



Isomorphic (Koebner) and Isotopic (Wolf's) Phenomenon of Post Herpes Zoster Psoriasis: A Compilation of Case Studies and Narrative Review

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ABSTRACT

Koebner phenomenon is defined as the development of psoriatic lesions on previously healthy skin of a psoriasis patient following skin trauma. A related skin reaction, known as Wolf's isotopic response, involves the appearance of a new skin condition in an area of healed dermatosis; in many cases, from herpes zoster. The exact cause of this link is not fully understood, but it may involve neuroimmune system and its neuromediators, particularly substance P. This paper serves as a reminder on the importance of recognizing dermatologic phenomena.

Keywords: Herpes zoster, Koebner phenomenon, psoriasis, Wolf's isotopic response.

ABSTRAK

Fenomena Koebner didefinisikan sebagai munculnya lesi psoriasis pada kulit penderita psoriasis yang sebelumnya sehat setelah mengalami trauma kulit. Reaksi kulit yang juga berkaitan, dikenal sebagai *Wolf's isotopic response*, adalah munculnya kelainan kulit baru di area dermatosis yang telah sembuh; kebanyakan dari infeksi herpes zoster. Hubungan antara herpes zoster dan munculnya lesi psoriasis atau kondisi kulit lainnya belum sepenuhnya dipahami, mungkin melibatkan sistem neuroimun dan neuromediator, khususnya substansi P. Makalah ini bertujuan untuk menjadi pengingat tentang pentingnya mengenali fenomena dermatologis. **Siauw Lidya Oktaviani, Yuliana Teguh. Fenomena Isomorfik (Koebner) and Isotopik (Wolf's) dari Psoriasis Pasca-Herpes-Zoster: Sebuah Kompilasi Studi Kasus dan Tinjauan Naratif.**

Kata Kunci: Herpes zoster, fenomena Koebner, psoriasis, *Wolf's isotopic response*.



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INTRODUCTION

Koebner phenomenon (KP) and Wolf's isotopic response (WIR) are two different yet similar or related skin reaction. Koebner phenomenon was first described by Heinrich Koebner as a skin lesions on previously unaffected skin, secondary to minor skin injury caused by traumas, burns, friction, insect bites, surgical incision, underlying skin diseases, and/or therapy. Another term for KP is isomorphic (meaning 'equal shape' in Greek) response.^{1,2} Lesions developing from KP will be in accordance with the underlying skin disease, particularly the emergence of new psoriatic lesions following injury or trauma to healthy skin areas of individuals with psoriasis. Several factors have been known to trigger the development of new psoriatic lesions, including tattooing, exposure to radiation, skin incision, viral infection, formation of stretch marks/striae.³

A similar but different phenomenon, the Wolf's isotopic response (WIR) some considered as a subtype of KP,⁴ was first described in 1955 by Wolf, *et al*, as a new skin disorder at the site of another, unrelated, and already healed skin disease. These definitions are still controversial.¹ Diseases that tends to manifest koebnerization include: psoriasis, vitiligo, lichen planus, and bullous dermatoses.² Some epidemiological studies found that KP incidence varies from 25%-30% in psoriasis patients after various trauma.⁴ There is still lack of data regarding KP or WIR of psoriasis and mostly report single case.

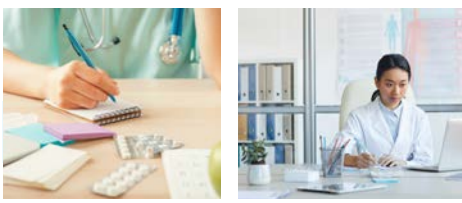
Herpes zoster is a viral infection from the reactivation of latent Varicella Zoster Virus (VZV) infection in the dorsal ganglia of spinal cord after the first attack of varicella. Several studies have found another cutaneous lesion emerging at the site of healed HZ infection.

