Granulomatous dermatitis as a postherpetic isotopic response in immunocompromised patients: A report of 5 cases

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INTRODUCTION

Granulomatous dermatitis (GD) describes disorders in which mixed inflammatory infiltrates composed primarily of histiocytes invade the skin. The pathogenesis of GD is unknown; however, GD has been noted to occur in areas previously affected by trauma, sun damage, or infection.[1] When GD presents at the same site of a healed, unrelated skin disease, it falls within the category of a Wolf's isotopic response.[2] The regional restriction of a Wolf's isotopic response is proposed to occur due to an area of localized immunocompromise known as an *immunocompromised district*.[3] This immunocompromised district is believed to result from various types of cutaneous damage that hinder lymph circulation, like chronic regional lymphedema or prior herpes virus infection (eg, varicella zoster virus [VZV] and herpes simplex virus [HSV]).[3] Postherpetic isotopic response (PHIR) is the most commonly reported isotopic response, and more cases of PHIR-GD have been reported than any other type of isotopic response.[3] It can occur within the same dermatomal distribution either immediately after primary lesion resolution (VZV>HSV) or many years later.[3] Persistent VZV DNA has been detected in PHIR lesions within 4 weeks after an acute episode[4,5] but not after 7 weeks.[6,7] The presence of viral DNA in some lesions has led to the proposal that VZV glycoproteins (gpI/II) may still be expressed at a sufficient level to initiate granuloma formation.[8]

Since the first report of granuloma annulare (GA) as an isotopic response,[9] 38% of the 32 cases have been reported in the setting of immunocompromise.[10] We now add 5 unreported cases and 16 literature cases (not reviewed in prior meta-analyses) of immunocompromised PHIR-GD. Our review of the literature has also added 23 cases of

Abbreviations used:

AML:	acute myelogenous leukemia
CLL:	chronic lymphocytic leukemia
GA:	granuloma annulare
GD:	granulomatous dermatitis
HSV:	herpes simplex virus
MM:	multiple myeloma
PHIR:	postherpetic isotopic response
PHIR-GD:	postherpetic isotopic response-granulomatous dermatitis
PHN:	postherpetic neuralgia
SCT:	stem cell transplant
SLE:	systemic lupus erythematous
SS:	Sjogren syndrome
VZV:	varicella zoster virus

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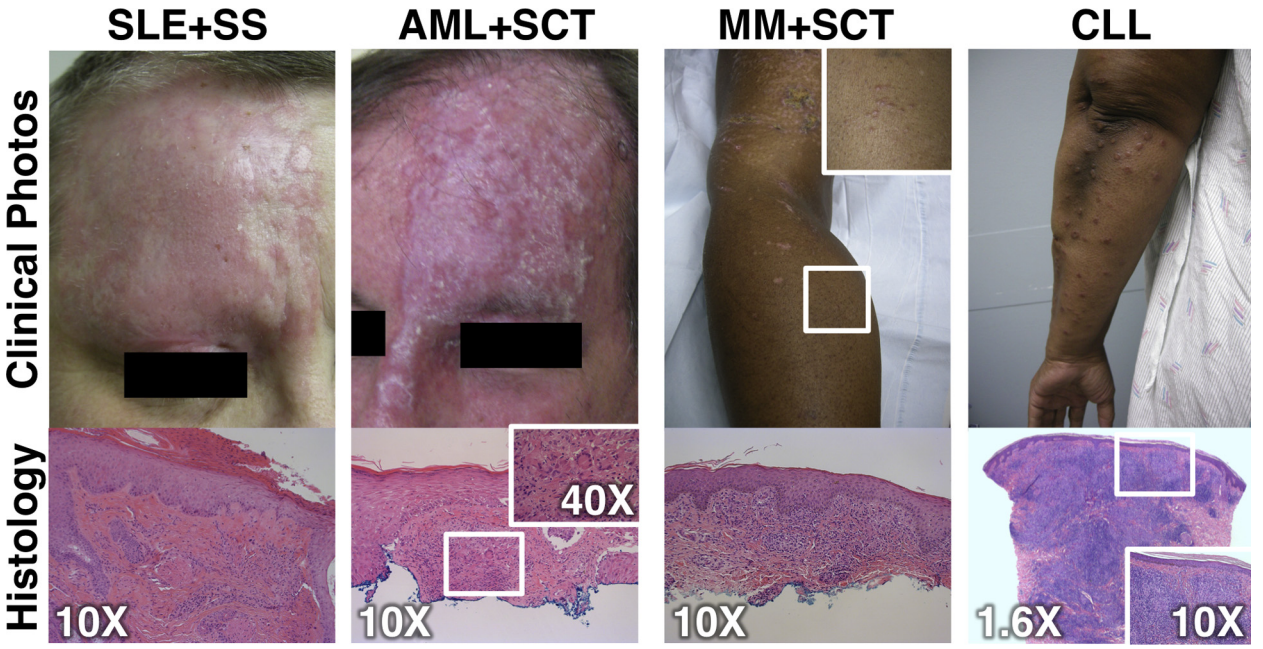

