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Case Report

Subcorneal Pustular Dermatosis at the Site of Healed Herpes Zoster Infection: *Wolf*'s Isotopic Response

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Abstract

Observations: A 57 year-old male patient presented with slightly itchy and grouped vesiculopustular eruption on an erythematous base on the right side of the neck. The lesions started 4 weeks before admission, and the patient was treated with systemic acyclovir for herpes zoster at the same location 3 months ago. *Tzanck* and KOH smears, bacterial and fungal cultures were all negative. Histopathological findings were consistent with subcorneal pustular dermatosis and the patient was successfully treated with topical corticosteroids. Based on clinical and histological findings, the patient was diagnosed as *Wolf*'s isotopic response. To our knowledge, this is the first report of subcorneal pustular dermatosis that occurs at the site of healed herpes zoster infection.

Introduction

The term, isotopic response was proposed by *Wolf* et al. in 1995 [1] and defined as the occurrence of a new skin disease at the site of a previously healed dermatological condition unrelated to each other. The primary disease is mostly herpes zoster, herpes simplex or varicella zoster virus (VZV) infection. The interval period between two diseases is variable ranging from days to months [2, 3, 4] *Wolf*'s isotopic response is a rare phenomenon and several different disorders have been described at the site of herpes zoster healed with or without scar formation. These diseases include fungal [4] or granulomatous folliculitis [3], granuloma annulare [5], granulomatous reactions [6] lichen planus [2], lichen sclerosus [7], rosacea [8], acneiform eruption [9] furunculosis, contact dermatitis [1], eosinophilic dermatosis [10], pseudolymphoma [3], and malignancies [11, 12, 13]. Individual cases of erythema annulare centrifugum [14] and acquired reactive perforating collagenosis [15] were also described. The present case suggestive of *Wolf*'s isotopic response presented with subcorneal pustular dermatosis (SCPD) at the site of healed herpes zoster.

Case Report

A 57-year-old male was admitted with a 4-week history of slightly itchy eruption on the neck. The patient had been diagnosed as herpes zoster at the same location and treated successfully with oral acyclovir without scar formation 3 months ago. However, he did not benefit from systemic acyclovir represcribed for the current lesions. He did not describe trauma and denied intake of medications or application of topical agents to that area. The family history was not remarkable.

On examination, superficial vesiculopustular lesions with coalescing tendency were observed on