The pathogenesis remains unclear, but some theories had been suggested.⁵ Koebner phenomenon after HZ infection are rare,⁶ but herpes zoster is the most frequently observed initial disease prior to the occurrence of Wolf's isotopic response.⁴ It is likely linked to disruption of the immune system, blood vessels, and nerves associated with viral infection. Interval between HZ and WIR vary significantly, ranging from few days to several years with no established pattern.⁴

MATERIALS AND METHODS

A literature search was performed to collect studies regarding isomorphic or isotopic phenomenon of psoriasis in post-herpes zoster patients. Literature published from year 2000 and after was obtained from PubMed, Embase, Wiley and, Google Scholar using keywords: 'Wolf's isotopic response', 'isotopic response', or 'Koebner phenomenon', 'isomorphic response',

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with 'psoriasis', and 'herpes zoster'. Selected literature was full papers or abstracts restricted to English language. Case series or case reports that include reports of patient's age, gender, dermatomal distribution of herpes zoster, interval between herpes infection to psoriatic Koebner Phenomenon (KP) or Wolf's isotopic response (WIR), including treatment of psoriatic KP or WIR were analysed and reviewed. Other articles or studies regarding Koebner phenomenon, Wolf's isotopic reaction, psoriasis, and herpes zoster will be used as references of discussion and narrative review.

RESULTS

Most studies regarding KP or WIR psoriasis in post-herpes zoster patients are case series or case reports, and are currently limited. Other papers on isotopic response and herpes zoster, include lichen planus, impetigo, keloid, bullous pemphigoid, lichen sclerosis, and vitiligo. Nine published case reports on KP and WIR psoriasis related to herpes zoster infection were sorted in accordance with our inclusion criteria. Two reports did not include treatment for psoriatic KP or IP and five reports did not state previous herpes zoster treatment. Most studies provided histopathological evidence of psoriasis (including parakeratosis, psoriasiform hyperplasia, hypogranulosis,

munro-microabscess, supra papillary thinning, dilated capillaries, and perivascular lymphocytes in dermis). Out of these 9 studies, 4 are Koebner phenomenon and 5 Wolf's isotopic response.

Data were summarized in **Table 1**.

The average age of patients who developed KP or WIR psoriasis from HZ lesions was 50 years old, with equal distribution of young (25-44 yo), middle (44-60 yo), and elderly age (60-75 yo). Dominant locations were in the right side (n=5) and thoracal region (n=9) (**Table 2**). The interval from herpes zoster infection to the emergence of psoriasis KP or WIR were mostly 6-12 months (n=3). One patient had positive HIV infection. Treatment of herpes zoster were mostly with oral antiviral (acyclovir or valacyclovir) and topical antibiotics as adjuvant. Treatment of KP or WIR psoriasis were topical steroids. Some steroids mentioned were clobetasol propionate cream 0,05% (with or without calcipotriol compounds), betamethasone cream in combination with calcipotriol, one study used NBUVB, as well as combination of betamethasone, sulphur salicylic acid 5% ointment, and ARV in the HIV case.

DISCUSSION

Koebner phenomenon (KP) was first described by a German dermatologist Heinrich Koebner, as a formation of psoriatic lesions on a previously healthy skin of a psoriasis patient after trauma (excoriations, tattoos, and horse bites).³ Other dermatoses noticed to have a same reaction, include vitiligo, lichen planus, Darier's disease, and bullous dermatoses.³ Koebner phenomenon are reported due to some factors or agents such are megavoltage irradiation, radiotherapy, Mantoux test, surgical incision, acupuncture, prosthesis, secondary syphilis, striae distensae or gravidarum, itching, or viral infection.³

There are two essential steps in KP. First is the non-specific inflammation, which contributes to the production of inflammatory substances (cytokines, proteins, adhesion molecules, autoantigens). Second is a disease-specific reactions (stimulation of T-cells, B cells, autoantibodies, and immune deposits).² The appearance of psoriatic lesions at the site of herpes zoster infection led to the assumption that nerve growth factor, tumor necrosis factor- α , substance P, as well as interleukin-1 play important roles in the pathogenesis of koebnerization.² The occurrence of psoriatic koebnerization at the site of shingles and varicella was mediated by neuropeptides such

Table 1. Summary of characteristics of patients with psoriasis KP/WIR post-herpes zoster infection .