Fig 1. Clinical and histologic images. Four of the immunocompromised patients with granulomatous PHIR from this case series are shown with their clinical photographs above and the corresponding H&E pathology immediately below. Inset images show magnified areas of rash/histology. Immunocompromise etiology and microscopic magnifications are listed. No clinical/histologic images were available for the heart transplant subject in our case series.

nonimmunocompromised PHIR-GD. Our analysis of 33 immunocompromised and 43 immunocompetent cases highlights PHIR-GD associations with immunocompromise, chronic lymphocytic leukemia (CLL), and male sex.

METHODS

We conducted a retrospective study of 5 immunocompromised PHIR-GD patients at Barnes Jewish Hospital in St Louis, Missouri between 2008 and 2015. Through a literature search of PubMed, we reviewed all previous cases of PHIR-GD. Search terms included *Wolf's isotopic response*, *postherpetic isotopic response*, *granulomatous dermatitis*, *granuloma annulare*, and perturbations of these terms. References from the identified literature were used to expand our search.

RESULTS

Case 1

A 53-year-old white woman with systemic lupus erythematosus (SLE), Sjögren syndrome (SS), and IgM deficiency on methotrexate, Plaquenil, prednisone, and sulfasalazine presented with right V1 dermatome VZV reactivation. Treatment included valacyclovir, tobramycin ophthalmic ointment, and gabapentin. Less than a month after the lesions resolved, an erythematous, alopecic plaque appeared in the same dermatome (Fig 1; SLE+SS) complicated by severe postherpetic neuralgia (PHN) and trigeminal trophic syndrome with ulceration and superinfection (methicillin-resistant *Staphylococcus aureus*, *Candida* keratitis). Biopsy found no viral cytopathic changes (Fig 1; SLE+SS). HSV/VZV assays were negative. She received valacyclovir, corticosteroids (topical, intralesional, oral), and calcineurin inhibitors (tacrolimus, pimecrolimus) for her PHIR-GD. Her PHN required oral gabapentin, pregabalin, duloxetine, hydroxyzine, and topical lidocaine. Autoimmune treatments were replaced with abatacept 6 months after PHIR-GD onset. Over 19.5 months, her cutaneous disease and PHN significantly improved, but her PHN never resolved completely.

Case 2

A 56-year-old white man with a history of acute myelogenous leukemia (AML) treated with chemotherapy and unrelated donor stem cell transplant (SCT) later complicated by chronic graft-versus-host disease presented for suture removal after Mohs micrographic surgery for squamous cell carcinoma of the left side of the forehead. He was found to have VZV reactivation of the left V1 dermatome. He received intravenous acyclovir, oral valacyclovir, and gabapentin for PHN. Less than a month later, an erythematous, sclerotic plaque developed in the