Letter to the Editor / Editöre Mektup

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Morphea as a rare isotopic response following herpes zoster: A case report and literature review

Herpes zoster sonrası nadir görülen izotopik yanıt olarak morfea: Bir olgu raporu ve literatür incelemesi

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To the Editor,

Wolf et al.[1] isotopic response is a rare phenomenon characterized by the emergence of a new skin disorder at the site of a previously healed dermatosis, without any causal link between the two conditions. Wolf et al.[1] first introduced this definition in the literature in 1995, and the most common primary disease in which an isotopic response is observed is herpes zoster. In this article, we report a case of morphea as an isotopic response on the same dermatome of a patient with a history of herpes zoster 5 years ago. A pathophysiological discussion is provided in the context of relevant literature.

A 35-year-old woman presented with violaceous atrophic plaques extending from her right back to her right upper abdomen over the past month. She had a history of herpes zoster in the same region five years earlier, which resolved with antiviral therapy, although she continued gabapentin use for postherpetic neuralgia. Dermatological examination revealed livid, atrophic plaques along the T4-T7 dermatomes (Figure 1a and 1b). Serological testing for *Borrelia burgdorferi* was negative, and the patient had no chronic illnesses. Hematoxylin and eosin staining of the skin biopsy specimen revealed mesh-like hyperkeratosis, hypogranulosis, and atrophy in the epidermis, as well as increased dermal collagen fibers (fibrosis), decreased skin attachments, and a superficial, mild, perivascular lymphocytic infiltrate in the dermis (Figure 1c). Masson trichrome staining showed positive staining of collagen fibres (Figure 1d). Although the epidermal atrophy and hyperkeratosis raised the possibility of a clinicopathological overlap with lichen sclerosus, the absence of follicular plugging and dermal hyalinization, together with the marked dermal fibrosis on Masson trichrome staining, favored a diagnosis of morphea. These clinical and histological findings supported the diagnosis of morphea as an isotopic response in a previously healed herpes zoster site. The patient in this manuscript has given written informed consent to the publication of her case details.

The most commonly reported isotopic responses include granulomatous and lichenoid reactions, hematologic infiltrates, infections and malignancies. Non-specific granulomatous dermatitis

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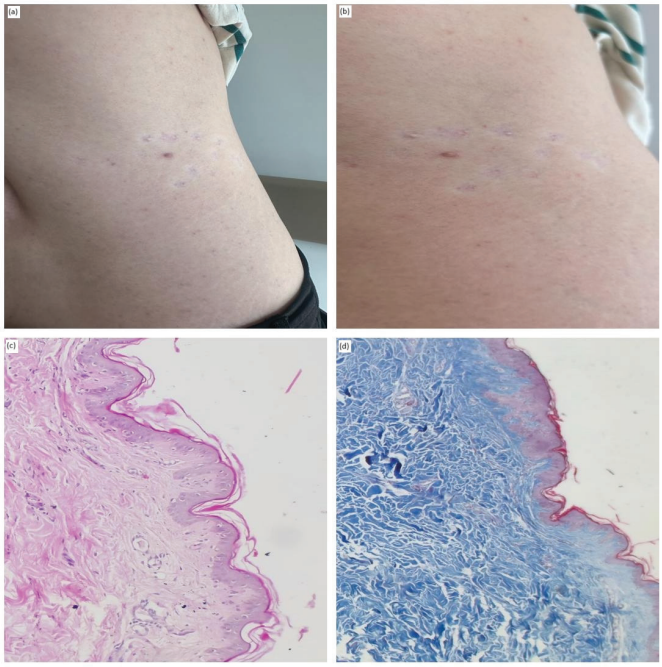