Case	Author	KP/ WIR	Age (Years)	Gender	Dermatome	Interval (HZ to KP/WIR)	Treatment of HZ	Treatment of Psoriasis KP/WIR
1	Chiriac, <i>et al.</i> ⁷	KP	64	F	Right T7	10 days	Acyclovir oral 7 days	Topical steroid
2	Zhao, <i>et al.</i> 2015. ²	KP	30	M	Right T2-T4	6 days	Valacyclovir oral	Topical clobetasol propionate + calcipotriol
3	Subedi, <i>et al.</i> 2018. ⁸	WIR	56	F	Right T7-T9	5 months	Acyclovir IV + topical calcipotriol	Topical clobetasol propionate cream 0,05%
4	Kurtipek, <i>et al.</i> 2015. ⁶	KP	74	F	Right T10-T12	15 days	Systemic antiviral + topical antibiotic	Topical steroid
5	Neema, <i>et al.</i> 2017. ⁹	WIR	35	F	Left T8-T10	6 months	NA	NA
6	Yao, Liu. 2022. ¹⁰	WIR	61	M	Left C8-T3	2 weeks	NA	NA
7	Garcia-Souto, <i>et al.</i> 2019. ¹¹	WIR	36	M	Left T	6 months	NA	Calcipotriol+betamethasone cream
8	Allegue, <i>et al.</i> 2007. ¹²	WIR	47	M	Right T10	6 months	NA	Calcipotriol+betamethasone cream+ NBUVB
9	Anaba, <i>et al.</i> 2018. ¹³	KP	48	M (HIV +)	Predominant Left (Thoracal, Lumbal)	3 months	NA	ARV+betamethasone cream+sulphur salicylic acid 5% ointment



as substance P, an endogenous neuropeptide being potentiated by viral infection and acting as a chemomediator of nociceptive impulse from periphery to central nervous system, plays an important role in the HZ-associated pain.² Viral infection intensifies the effect of substance P by reducing the degradation of its breakdown enzyme. Substance P has also been demonstrated to increased in psoriatic lesions.²

Wolf's isotopic response is characterized by the emergence of a new skin disease in an area of a healed dermatosis. In most cases, the initial dermatosis was herpes zoster (HZ), also known as shingles.¹⁴ The skin appearance associated with Wolf's isotopic response typically include granulomatous and lichenoid reactions, malignancies, skin tumors, and other infections.¹⁴

Several potential mechanisms that may contribute to Wolf's isotopic response are:¹⁵

1. Viral particles may persist in tissues, leading to the development of a second disease (although recent investigations have not found viral DNA in specimens, possibly due to the duration of lesions, typically detected in early stages only).
2. Viral infections can trigger skin immunological changes, making it more susceptible to the development of a subsequent disease.
3. Local inflammation-induced alterations in microcirculation may "memorize" the site's response to future insults.

Table 2. Characteristics of patients with psoriasis KP/WIR post herpes zoster infection (compilation of 9 studies).

Characteristics		n	%
Age	25 - 44 (Young age)	3	34
	44 - 60 (Middle age)	3	33
	60 - 75 (Elderly age)	3	33
Gender	Male	5	55
	Female	4	44
Location of Lesion	Right	5	55
	Left	4	44
	Thoracic	9	100
	Cervical	1	11
	Lumbal	1	11

Herpes zoster damages A δ and C nerve fibers in the mid and lower dermis. Destruction of nerve fibres by the virus can indirectly influence the local immune system, leading to the release of neuromediators in the skin. KP, while not directly involved in the pathogenesis of the new dermatosis, is believed to exert an indirect influence through interactions with the immune system. Nerve injuries result in immune dysfunction associated with the release of neuropeptides in the affected dermatome. Neuropeptides like substance P, released from damaged nerve endings, may play a pivotal role in inducing epidermal changes at the site of previously healed herpes zoster. Studies have reported that treating trigeminal neuralgia with capsaicin after trauma can alleviate pain and acne, suggesting that local nerve abnormalities can lead to skin tissue lesions by altering the concentration of substance P.¹⁵

LIMITATIONS

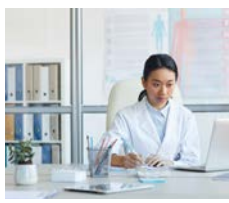
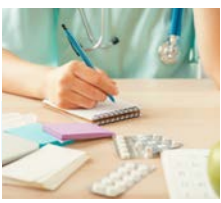
Study on psoriasis Koebner phenomenon or Wolf's isotopic response post herpes infection are still lacking. Reports did not mention other underlying diseases that might have influenced the pathogenesis. No family histories of psoriasis or other diseases were mentioned. Some studies did not include the complete treatment of herpes zoster or psoriasis KP or WIR.

CONCLUSION

The underlying causes of Koebner phenomenon (KP) and Wolf's isotopic response (WIR) remain unclear, neuroimmune instability at sites of viral infection may trigger the development of psoriasis KP or WIR.

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