



CASE REPORT

A Case of Herpes Zoster Granulomatous Dermatitis: Report of Wolf's Isotopic Response

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Wolf's isotopic response refers to the occurrence of a novel skin disease at the site of a preceding treated or untreated skin disease. Although the most common preceding skin disease was found to be herpes zoster (HZ), HZ-related dermatological phenomena are not well known in the literature. We report a case of HZ granulomatous dermatitis in a 77-year-old female with a previous history of hypertension, diabetes mellitus, chronic kidney disease, and HZ. She presented with a 3-month history of a pruritic skin lesion on her right thigh. The location of the lesion was consistent with a previous HZ site. Histopathological examination revealed lympho-histiocytic infiltration in the superficial dermis, forming a granulomatous structure. Based on clinical and histopathological findings, we made a diagnosis of granulomatous dermatitis at a previous HZ site. We assumed that the lesion arose from an isotopic response of Wolf. The patient was treated with topical steroids for 3 months and showed clearance of the lesion and symptom. We suggest that treatment should be based on the individual disease, which in our case was topical steroid. (**Ann Dermatol 33(2) 186~189, 2021**)

-Keywords-

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INTRODUCTION

Herpes zoster (HZ) is a common skin infective disorder caused by the reactivation of a previous varicella zoster virus (VZV) infection. VZVs affect the skin via an innervated sensory neuron. Therefore, the distribution of the skin lesions is consistent with the dermatome. HZ could cause various complications, including post-herpetic neuralgia, neurological complications (motor palsy), and ophthalmological complications (keratitis, conjunctivitis, and rarely, visual defect) when cranial nerve V1 was involved¹. However, its dermatological phenomena are not well known in the literature. An isotopic response of Wolf, or Wolf's isotopic response, refers to the occurrence of a novel skin disease at the site of a preceding treated or untreated skin disease². The most common preceding skin disease was found to be HZ³. Here, we report a case of HZ granulomatous dermatitis, which was presumed to be an isotopic response of Wolf.

CASE REPORT

A 77-year-old female with a previous history of hypertension, diabetes mellitus, chronic kidney disease, and HZ, presented with a 3-month history of pruritic skin lesions on her right thigh. On physical examination, localized erythematous to brown-colored tiny flat-topped papules and macules with a scar were found on the right thigh (Fig. 1). Notably, the site of the lesions was consistent with the site that was affected by a previous HZ. Before her visit to our clinic, the patient had been on medication (non-steroid anti-inflammatory drugs, tramadol) for post-herpetic pain for a year. She denied any medication change or contact with an unusual material in the recent 6 months. Suspecting lichenoid disorders, a histopathological examination was performed for differential diagnosis. Histopathologically, no

remarkable finding was noted in the epidermis. Infiltration of lymphocytes and histiocytes was noted in the superficial dermis, forming a granuloma rather than the typical lichenoid pattern, which involves the dermo-epidermal junction (Fig. 2). Based on clinical and histopathological findings, the initial diagnosis was revised to granulomatous dermatitis at a previous HZ site. Considering the history of HZ infection, we presumed that the disease was an isotopic response of Wolf. The patient was treated with a topical prednisone 20% lotion twice daily. No antiviral agent was used. The symptom and lesions gradually resolved after 3 months of treatment (Fig. 3).

We received the patient's consent form about publishing all photographic materials.

DISCUSSION

"Isotopic response of Wolf" or "Wolf's isotopic response" was first proposed by Wolf et al.² in 1995, to explain the pathogenesis of a novel skin disorder at the site of another treated or untreated skin disease⁴. The concept of this phe-

nomenon is different from the Koebner phenomenon, which refers to the occurrence of an existing skin disease at the site of trauma or irritation⁴. The most common preceding skin disease was found to be HZ, followed by herpes simplex infection. A wide spectrum of novel diseases could occur, including a granulomatous reaction, lymphoma, and malignancy.

