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Case Report

Imiquimod triggering varicella zoster reactivation in an immunocompetent patient

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ABSTRACT

Imiquimod is widely used for the treatment of superficial basal cell carcinoma as well as several other dermatologic conditions. While its local immunostimulatory action is well proven, its potential for systemic immunomodulation has been less well described. We report the first case (to our knowledge) of varicella zoster reactivation caused by Imiquimod in an immunocompetent patient.

Keywords: Drug reaction, Imiqumod, Varicella zoster reactivation

INTRODUCTION

Herpes zoster or 'shingles" is a painful dermatomal cutaneous eruption caused by reactivation of latent varicella zoster virus (VZV). Virus reactivation is most frequently triggered by stress and/or disease- and druginduced immunosuppression. Medications, led by glucocorticoids and disease modifying anti-rheumatic

drugs account for around 10% of cases.¹ Therapeutic use of topical anti-cancer agents including Imiquimod has been shown to effect systemic immunomodulation leading to local as well as distant adverse sequelae.^{2,3}

We present a case of imiquimod triggering varicella zoster reactivation in an immunocompetent patient.

CASE REPORT

A 70-year-old caucasian male presented to a private dermatology clinic with a 2cm brown plaque on his right chest of six-months duration. He recounted primary VZV infection as a child but refuted any episodes of reactivation. He was medicated with Rosuvastatin (20mg daily) for hypercholesterolemia but specifically denied knowledge of any immunosuppressive illnesses or medications.

Shave biopsy confirmed a superficial basal cell carcinoma (0.3mm). Surgical and non-surgical options were discussed with the patient and he elected for the standard regime of topical Imiquimod five times weekly for six weeks.



Figure 1: Anterior distribution of vesicular eruption.

Ten days after starting, the patient developed a grouped vesicular eruption overlying the contralateral lumbar 1 and 2 dermatomes anteriorly and posteriorly (Figures 1 and 2). He had also developed headaches, myalgia and arthralgia and exhibited an intense localised skin reaction. He had received a Hepatitis A booster three days prior but denied any antecedent stressors or trauma.

Viral PCR of the vesicles detected Varicella Zoster DNA. Blood testing and chest radiography excluded chronic immunosuppressive disease and occult malignancy. The Imiquimod was ceased and he responded completely to antiviral therapy. Notably, his systemic symptoms persisted four days into antiviral therapy.

DISCUSSION

Topical Imiquimod is adversely most frequently associated with localised skin reactions (e.g. erythema, irritation).

However, there have also been reports of systemic adverse effects including fever, headache, myalgia and arthralgia. Systemic absorption is understood to be minimal but may be augmented by various factors such as dosing, topographic location and intensity of localised skin reaction.^{4,5}



Figure 2: Posterior distribution of vesicular eruption.

Transdermal skin thickness may also affect topical drug delivery and our patient undergoing shave biopsy may have aided systemic absorption. Imiquimod might be best avoided for 'raw' areas. It has been hypothesised that any systemic effects resulting from Imiquimod use may be caused not by the drug itself but by the locally produced cytokines spreading into the systemic circulation.⁶

Imiquimod acts on toll-like receptors (TLR) 7 and 8 inducing a pro-inflammatory response. At the same time, it mediates a regulatory response chiefly through interleukin-10 (IL-10) and regulatory T cells, which acts to temporise inflammation.⁷

Some CD4+ polymorphs secrete relatively more IL-10, restricting downstream production of effector T cells, tipping the immune balance in favour of suppression. Repetitive TLR 7/8 administration with single agonist not exhibiting any virulence or invasive properties can induce effector T cell immunosuppression. ^{8,9}

Primed IL-10-secreting Tregs can be amplified by viral vaccination. 10

Causality is seldom proven in these cases deferring rather to a test of probability. Our analysis suggests that topical

imiquimod is a probable cause of the patient's herpes zoster satisfying requirements of timing, dechallenge and systemic effects consistent with oral toxicity.

Mounting evidence of generalised and distant effects resulting from topical imiquimod use suggest that it is indeed a systemic medication and should be considered as such. Factors relating to dosing, topographic location, intensity of localised skin reaction as well as skin condition may dictate individual propensity to systemic reactions, including latent viral reactivation.

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