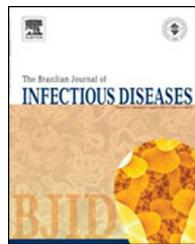




# The Brazilian Journal of INFECTIOUS DISEASES

[www.elsevier.com/locate/bjid](http://www.elsevier.com/locate/bjid)



## Letter to the Editor

### Pityriasis rosea following human papillomavirus vaccination<sup>☆</sup>



Dear Editor,

We read with great interest the review by Gonçalves et al.<sup>1</sup> about safety, tolerability and side effects of human papillomavirus (HPV) vaccines, discussing the most frequently reported events related to the vaccine. We agree that safety is not a major barrier to vaccination since most of the reported adverse events have been mild or moderate in intensity. We would like to describe two patients who developed pityriasis rosea (PR) following the last dose of the quadrivalent HPV vaccine. To our knowledge, they are the first two cases of PR secondary to HPV vaccine.

The first of our patients was a 17-year-old woman who presented with a typical PR, which developed one month after the third dose of HPV vaccination. The exanthema, preceded by general malaise and headache, started with a herald patch on the trunk and progressed with secondary eruptions on trunk, arms and neck two weeks later. Routine investigations yielded unremarkable results. Serology disclosed IgG (1/160) and IgM (1/320) antibodies against human herpesvirus 7 (HHV-7) and IgG antibody against human herpesvirus 6 (HHV-6) (1/40). HHV-7 DNA in plasma (170 genome equivalents/mL) and in peripheral blood mononuclear cells (PBMCs) (657 genome equivalents/mL) were found by calibrated quantitative real-time polymerase chain reaction, as reported.<sup>2</sup> HHV-6 DNA was neither found in plasma nor in PBMCs. Her lesions and symptoms gradually improved in the following eight weeks. After recovery, HHV-7 DNA was not any longer detected in plasma.

Our second patient was a 20-year-old woman who developed a typical PR two months after the third dose of HPV vaccination. The skin eruption was preceded by headache, inability to concentrate, and insomnia, initiated over the trunk and then spread to the abdomen and neck without a herald patch. Routine investigations turned out normal. IgG antibodies against HHV-6 and HHV-7 were present (1/320 and 1/160, respectively) whereas IgM was negative. HHV-6 and HHV-7 DNAs were positive in plasma (137 and 85 copies/mL) and in

PBMCs (570 and 464 copies/mL). The lesions improved in eight weeks. HHV-6 and HHV-7 DNAs were no longer detected after recovery.

Pityriasis rosea (PR) is a self-limiting exanthematic disease, due to an endogenous reactivation of HHV-6 and/or HHV-7.<sup>2</sup> PR and PR-like eruptions have very rarely been described after vaccination against diphtheria, tuberculosis, poliomyelitis, tetanus<sup>3</sup> but never after HPV vaccination. PR, usually, develops a few weeks after vaccination.

According to the criteria recently described,<sup>4</sup> in our patients, the detection of HHV-7 and HHV-6 viremia, together with anti-HHV-7 IgM antibodies in the plasma of the first patient, confirmed that the exanthematic lesions were typical PR instead of PR-like eruptions.

The pathogenetic mechanisms leading to post-vaccination PR is unknown. We believe that the non-specific immune stimulation and the subsequent release of cytokines<sup>5</sup> may trigger HHV-6 and/or HHV-7 reactivation and therefore the occurrence of PR. However, PR is a self-limiting exanthema and its occurrence does not require discontinuation of the vaccination schedule.

#### Conflicts of interest

The authors declare no conflicts of interest.

#### REFERENCES

1. Gonçalves AK, Cobucci RN, Rodrigues HM, de Melo AG, Giraldo PC. Safety, tolerability and side effects of human papillomavirus vaccines: a systematic quantitative review. *Braz J Infect Dis.* 2014; pii:S1413-8670(14)00069-5.
2. Broccolo F, Drago F, Careddu AM, et al. Additional evidence that pityriasis rosea is associated with reactivation of human herpesvirus-6 and -7. *J Invest Dermatol.* 2005;124:1234–40.
3. Bjornberg A, Hellgren L. Pityriasis rosea: a statistical, clinical and laboratory investigation of 826 patients and matched

<sup>☆</sup> Report of the first two cases of exanthema secondary to HPV vaccination.

- healthy controls. *Acta Derm Venereol Suppl (Stockh).* 1962;42:1–68.
4. Drago F, Broccolo F, Agnoletti A, Drago F, Rebora A, Parodi A. Pityriasis rosea and pityriasis rosea-like eruptions. *JAAD.* 2014;70:196.
  5. Drago F, Javor S, Bruzzone L, Drago F, Parodi A, Picciotto A. Pityriasis rosea in a hepatitis-positive patient treated with pegylated interferon  $\alpha$ : report of a case and review of the literature. *Dermatology.* 2014;228:10–3.

Francesco Drago, Giulia Ciccarese\*, Alfredo Rebora,  
Aurora Parodi  
DISSAL, Department of Dermatology, IRCCS A.O.U. San Martino-IST,  
Genoa, Italy

\*Corresponding author at: DISSAL, Department of Dermatology, IRCCS Azienda Universitaria Ospedaliera San Martino-IST, Largo Rosanna Benzi, 10, 16132 Genoa, Italy.  
E-mail address: [giuliaciccarese@libero.it](mailto:giuliaciccarese@libero.it) (G. Ciccarese).

Received 10 June 2014

Accepted 26 October 2014

Available online 17 December 2014

<http://dx.doi.org/10.1016/j.bjid.2014.10.006>

1413-8670/© 2014 Elsevier Editora Ltda. All rights reserved.