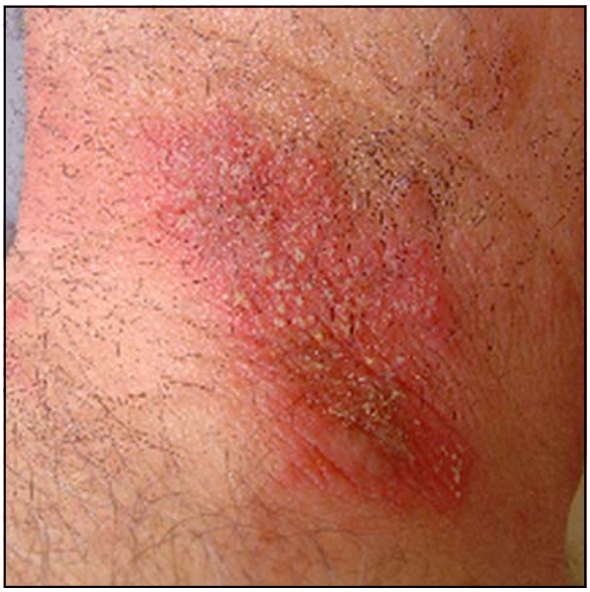

Figure 1. Pustular lesions on an erythematous base on the right side of the neck

a large, slightly scaling, erythematous plaque located on the right side of the neck (**Figure 1**). The lesions, some of which were erosive, were painless and did not cross the midline. He was otherwise healthy and laboratory investigation including complete blood count, erythrocyte sedimentation rate, CRP, fasting blood sugar, renal and hepatic function tests and urinalysis were all within normal limits except for total cholesterol levels. Serum IgA, G, M and E levels, and thyroid function tests were normal. ANA, RF, anti-HIV, anti-HCV, HBs and VDRL tests were negative. Serum and urine protein electrophoresis were normal. Tzanck and KOH smears, bacterial and fungal cultures of the pustular lesions were all negative. Skin punch biopsy showed focal parakeratosis, mild hyperkeratosis and subcorneal pustule filled with polymorphonuclear leukocytes. There was a mixed perivascular inflammatory infiltrate composed of polymorphonuclear leukocytes and mononuclear cells in the superficial dermis. Variable number of migrating inflammatory cells were observed throughout the epidermis (**Figure 2**). A periodic acid-Schiff staining for fungal organisms was negative. Direct immunofluorescence was negative and IgA deposition was not detected. Based on the clinicopathological findings, the patient was diagnosed as SCPD and treated with mildly potent topical corticosteroids. Improvement started within the first week of treatment and the lesions healed with mild hyperpigmentation at the end of 4 weeks (**Figure 3**).

Discussion

SCPD is an uncommon, pustular dermatosis described by *Sneddon* and *Wilkinson*,

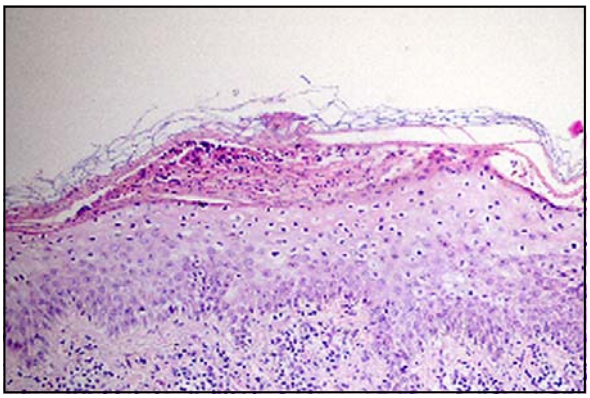

Figure 2. Punch biopsy: Subcorneal pustule filled with polymorphonuclear leukocytes and mixed perivascular inflammatory infiltrate composed of polymorphonuclear leukocytes and mononuclear cells in the superficial dermis. (Hematoxylene eosine X100)

and characterized by asymptomatic eruption of grouped pustules that usually coalesce to form annular or polycyclic shapes. SCPD usually appears on the flexures and trunk. The lesions commonly lead to scaling and sometimes to mild hyperpigmentation [**16**]. The differential diagnosis of SCPD includes subcorneal-type of IgA pemphigus, pemphigus foliaceus, dermatitis herpetiformis, pustular psoriasis, and bacterial impetigo [**17**]. Subcorneal-type of IgA pemphigus differs in that immunofluorescence demonstrates positive intraepidermal IgA deposits [**16, 17**]. In our patient, direct immunofluorescence was negative, ruling out the diagnosis of subcorneal-type of IgA

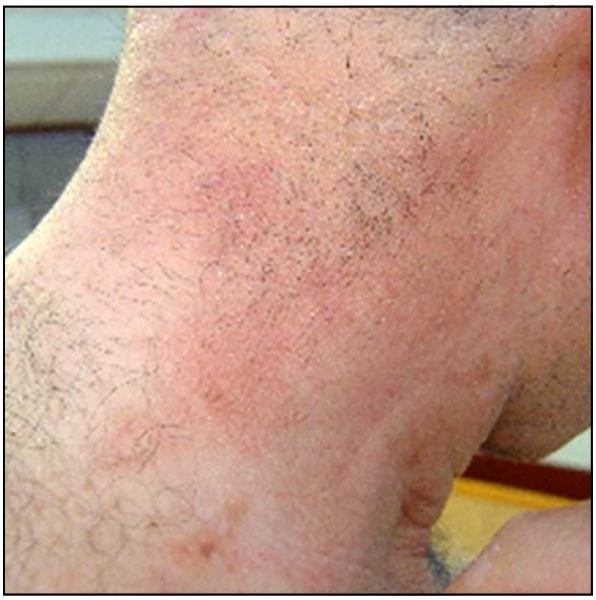

Figure 3. Clinical appearance of the patient after treatment

pemphigus. The diagnoses pemphigus foliaceus and dermatitis herpetiformis were unlikely in the present case, because of the absence of acantholysis or subepidermal vesicles, as well as negative immunofluorescence findings. The absence of psoriasiform hyperplasia and loss of granular layer, thinning of the suprapapillary plates on histopathology excluded the diagnosis of pustular psoriasis [**17, 18**]. Negative KOH smears and negative bacterial and fungal cultures excluded bacterial and fungal infections in our patient.