Figure 1. (a, b) Violaceous, atrophic plaques extending from right back to right upper abdomen. (c) Mesh-like hyperkeratosis, hypogranulosis, atrophy in the epidermis, increased dermal collagen fibres, decreased skin attachments, and superficial perivascular lymphocytic infiltrate in the dermis (H&E, x10). (d) Positive staining of collagen fibres (Masson trichrome, x5)
H&E: Hematoxylin and eosin

and granuloma annulare are frequently reported. Morphea is very rare within this spectrum. Morphea (localised scleroderma) is a chronic dermatosis characterised by inflammation and fibrosis of the connective tissue. The emergence of fibrotic dermatoses following herpes zoster underscores the immunologically mediated nature of the isotopic response and offers novel insights into the underlying pathogenic mechanisms. Six previously reported cases of morphea as an isotopic response after herpes zoster infection, along with the present case, are summarized in Table 1, as documented in the English literature. Although the pathophysiology of Wolf's isotopic response is still not fully understood, several hypotheses have been proposed.

The neurohumoral mechanism is the most commonly adopted theory. Herpes zoster affects the dorsal ganglia, disrupting nerve function in the dermatomal area and resulting in altered neuropeptide release. These abnormally secreted neuropeptides can either directly initiate an isotopic response in the skin or indirectly mediate this response by activating immune cell receptors. According to the viral antigen residue hypothesis, viral DNA or protein residues may remain in the area after herpes zoster infection, triggering non-specific immune responses and leading to the development of secondary dermatoses. However, one study found that viral DNA could not be isolated from any of the isotopic responses that developed between one month and four years after the onset of herpes zoster. The vascular damage hypothesis suggests that memory of localised microcirculatory damage secondary to herpes zoster may contribute to the development of secondary dermatoses[2]. Ruocco's concept[3,4] of the "immunocompromised cutaneous district" offers a novel perspective on this phenomenon. For example, trauma and infections can cause localized disruption of the immune system and other functions of the skin. This theory may help understand the basics of isotopic and isomorphic phenomena. Areas that have healed after herpes zoster infection become immunocompromised micro-areas where immune control is impaired. This may create favourable conditions for secondary dermatoses. The five-year interval observed in the present case is notably longer than the 1-month to 2-year latency reported in previous cases. However, the precise anatomical correspondence between the healed herpes zoster dermatome and the site of morphea onset argues against a purely coincidental occurrence, and instead supports Ruocco's concept[3,4] of a persistently immunocompromised cutaneous district, in which local immune dysregulation may remain latent for years before manifesting as a secondary dermatosis.

The development of morphea following herpes zoster has rarely been reported in the literature. This case, in which morphea is localised to the same dermatome, is evaluated in the context of Wolf's isotopic response, highlighting the importance of clinical awareness when diagnosing atypical cutaneous lesions. Such cases contribute to a deeper understanding of dermatoimmunological interactions and may lay the groundwork for future clinical and pathogenetic investigations. Therefore, recognizing the phenomenon of isotopic response is crucial for achieving diagnostic accuracy and managing patients effectively.

Table 1. Summary of the cases of morphea as an isotopic response after herpes zoster reported in the English literature

Case	Age/gender	Involvement sites/dermatomes	Time after herpes zoster	Past medical history
Present case	35/F	T4-T7	5 years	None
Forschner et al.[5]	40/F	C4-C7	1 month	None
López et al.[6]	45/M	D2-D4	2 years	HIV infection
Noh et al.[7]	59/M	T2-T4	3 months	Diabetes mellitus
Ruiz-Villaverde et al.[8]	19/F	T5-T7	2 years	None
Wang et al.[9]	24/M	Left abdomen	>100 weeks	NA
Wang et al.[9]	52/M	Left back	>100 weeks	NA

NA: Not available, F: Female, M: Male, HIV: Human immunodeficiency virus

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Ethics

Informed Consent: Written informed consent was obtained from the patient for the publication of her clinical information and accompanying images.

Footnotes

Authorship Contributions

Surgical and Medical Practices: E.Z., G.S., Concept: E.Z., M.T., Design: E.Z., M.T., A.O.N., Data Collection or Processing: E.Z., A.O.N., G.S., Analysis or Interpretation: E.Z., A.O.N., G.S., Literature Search: E.Z., M.T., A.O.N., Writing: E.Z., A.O.N.

Conflict of Interest: The authors declare no conflicts of interest.

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