Recurrence of Hepatitis C Virus Infection during Pityriasis Rosea

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Pityriasis rosea (PR) is a common, self-limiting exanthematous skin eruption that usually resolves spontaneously within 4–8 weeks. Systemic active infection with human herpes viruses 6 (HHV-6) and/or 7 (HHV-7) has been implicated recently in PR pathogenesis (1, 2). We describe here a patient with hepatitis due to hepatitis C virus (HCV) who experienced a worsening of her hepatic disease during PR.

CASE REPORT

A 34-year-old woman presented with erythematous papulosquamous lesions on her trunk and limbs and a "herald patch" on the right upper arm. The clinical lesions were suggestive of PR. The patient had reported severe prodromal symptoms, such as fatigue, headache, irritability, insomnia and difficulty concentrating for 3 weeks prior to consultation. She denied any drug intake prior to the onset of the skin eruption.

A biopsy specimen of a lesion showed patchy parakeratosis and dyskeratotic cells in the epidermis, oedema, and perivascular infiltration of lymphocytes and histiocytes in the papillary dermis with some extravasated erythrocytes, all consistent with the diagnosis of PR.

In 2005, the patient had been diagnosed as having chronic hepatitis C infection (genotype 2). She was treated with 18 μg/kg/week PEGylated interferon α-2a combined with 800 mg/day ribavirin for 24 weeks, and her liver enzymes returned to normal levels and HCV-RNA became undetectable. The patient was treated only for 24 weeks in 2005 and after that, she did the laboratory exams requested for her hepatitis (as follow-up) 3 times a year, since 2012, when PR developed.

During the next 2 weeks, her severe constitutional symptoms persisted and new lesions involved most of her skin surface. Blood and lesional skin samples were taken to test for HHV-6 and HHV-7 DNA by quantitative calibrated real-time PCR, and this revealed abnormal loads of both viruses (Table I). In addition, the HCV-RNA titre increased (Table I). A course of PEGylated interferon α-2a (12 μg/kg/week) and ribavirin (600 mg/day) was prescribed. PR lesions and constitutional symptoms resolved in a month (10 weeks from the onset of the eruption) with a simultaneous improvement in the laboratory tests. Both HCV-RNA and HHV-7 DNA became undetectable, while HHV-6 DNA reduced to < 10 equivalents/ml (Table I).

Table I. *Laboratory findings before and after treatment*

Serum levels	Before treatment	After treatment
AST, U/l	140	Normal range
ALT, U/l	115	Normal range
HCV-RNA, IU/ml	110×10^3	Undetectable
HHV-6 DNA, eq/ml	50	<10
HHV-7 DNA, eq/ml	40	Negative

Elevated serum levels of transaminases, HCV-RNA and cell-free genome equivalents of HHV-6 and HHV-7 DNA during PR and HCV reactivation. These parameters declined considerably after the treatment with PEGylated interferon α-2a (12 μg/kg/week) and ribavirin (600 mg/day).

DISCUSSION

PR is a common self-limiting papulosquamous skin disorder, which is thought to be caused by systemic reactivation of HHV-6 and/or HHV-7 (1, 2). Although constitutional symptoms are not rare in PR, they were particularly severe in our patient and were accompanied by a simultaneous increase in HCV-RNA and hepatic enzymes titres.

Target cells of HHV-6 are, in fact, $CD4^+$T lymphocytes, $CD8^+$T lymphocytes and natural killer (NK) cells. It is not surprising, therefore, that HHV-6 is the most immunosuppressive of the currently known herpes viruses (3), promoting the release of cytokines, activating Kupffer cells and inducing transforming growth factor-β1, which are dominant factors in the cascade of hepatic fibrogenesis (4). In fact, the reactivation of one or more herpes viruses after transplantation has been shown to increase HCV replication and promote relapses in HCV hepatitis (5).

We suggest that, in our patient, HHV-6 reactivation, demonstrated by the high HHV-6 viraemia and by development of PR, simultaneously reactivated the latent HCV infection. To our knowledge, an association between HCV reactivation and PR has not been reported previously. This connection, although plausible, may just be accidental, so this needs further investigations.

The authors declare no conflicts of interest.

REFERENCES

1. Drago F, Ranieri E, Malaguti F, Losi E, Rebora A. Human herpesvirus 7 in pityriasis rosea. Lancet 1997; 349: 1367.
2. Broccolo F, Drago F, Careddu AM, Foglieni C, Turbino L, Cocuzza CE, et al. Additional evidence that pityriasis rosea is associated with reactivation of human herpesvirus-6 and -7. J Invest Dermatol 2005; 124: 1234–1240.
3. Singh N, Husain S, Carrigan DR, Knox KK, Weck KE, Wagener MM, Gayowski T. Impact of human herpesvirus-6 on the frequency and severity of recurrent hepatitis C virus hepatitis in liver transplant recipients. Clin Transplant 2002; 16: 92–96.
4. Friedman SL. Cytokines and fibrogenesis. Semin Liver Dis 1999; 19: 129–140.
5. Humar A, Kumar D, Raboud J, Caliendo AM, Moussa G, Levy G, Mazzulli T. Interactions between cytomegalovirus, human herpesvirus-6, and the recurrence of hepatitis C after liver transplantation. Am J Transplant 2002; 2: 461–466.