

Clearance of Psoriasis After Ischemic Stroke

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PRACTICE POINTS

- Psoriasis is exacerbated in the presence of stress, and psoriatic lesions often have a symmetric distribution, which is evidence that the nervous system is involved in the pathophysiology of the condition.
- Various neuropeptides are involved in the pathophysiology of psoriasis, including substance P, nerve growth factor, calcitonin gene-related peptide, and vasoactive intestinal peptide.
- Peripheral nerve damage results in decreased secretion of neuropeptides, which can lead to remission of psoriasis.

The role of the nervous system in the pathogenesis of psoriasis is not well elucidated. However, its involvement is clinically apparent with sparing of areas affected by neurologic disease, such as poliomyelitis, and remission of psoriasis in cases of nerve damage. Several neuropeptides, including substance P (SP), nerve growth factor, calcitonin gene-related peptide, and vasoactive intestinal peptide have been hypothesized to play a part in the development of psoriasis and its symptoms. We report a case of a patient with psoriasis who experienced complete remission following ischemic stroke.

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The etiology of psoriasis is multifactorial, and it is attributed to both genetic and environmental components.¹ One of the lesser-studied aspects of psoriasis pathogenesis is the involvement of the nervous

system. It is thought that the pathogenesis involves inflammation of the cutaneous nerves,² and cutaneous denervation has been shown to improve acanthosis and IL-23 expression in mice with psoriasiform skin.³ There also have been reports of psoriasis remission following peripheral and central nervous system injury from surgical nerve resection⁴ as well as cerebrovascular accident.⁵ We present a case of total psoriasis clearance following ischemic stroke.

Case Report

A 52-year-old man with psoriasis presented to the dermatology clinic for follow-up. The patient had been using topical clobetasol and apremilast with limited success but had not previously tried biologics. On physical examination he was noted to have erythematous, scaly, indurated papules and plaques on the chest, abdomen, back, arms, and legs, consistent with psoriasis. Affected body surface area was approximately 10%. Ustekinumab was prescribed, but the patient did not pick it up from the pharmacy.

Approximately 1 month later, the patient presented to the emergency department with left-sided weakness and numbness. He was hospitalized for treatment of stroke. During hospitalization, the patient was started on lisinopril, aspirin, and atorvastatin. He also was given subcutaneous enoxaparin with plans to initiate warfarin as an outpatient. His psoriasis was not treated with topical or systemic medications during the course of his admission. He was discharged to a skilled nursing facility after 3 days.

Three months following discharge, the patient returned to the dermatology clinic for follow-up. After his stroke,

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he reported that his psoriasis had cleared and had not returned. On physical examination his skin was clear of psoriatic lesions.

Comment

The nervous system is thought to play an important role in the pathophysiology of psoriasis. Evidence for this involvement includes the exacerbation of psoriasis with stress and the often symmetric distribution of psoriatic lesions.⁶

Moreover, numerous neuropeptides have been identified in the pathophysiology of psoriasis. Farber et al⁷ first proposed that release of substance P (SP) from cutaneous sensory nerve fibers causes a local neurogenic response that triggers psoriasis in predisposed individuals. The role of SP in psoriasis is unclear, as there have been reports of both higher⁸ and lower⁹ levels in involved and non-involved skin of psoriatic patients compared to skin in healthy individuals. It has been suggested that numerous other neuropeptides, including nerve growth factor (NGF), calcitonin gene-related peptide, and vasoactive intestinal peptide, play a part in psoriasis.^{2,10} Specifically, NGF prevents apoptosis of keratinocytes¹¹ and is found in higher levels in psoriatic skin compared to controls.¹² Calcitonin gene-related peptide has been shown to stimulate keratinocyte proliferation¹³ and has been found at increased levels in psoriatic skin.¹⁴ Vasoactive intestinal peptide-positive nerve fibers in the epidermis and dermis are found in higher quantities in psoriatic plaques compared to nonlesional and normal skin.⁸

Neuropeptides also might play a role in the itching and Köbner phenomenon that accompany psoriasis. Increased levels of NGF in nonlesional skin of patients with psoriasis is thought to contribute to the development of psoriatic plaques following trauma by inducing an inflammatory response that upregulates other neuropeptides, such as SP and calcitonin gene-related peptide. These neuropeptides induce keratinocyte proliferation, which further increases NGF expression, thus creating a cycle of inflammation and formation of psoriatic lesions.⁶ Moreover, there is a notable correlation between pruritus severity and density of NGF-immunoreactive keratinocytes, high-affinity NGF receptors, protein gene product 9.5-immunoreactive intraepidermal fibers, and immunoreactive vessels for E-selectin.¹⁵

Spontaneous remission of psoriasis after cerebrovascular accident was first reported in 1998.⁵ Moreover, there have been cases of protective effects from psoriasis and psoriatic arthritis in limbs affected by poliomyelitis.^{16,17} In cases in which patients regained neurologic function, Zhu et al¹⁰ found that recurrence of skin lesions in areas corresponding to nervous system injury also occurred. However, in cases of permanent nerve damage, psoriasis did not return,¹⁰ confirming the role of peripheral nerves in the pathogenesis of psoriasis. It is thought that peripheral nerve damage results in decreased secretion of neuropeptides³ and that central nervous system injury also can cause similar downstream effects.¹⁰

Other reasons for the patient's remission also were considered. Although it is possible that the sudden change in the patient's usual environment could have induced remission of psoriasis, it seems more likely that the stress of the situation would have worsened his symptoms. Medications used during the patient's hospitalization also were considered as reasons for symptom improvement. One study using a case-control and case-crossover design found psoriasis to be associated with nonsteroidal anti-inflammatory drugs and angiotensin-converting enzyme inhibitors (odds ratio, 4.0 and 2.1, respectively).¹⁸ Atorvastatin has been investigated as a potential treatment of psoriasis, though no therapeutic benefit has been proven.^{19,20} Heparin has been shown in case reports to improve psoriasis symptoms but was used in addition to standard psoriasis therapies and not as monotherapy.²¹

A more thorough understanding of which neuropeptides are directly implicated in the neurologic-mediated clearance of psoriasis might contribute to better targeted therapies. For example, infusion of peptide T, a vasoactive intestinal peptide analogue, was shown to have some effect in clearing the skin in 14 psoriasis patients.²² Although this finding has not been replicated, it demonstrates the potential utility of therapies targeted toward the neurologic aspects of psoriasis. More research is needed to evaluate the potential of targeting other neuropeptides for treatment of psoriatic plaques.

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