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Pityriasis rosea manifesting only with a herald patch

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Ethics approval and consent to participate: the study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the coordinating center (Liguria Region Ethics Committee, registry number 163/2020). Informed consent was obtained from the patients included in this study.

Availability of data and materials: data supporting the findings of this study are available from the corresponding author upon reasonable request.

Dear Editor,

Pityriasis rosea (PR) is an acute, self-limited exanthematous disease associated with the endogenous systemic reactivation of human herpesvirus (HHV)-6 and/or HHV-7. The disease typically begins with a single erythematous plaque called the "herald patch" (HP), followed by a secondary generalized, symmetrical eruption.[1,2] Rarely, PR can be limited only to the herald patch.[2-4] The clinical and laboratory features of these atypical PR have been poorly investigated.

To assess the differences from the classical form, we did a retrospective case-control study on 19 patients presenting with HP as the only sign of PR (cases) (Table 1) and on 19 age- and sex-matched, otherwise healthy, immunocompetent patients with a typical PR (controls) (Table 2). No patients were taking any drugs before and during the eruption. Mycological examination and Treponema pallidum hemagglutination assay (TPHA) were negative in all patients with only HP. We recorded the site of the herald patch for each patient, the eruption duration, the presence of mucosal lesions, and associated systemic symptoms. Furthermore, we evaluated the titers of HHV-6 and HHV-7 antibodies and their DNA loads in plasma by quantitative real-time PCR, as described.[1] All the patients gave informed consent for blood sampling, to collect their data, and to be included in this study. Considering the site of the HP, mucosal lesions, and systemic symptoms, no statistically significant differences were found between the two groups of patients at $\chi 2$ test with Yates correction. Similarly, HHV-6 IgG and IgM antibody titers and HHV-7 IgG and IgM antibody titers showed no statistically significant differences between the two groups.

Conversely, the cases showed a shorter duration of PR and a lower HHV-6 DNA and HHV-7 DNA viral load in plasma than the controls with high statistical significance (T-test $p<0.00001$, $p<0.00001$, and $p=0.007275$, respectively, considering $p<0.05$ statistically significant).

Several review articles about the clinical variants of PR reported the possibility that the disease may present only with the HP, not followed by the secondary eruption.[2-4] However, the present study is the first to investigate the clinical and laboratory features of this atypical form of PR compared with the classic PR. Our study did not show significant clinical and serological differences between classic PR and PR with HP alone. Notably, the findings concerning the duration of HP and its HHV-6 and HHV-7 viral load in the plasma compared to the eruption of typical PR may suggest differences in pathogenesis for these two forms of PR. Generally, the mechanisms underlying the different forms of PR (namely classic, relapsing, persistent, and pediatric)[2] depend on the different interactions between the systemic activation of HHV-6 and HHV-7 and the host's immunological response. We found that when PR manifests with only the HP, it has a shorter duration, and the mean HHV-6 and HHV-7 DNA load in plasma was lower than the classic form. Therefore, this rare variant of PR may

be considered an abortive form of the disease occurring when the HHV-6 and/or HHV-7 reactivation from latency is countered by an immunological response that is more effective than in classic PR.

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Table 1. Clinical and laboratory features of the patients with HP as the only evidence of PR.

Patient n°	**Age**	**Sex**	**Herald patch site**	**Eruption duration (days)**	**Enanthem**	**Prodromal symptoms**	**DNA cp/mL plasma HHV-6**	**DNA cp/mL HHV-7**	**HHV-6 antibody titer IgG**	**HHV-6 antibody titer IgM**	**HHV-7 antibody titer IgG**	**HHV-7 antibody titer IgM**
1	26	m	trunk	32	no	headache, sore throat	≤15	≤15	1/80	1/40	1/80	NEG
2	19	f	trunk	28	no	fatigue, irritability	23	≤15	≥1/160	1/80	1/80	NEG
3	31	m	thigh	25	no	fatigue, inappetence	≤15	≤15	1/80	1/80	1/40	NEG
4	18	f	trunk	20	yes	sore throat, irritability	20	≤15	≥1/160	≥1/160	1/80	1/40
5	23	f	trunk	30	no	fatigue, lack of appetite	18	NEG	≥1/160	1/80	1/40	NEG
6	29	f	trunk	28	yes	headache, irritability	≤15	≤15	≥1/320	1/80	1/80	1/80
7	34	m	trunk	20	no	no	≤15	NEG	≥1/160	1/80	1/40	NEG
8	30	m	trunk	25	no	fatigue, inappetence	≤12	NEG	≥1/320	1/80	1/80	1/40
9	26	m	trunk	28	no	sore throat	18	≤15	≥1/160	1/80	≥1/160	1/80
10	20	m	trunk	25	no	fatigue	18	≤15	1/80	≥1/160	≥1/160	1/80