Although the exact pathophysiology of SCPD is unknown, the role of triggering factors such as preceding or concomitant infections has remained speculative. Immunologic mechanisms have also been implicated [17, 19]. Histopathologically, sterile subcorneal pustules filled with neutrophils, absence of acantholysis, and negative immunofluorescence examination are key features of SCPD [**16, 17**]. This hyperactivation of neutrophils suggests the presence of chemotactic factors in the uppermost epidermis [**16, 19**]. Tumor necrosis factor (TNF)-α may be a principal chemotactic factor, as shown by the excessive TNF-α levels found in serum samples and blister fluid of patients with SCPD. Levels of interleukin-8 and C5a have also been found to be raised in scale extracts of affected patients [**16, 17**]. Treatment with infliximab achieved immediate control in two severe recalcitrant cases [**20, 22**], although in one case the improvement was only temporary [**23**]. Evidence that TNF-α may be involved in the pathogenesis of SCPD, coupled with the reported association of SCPD and inflammatory bowel disease, pyoderma gangrenosum, rheumatoid arthritis and *Sjögren* syndrome support the role of anti-TNF agents as therapeutic options [**16, 20, 21, 23**]. None of the previously known associations was present in our case.

The term "*Wolf*'s isotopic response" was defined as the occurrence of a new skin disease at the site of a previously healed and unrelated skin disorder, especially herpes zoster. The pathogenesis and underlying mechanisms leading to the development of the second disease are unknown and viral genome has been detected only in early lesions. It has been suspected that viral particles persisting in the tissue might be responsible for the occurrence of the second disease [**24**]. In many of the reported cases, the first disease was herpes zoster or simplex; however, viral DNA has not been isolated from the skin lesions of the second disease. It has been suggested that viral infection could alter local cutaneous immunity leading to *Wolf*'s isotopic response [**5, 7, 24**].

TNF-α is a major cytokine in defense with adaptive immunity and it has well known antiviral activity. TNF-α related cytokines are important effector molecules in the immune response against viruses. This cytokine is increased in the primary immune response against VZV infection, in re-exposure to VZV and during herpes zoster infection [**20, 25**]. Furthermore, TNF-α has been speculated to play a causal role in several inflammatory diseases, including SCPD, psoriasis, and its role in innovating and maintaining granulomas at multiple levels is also known [**17, 20**].

To our knowledge, this is the first report of SCPD in the setting of healed herpes zoster virus infection. Although the pathogenesis of Wolf's isotopic response is unknown, over expression of TNF-α, induced locally by VZV infection, might be responsible for the development of SCPD by altering the local immunity.

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References

1. Wolf R, Brenner S, Ruocco V, Filioli FG. Isotopic response. Int J Dermatol 1995; 34: 341-348. PMID: 7607796
2. Shemer A, Weiss G, Trau H. Wolf's isotopic response: a case of zosteriform lichen planus on the site of healed herpes zoster. J Eur Acad Dermatol Venereol 2001; 15: 445-447. PMID: 11763387
3. Schena D, Barba A, Chieregato C. Granulomatous folliculitis as a manifestation of post-herpetic isotopic response. J Eur Acad Dermatol Venereol 2001; 15: 473-475. PMID: 11763396
4. Tüzün Y, İşçimen A, Göksügür N, Demirkesen C, Tüzün B. Wolf's isotopic response: Trichophyton rubrum folliculitis appearing on a herpes zoster scar. Int J Dermatol 2000; 39: 766-768. PMID: 11095197
5. Ruocco E, Baroni A, Cutri FT, Filioli FG. Granuloma annulare in a site of healed herpes zoster: Wolf's isotopic response. J Eur Acad Dermatol Venereol 2003; 17: 686-688. PMID: 14761138

6. Fernández-Redondo V, Amrouni B, Varela E, Toribio J. Granulomatous folliculitis at sites of herpes zoster scars: Wolf's isotopic response. J Eur Acad Dermatol. Venereol 2002; 16: 628-630. PMID: 12482051

7. López N, Alcaraz I, Cid- Mañas J, Camacho E, Herrera-Acosta E, Matilla A, et al. Wolf's isotopic response: zosteriform morphea appearing at the site of healed herpes zoster in a HIV patient. J Eur Acad Dermatol Venereol 2009; 23: 90-92. PMID: 18355190

