



# Nonphoto-exposed initial cutaneous manifestation of lupus after zoster: A case of Wolf's isotopic reaction

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## INTRODUCTION

An isotopic reaction describes a novel cutaneous condition occurring in a distribution previously affected by another disease, a dermatologic example of locus minoris resistentiae (LMR). LMR represents a physiologic Achilles heel in the skin in which a congenital or acquired altered defense capacity causes a certain region of skin to be more vulnerable and easily affected by a trigger or new disease than others. Since its initial description in 1995, Wolf's isotopic reaction has been characterized as a type of isotopic reaction in which a classically nondermatomal skin reaction presents in the same dermatome after an initial pathologic insult of a herpes zoster infection (or other herpes viruses).

Multiple cutaneous diseases are reported to arise confined to dermatomes previously affected by these viruses, including malignancies, fungal infections, granulomatous diseases, and connective tissue diseases.<sup>1</sup> Hypotheses such as altered immune environment, neuronal damage, and vulnerable connective tissue have been implicated in the development of this response. In vitro studies found that varicella zoster virus alters gene expression affecting cytokeratins, desmosomes, and proteases in keratinocytes.<sup>2</sup> In addition to keratinocytes, the sensory nerve fibers, which modulate the skin immune response secreting neuromediators such as substance P, vasoactive intestinal peptide and calcitonin gene-related peptide interact with membrane receptors of immune cells in the skin.<sup>3</sup> Immune dysregulation is supported by comparative patch testing studies in which skin previously affected by herpes viruses responded differently compared with unaffected skin when in contact with an allergen.<sup>4</sup>

### Abbreviations used:

LMR: locus minoris resistentiae  
 SLE: systemic lupus erythematosus

## CASE REPORT

A 56-year-old white woman with a history of systemic lupus erythematosus (SLE) diagnosed in her 20s and Sjögren's disease, presented with a chief complaint of a rash on her left leg and thigh, present for 1 year. After a knee surgery 1 year before presentation, the patient incurred a herpes zoster infection on her left leg. The patient completed a course of valacyclovir, and the rash resolved; however, the patient stated that the skin lesions for which she presented developed in the same area months later after clearance of her shingles infection. Review of systems was positive for joint pain, dry mouth, and dry eyes. The patient's medications included hydroxychloroquine, 400 mg daily, for SLE and tramadol, 100 mg daily, for joint pain. A rheumatologist managed the patient's SLE until she presented, and she never experienced any skin manifestations of the disease. Physical examination found numerous blanching and nonblanching, faintly erythematous to slightly violaceous, and salmon-colored macules and thin scaly papules in a dermatomal configuration on the anterior and lateral aspect of the left thigh extending vertically down the left leg (Fig 1). No vesicles or pustules were observed.

Laboratory results for antinuclear antibody; anti-dsDNA; C-reactive protein; complement, rheumatoid factor, Ro, La, and Smith antibodies; and anti-ribonucleoprotein were all within normal limits

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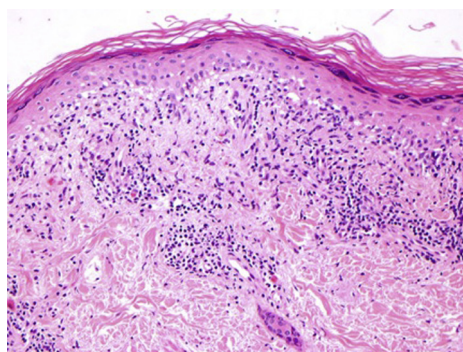
**Fig 1.** Cutaneous lupus in dermatomal distribution. Erythematous papules in a dermatomal distribution along the patient's left lower extremity.

at the time of presentation. The patient reported that antinuclear antibody and other markers of autoimmune disease were positive at the time of diagnosis and fluctuated over her 20-year course of disease. A complete blood count showed mildly decreased white blood cells and was otherwise within normal limits. Her anti-cyclic citrullinated peptide was elevated. Two punch biopsies of affected skin within the dermatomal band of lesions on the left knee and left distal thigh were performed. Histopathology of the tissue found interface dermatitis with dyskeratosis, superficial perivascular lymphocytic infiltrate, focal red blood cell extravasation, and pigment incontinence (Fig 2). No fungal organisms were identified on periodic acid–Schiff stain. Immunohistochemistry for herpes simplex virus and varicella zoster virus were negative. Neither vasculitis nor viral cytopathic changes were seen. Colloidal iron stains showed increased mucin (Fig 3). Clinical pathologic correlation was consistent with the patient's underlying connective tissue disease.

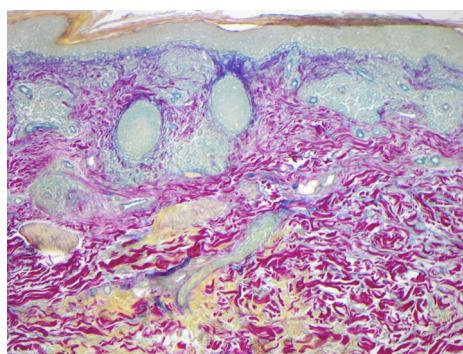
The patient was prescribed triamcinolone to affected areas, which did not improve her symptoms. She was subsequently prescribed clobetasol to affected areas twice daily, under occlusion, which she found helpful. With continued use of clobetasol ointment, the patient's skin lesions began to fade and transitioned from pink and erythematous in color to hyperpigmented, with significantly decreased pruritus.

## DISCUSSION

Cases of systemic lupus erythematosus and discoid lupus have been reported after herpes zoster infections in a dermatomal distribution.<sup>5,6</sup> Despite a 20-year history of systemic lupus, the only lupus-related skin findings that the patient experienced were nonphoto-exposed and within the dermatome previously affected by zoster. She denied ever having



**Fig 2.** Cutaneous lupus. Biopsy of the left distal thigh shows interface dermatitis, dyskeratosis, superficial perivascular lymphocytic infiltrate, focal red blood cell extravasation, and pigment incontinence.



**Fig 3.** Colloidal iron stain shows increased mucin.

had any other typical skin findings of photosensitive dermatitis, such as a malar rash, at presentation. The patient's concomitant hydroxychloroquine therapy may provide an explanation for lack of other cutaneous lupus findings. Zoster infection, and thus keratinocyte neuromediators and immune alteration in the affected dermatome, could have produced a vulnerable cell line resistant to the patient's current dose of hydroxychloroquine. Lichen striatus was also in the original differential, as both lupus and lichen striatus have been reported to exhibit Wolf's isotype response after herpes zoster infection.<sup>3</sup> The presence of mucin on histopathologic analysis supported lupus as the pathology. Furthermore, the bandlike pattern of the eruption was more consistent with a dermatomal distribution rather than a thinly whorled Blaschkoid distribution on the leg.<sup>7</sup> The occurrence of cutaneous lupus after a zoster infection and the dermatomal distribution of the eruption support an isotopic reaction in this case. Thus, remembering the old concept of *locus minoris resistentiae*, a region of the skin that behaves as a dermatologic Achilles heel, continues to inform our understanding, workup, and diagnosis of dermatologic diseases that present in atypical distributions.

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