

Case Letter

Woronoff Ring Associated With Adalimumab Therapy for Psoriasis

To the Editor:

In 1926, Woronoff¹ first described a hypopigmented ring surrounding psoriatic plaques during UV treatment. Since then, the Woronoff ring has been noted with the use of psoralen plus UVA therapy, corticosteroids, the Goeckerman treatment, coal tar, anthralin, fumaric acid esters, and methotrexate, as well as over the natural course of untreated psoriasis.²⁻⁶ However, there is limited research investigating this phenomenon and only 1-sentence descriptions are typical in dermatologic textbooks.⁷⁻¹⁰ We report a case of Woronoff ring in association with adalimumab. Its presentation with the use of any biologic agent is unique.

A 27-year-old Asian man with generalized plaque psoriasis of 4 years' duration presented for follow-up 1 month after the initiation of adalimumab. He had suboptimal responses to tar preparations, superpotent topical steroids, phototherapy, and methotrexate prior to presentation. On presentation, the patient had a 10% decrease in psoriasis area and severity index score from baseline. The patient reported a marked decrease in disease severity and pruritus with no adverse effects. Physical examination revealed involuting psoriatic plaques located on the scalp, extremities, and trunk that were individually circumscribed with a discrete hypopigmented halo (Figure). Although the patient previously had been treated with topical and systemic therapies, he had not presented with changes consistent with Woronoff ring until treatment with adalimumab.

The Woronoff ring is characterized by a 3- to 5-mm hypopigmented and blanched halo that uniformly

circumscribes a psoriatic plaque. The Woronoff ring is more common on the trunk than the extremities.³ Histologically, biopsies of this perilesional pallor show a 40% increase in epidermal thickness compared with normal skin, minimal acanthosis, and a remarkable decrease in basal melanin.¹¹

The pathogenesis of the Woronoff ring is unclear. It has a relative deficiency of prostaglandin E₂ due to local inhibition of prostaglandin E₂ synthesis.⁷ This deficiency decreases vasodilation and consequently decreases erythema, which suggests that the



Psoriatic plaques circumscribed with the Woronoff ring on the trunk.

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ring arises from the release of a local inhibitor or mediator of prostaglandin synthesis produced by the active psoriatic plaque during regression.⁷ It also has been observed that local cutaneous blood flow varies remarkably from the psoriatic plaque, the Woronoff ring, and nonlesional skin; however, subcutaneous blood flow is the same in the plaque and ring.⁹ Furthermore, the glycoprotein endoglin, which is upregulated in psoriatic cell proliferation, is found in decreased levels in the plaque circumference and may play a role in the pathogenesis of the ring.⁸

Adalimumab is a fully human monoclonal antibody and tumor necrosis factor α (TNF- α) antagonist that theoretically prevents TNF- α -mediated events such as the release of cytokines and acute phase reactants. The exact mechanism of action of adalimumab is unknown. Because the Woronoff ring has been observed in association with cases of spontaneous regression, phototherapy, systemic and topical therapy, and now biologic therapy,²⁻⁶ there may be a common mechanism of action that leads to involution of psoriatic lesions and the appearance of the Woronoff ring. All therapies offer a degree of immunosuppression, disruption of DNA synthesis, and modulation of cytokines and inflammatory mediators. Because adalimumab promotes downregulation of multiple TNF- α -mediated pathways, these treatments may all mediate a common factor or factors that are part of the affected TNF- α inflammatory cascade.

The Woronoff ring may not be specific to adalimumab or any other antipsoriatic therapy. Rather, it may be a sign of psoriasis improvement. We observed the Woronoff ring in our patient after 4 weeks of treatment with adalimumab, and it also has been observed as early as 1 week after initiation of treatment with topical tar.⁹ Therefore, the Woronoff ring may be clinically used to determine therapeutic efficacy, even at early stages of treatment. Further research is needed to elucidate the etiology and pathogenesis of this phenomenon, which also may aid in determining the mechanism of action of adalimumab and other psoriasis treatments and in facilitating the development of new therapies.

Despite the association of the Woronoff ring with multiple therapies, its pathogenesis still is unclear. Decreased prostaglandin and endoglin have been observed, but their exact mechanism of action in the

ring has yet to be substantiated.^{7,8} In our patient's presentation, the Woronoff ring may have been due to the anti-inflammatory activity induced by adalimumab, specifically mediators that are triggered during psoriasis plaque involution from treatment. Further investigation of the Woronoff ring and its relationship with adalimumab is needed.

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