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Lichen planus-like eruption following imiquimod treatment for genital warts

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Abstract

We report the case of a 37-year-old male patient, who developed a lichen planus-like eruption following imiquimod treatment for recurrent genital warts. We believe this is due to immune activation by imiquimod, which elicited an autoinflammatory reaction leading to an LP-like eruption in the setting of HPV infection. Our main objective was to open the way to greater understanding of this possible adverse event of imiquimod, commonly used in the treatment of human papillomavirus lesions. Moreover, the clinical implication is to maintain a high index of suspicion for imiquimod induced LP-like eruption, when encountering erythematous plaque lesions of the genitals in patients under treatment for recurrent genital warts.

Keywords: Lichen planus; Genital warts; Imiquimod; Lichenoid reaction; Adverse events.

Introduction

Genital warts is a common sexually transmitted disease of the genital skin and mucous membranes, caused by certain types of Human Papillomavirus (HPV). A wide range of options are currently available for the treatment of genital warts targeting at the removal of the warty growth; Imiquimod is considered to be among the first-line treatments [1]. Imiquimod 5% cream is a patient-applied topical immunomodulatory agent, with highly effective antiviral and anti-tumor activity [1]. We report the case of a male patient, who developed a Lichen Planus (LP)-like eruption following imiquimod treatment for recurrent genital warts.

Case presentation

A 37-year old male patient was referred to our clinic for recurrent genital warts. Personal and family history was otherwise unremarkable. On clinical examination, four skin-colored, verrucous plaques approximately 3 mm each, were identified on the glans penis near the urethral meatus and on the sulcus area. The rest of the anogenital area was clear. He was treated with liquid nitrogen cryotherapy; the warts cleared within 10 days. No residual lesions were identified two weeks after cryotherapy. A course of imiquimod cream 5%, 3 times weekly for 4 weeks was offered to the patient aiming at sub-clinical lesions. Mild erythema and discomfort were noted after the 5th application which lasted for about one week. On 2-week follow up visit after end of imiquimod course, no active lesions were present, but 4 weeks later, new lesions appeared on the glans penis. Clinical examination revealed a group of asymptomatic pinkish-red, flat papules, 6-8 in number and 2 mm in size, over an ill-defined, subtle patch of background erythema of the glans penis (Figure 1). Differential diagnosis included re-activation of HPV infection, as well as inflammatory dermatoses, such as psoriasis or LP.

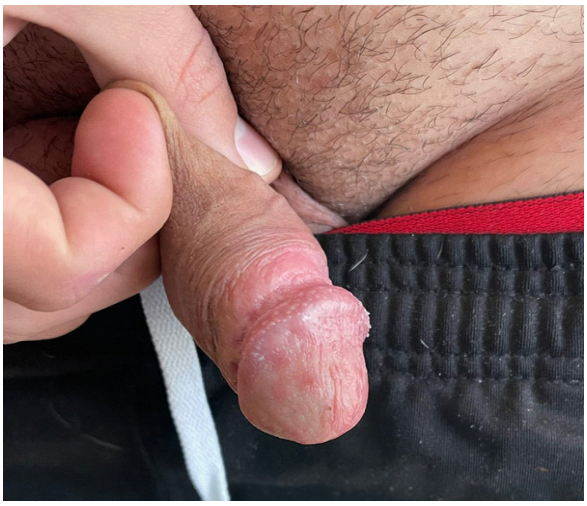

Figure 1: A group of asymptomatic pinkish-red, flat papules, 6-8 in number and 2 mm in size, over an ill-defined, subtle patch of background erythema of the glans penis of a patient treated with imiquimod for recurrent genital warts.

A biopsy was performed; histology revealed parakeratosis, basal layer hydropic degeneration and lichenoid inflammation of the upper dermis, findings consistent with LP. The lesions cleared after a 4-week course of pimecrolimus cream 1% twice daily.

Discussion

Lichen planus is an auto-inflammatory, T-cell mediated disease of obscure etiology, affecting skin and mucosae. It has been reported in association with chronic active hepatitis (B or C), primary biliary cirrhosis; as a complication of hepatitis B vaccination; in association with viral and bacterial antigens; trauma (via koebnerization), and several medications, including imiquimod. There are only four reported cases, all in male patients aged 21-54 years, who developed LP-like lesions after treatment of genital warts with topical imiquimod [1-3].

There are only four reported cases, all in male patients aged 21-54 years, who developed LP-like lesions after treatment of genital warts with topical imiquimod [1-3]. Duration of treatment with imiquimod ranged from 4 to 12 weeks and time between treatment onset and LP development varied between 6 to 12 weeks [1-3].

In our patient, the time elapsed from administration of imiquimod to the onset of LP was 10 weeks, while duration of treatment with imiquimod was 4 weeks, in accordance with previous experience.

The mechanism of imiquimod-induced LP is largely unknown. Imiquimod interacts with Toll-like receptors, leading to activation of cytokines that cause recruitment of cytotoxic Th1 and plasmacytoid dendritic cells [4]. The latter, in turn, produce large amounts of type I Interferons (IFNs), which we know that play a major role in LP pathogenesis [5]. IFN-inducible chemokines, CX19 and CXC110, and an IFN-inducible cytotoxic attack targeting the basal keratinocytes appear to play a crucial role in the development of LP pattern [5]. Further research is needed to elucidate the exact pathogenesis of these cases.

Clinical implications arising from the present case include mostly the addition of the imiquimod-induced LP-like eruption in our differential diagnostic approach, when encountering erythematous plaque lesions of the genitals in patients under treatment for genital warts.

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