Due to lack of large population based study regarding isotopic response after HZ, exact incidence is not known in the literature. Granulomatous reaction, such as granuloma annulare and granulomatous dermatitis, is one of the common subsequent diseases³. Granuloma annulare seems to be the most common granulomatous reaction. Other non-specific granulomatous dermatitis is also possible. Ferenczi et al.⁴ investigated the histopathological characteristics of HZ granulomatous dermatitis in 26 cases and reported various granulomatous reactions. The inflammatory responses included epithelioid granuloma, interstitial granulomatous reaction, elastophagocytosis, and perineural and periadnexal inflammation⁴. Additionally, lichen planus, skin cancer, leukemic reaction, and infection have been reported as sec-



Fig. 1. Localized erythematous to brown-colored tiny flat-topped papules and macules with a scar were found on the right thigh.



Fig. 3. The lesions were resolved after 3 months of treatment.

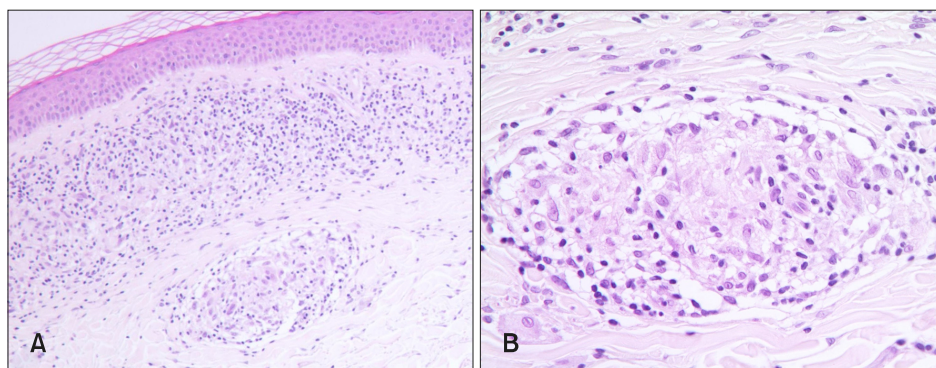


Fig. 2. Histopathological findings of the lesion. (A) Band-like lymphohistiocytic infiltration in the superficial dermis was noted. Vague granulomatous change was found. (H&E, $\times 100$). (B) A granulomatous structure, which comprises lymphocytes and histiocytes, was found in the dermis (H&E, $\times 400$).

ondary diseases in the literature⁵⁻⁷. The interval between the primary and secondary disease has been shown to vary from a few days to several years. Concerning granulomatous dermatitis, McCoy et al.⁶ reported that the subsequent disease occurred after an average of 4.2 months (range, 0.1 ~ 36 months) from the first disease. HZ granulomatous dermatitis showed male predominance (2.8:1) whereas granuloma annulare is more common in females⁶. Interestingly, immunocompromised state of the patient has association with HZ granulomatous dermatitis. About 43.4% (33 of 76) of HZ granulomatous dermatitis cases in the literature were reported to be associated with an immunocompromised condition⁶. Chronic lymphocytic leukemia (CLL) was the most common reported cause of immunosuppression, followed by other forms of lymphoma/leukemia and connective tissue disease⁶. Considering that CLL is less common in Korea compared to Western countries, it can be inferred that the etiology of HZ granulomatous dermatitis in Korea may differ from those in previous reports⁸. In our case, the patient was in immunocompetent state and had no history of leukemia or lymphoma.

The exact pathogenesis of Wolf's isotopic response is unclear. Considering that HZ is the most common preceding disease, a viral association has been suspected⁹. However, the result of VZV detection in the lesion of the second disease seemed inconsistent^{4,7,10}. These reports imply that not only viral factors but also more complex host factors, such as vascular, immunologic, or neurologic factors may be involved in the pathogenesis of the response^{4,11,12}. The management for HZ granulomatous dermatitis is based on physician's personal experience and case reports. Most cases have been treated with topical, intralesional or systemic corticosteroid^{13,14}. Antiviral therapy has been tried in several cases¹². However, considering the inconsistency of viral DNA at lesion and complex pathogenesis, using antiviral agents lacks evidence and should be tried in recalcitrant case individually.

There are several case reports regarding isotopic response of Wolf after HZ, but the exact incidence or prevalence of this phenomenon remains unclear. Considering that HZ is a common infective disease, the risk of dermatological phenomena, including isotopic response, might have been underestimated. Further research will be needed to understand the exact pathogenesis and epidemiology of this response.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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DATA SHARING STATEMENT

Research data are not shared.

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