symptoms between different age cohorts and ethnic groups.

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