11	17	f	trunk	30	yes	fatigue, irritability	25	≤15	1/80	≥1/160	1/80	1/40
12	28	m	trunk	27	no	headache	30	≤15	≥1/160	≥1/160	1/40	1/40
13	31	m	trunk	25	no	fatigue	≤15	≤15	1/80	≥1/160	1/40	NEG
14	29	f	trunk	25	no	no	18	≤15	1/80	1/80	1/80	1/80
15	34	m	trunk	28	no	sore throat	≤12	≤15	≥1/160	1/40	1/80	1/40
16	30	m	trunk	30	no	no	25	≤15	1/80	NEG	1/80	NEG
17	24	f	trunk	24	no	fatigue, insomnia	≤15	≤15	≥1/160	≥1/160	≥1/160	1/40
18	35	m	trunk	30	no	fatigue, inappetence	20	≤15	1/80	1/40	1/80	1/40
19	31	f	trunk	24	no	fatigue, difficulty concentrating	≤15	≤15	1/80	1/80	1/80	NEG

Table 2. Clinical and laboratory features of patients with classic PR (controls).

Patient n°	**Age**	**Sex**	**Herald patch site**	**Eruption duration (days)**	**Enanthem**	**Prodromal symptoms**	**DNA cp/mL plasma HHV-6**	**DNA cp/mL HHV-7**	**HHV-6 antibody titer IgG**	**HHV-6 antibody titer IgM**	**HHV-7 antibody titer IgG**	**HHV-7 antibody titer IgM**
1	18	m	trunk	38	no	no	35	≤15	1/80	≥1/160	1/40	≥1/160
2	28	f	thigh	35	yes	fatigue, headache	30	≤15	≥1/160	≥1/160	1/80	1/80
3	32	m	trunk	42	yes	fatigue, inappetence	26	≤15	≥1/160	≥1/160	1/40	1/40
4	19	f	trunk	38	no	fatigue, pruritus	46	18	1/80	≥1/160	1/40	NEG
5	30	m	trunk	35	no	no	35	≤15	1/80	1/80	≥1/160	1/80
6	31	m	thigh	40	no	fatigue, irritability, headache	20	≤15	1/40	≥1/160	1/40	NEG
7	25	f	trunk	36	no	fatigue, sore throat	≤15	≤15	≥1/160	≥1/160	1/80	1/80
8	32	m	trunk	38	yes	fatigue, irritability	28	18	≥1/320	≥1/160	≥1/160	≥1/160
9	30	f	thigh	48	yes	fatigue, irritability, insomnia	36	≤15	1/80	≥1/160	1/40	1/40

10	28	m	trunk	40	no	headache, arthralgia, myalgia	32	≤15	≥1/160	1/80	1/80	NEG
11	22	f	trunk	35	yes	fatigue, irritability	56	20	1/80	≥1/160	1/40	1/80
12	33	m	trunk	32	no	fatigue, sore throat	42	≤15	1/80	≥1/160	1/40	1/40
13	21	f	trunk	40	yes	fatigue	35	≤15	1/40	1/80	1/40	NEG
14	21	f	trunk	38	no	fatigue, lack of appetite	46	≤15	1/80	1/80	1/80	1/40
15	32	f	trunk	35	yes	fatigue, headache	26	≤15	1/40	1/80	1/80	1/40
16	32	m	trunk	30	no	fatigue	20	≤15	1/80	1/80	1/40	1/40