8. Sezer E, Koseoglu RD, Filiz N. Wolf's isotopic response: rosacea appearing at the site of healed herpes zoster. Australas J Dermatol 2006; 47: 189-191. PMID: 16867001

9. Stubbings JM, Goodfield MJ. An unusual distribution of an acneiform rash due to herpes zoster infection. Clin Exp Dermatol 1993; 18: 92-93. PMID: 8440068

10. Mitsuhashi Y, Kondo S. Post-zoster eosinophilic dermatosis. Br J Dermatol 1997; 136: 465-466. PMID: 9115936

11. Aloi FG, Appino A, Puiatti P. Lymphoplasmocytoid lymphoma arising in herpes zoster scars. J Am Acad Dermatol 1990; 22: 130-131. PMID: 2298951

12. Niedt GW, Prioleau PG. Kaposi's sarcoma occurring in a dermatome previously involved by herpes zoster. J Am Acad Dermatol 1988; 18: 448-451. PMID: 3343414

13. Hudson CP, Hanno R, Callen JP. Cutaneous angiosarcoma in a site of healed herpes zoster. Int J Dermatol 1984; 23: 404-407. PMID: 6541210

14. Lee HW, Lee DK, Rhee DY, Chang SE, Choi JH, Moon KC, et al. Erythema annulare centrifugum following herpes zoster infection: Wolf's isotopic response? Br J Dermatol 2005; 153: 1241-1243. PMID: 16307675

15. Bang SW, Kim YK, Whang KU. Acquired reactive perforating collagenosis: unilateral umbilicated papules along the lesions of herpes zoster. J Am Acad Dermatol.1997; 36: 778-779. PMID: 9146541

16. Cheng S, Edmonds E, Ben-Gashir M, Yu RC. Subcorneal pustular dermatosis: 50 years on. Clin Exp Dermatol 2008; 33: 229-233. PMID: 18355359

17. Reed J, Wilkinson J. Subcorneal pustular dermatosis. Clin Dermatol 2000; 18: 301-313. PMID: 10856662

18. Wilkerson A, Smoller B. The pustular disorders. Semin Cutan Med Surg 2004; 23: 29-38. PMID: 15095913

19. Hönigsmann H, Trautinger F, Wolf K. Subcorneal Pustular Dermatosis (Sneddon-Wilkinson Disease). In: Friedberg IM, Eisen AZ, Wolff K, Austen KF, Katz SI, Fitzpatrick TB, eds. Fitzpatrick's Dermatology in General Medicine. 6th ed. Newyork: McGraw -Hill; 2003. p. 625-627.

20. Allegue F, Fachal C, Romo M, López-Miragaya MI, Pérez S. Psoriasis at the site of healed herpes zoster: Wolf's isotopic response: Actas Dermatosifiliogr 2007; 98: 576-578. PMID: 17919439

21. Grob JJ, Mege JL, Capo C, Jancovicci E, Fournerie JR, Bongrand P, et al. Role of tumor necrosis factor -alpha in Sneddon-Wilkinson subcorneal pustular dermatosis. A model of neutrophil priming in vivo. J Am Acad Dermatol 1991; 25: 944-947. PMID: 1761776

22. Voigtländer C, Lüftl M, Schuler G, Hertl M. Infliximab (anti-tumor necrosis factor alpha antibody): a novel, highly effective treatment of recalcitrant subcorneal pustular dermatosis (Sneddon-Wilkinson disease). Arch Dermatol 2001; 137: 1571-1574. PMID: 11735706

23. Bonifati C, Trento E, Cordiali Fei P, Muscardin L, Amantea A, Carducci M. Early but not lasting improvement of recalcitrant subcorneal pustular dermatosis (Sneddon-Wilkinson disease) after infliximab therapy: relationships with variations in cytokine levels in suction blister fluids. Clin Exp Dermatol 2005; 30: 662-665. PMID: 16197383

24. Requena L, Kutzner H, Escalonilla P, Ortiz S, Schaller J, Rohwedder A. Cutaneous reactions at sites of herpes zoster scars: an expanded spectrum. Br J Dermatol 1998; 138: 161-168. PMID: 9536241

25. Benedict CA. Viruses and the TNF- related cytokines, an evolving battle. Cytokine Growth Factor Rev 2003; 14: 349-357. PMID: 12787571