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Psoriasis as a manifestation of HIV-related immune reconstitution inflammatory syndrome

To the Editor: Immune reconstitution inflammatory syndrome (IRIS) is a paradoxical exacerbation of a pre-existing condition or emergence of a previously unknown disease occurring in an HIV-infected patient after initiating combined antiretroviral therapy (cART). IRIS begins days to months after starting cART, and is associated with decreasing viral load.[1] The skin accounts for 52% to 78% of presentations, including a range of infectious, inflammatory, and neoplastic conditions.[2] Inflammatory dermatoses such as eosinophilic folliculitis, seborrhea, and acne vulgaris have all been reported.[3,4] Here we present, to our knowledge, the first report of paradoxical worsening of psoriasis as a presentation of IRIS.

A 63-year-old man with type 2 diabetes mellitus, hypertension, hepatitis C, HIV diagnosed in 1997, and a history of mild, untreated less than 1% total body surface area psoriasis presented to dermatology 1 month after starting a new cART, Stribild (elvitegravir, tenofovir, cobicistat, emtricitabine). The patient was switched 1 month prior from his previous cART regimen of Truvada (emtricitabine and tenofovir disoproxil fumarate), darunavir, and ritonavir, to Stribild, a once-a-day cART, because of concerns of medication noncompliance. His most recent CD4 count, 5 months before presentation, was 204 cells/μL and his viral load was 177,857 copies/mL. Skin examination demonstrated confluent erythema, edema, and focal areas of platelike desquamation over the palmar surfaces of both hands; thick sharply demarcated plaques with silvery scale over the elbows; and an erythematous patch over the sacrum, with sparing of the feet and nails, affecting approximately 10% total body surface area. Despite reports of mild joint stiffness in his hands, plain film x-rays did not show signs of psoriatic arthritis. A repeated CD4 count was 138 cell/μL and viral load was 257 copies/mL. He met the proposed diagnostic criteria for IRIS, with worsening of a pre-existing condition (psoriasis) and a concomitant greater than log 10 reduction in viral load.[5] He was started on topical psoralen plus ultraviolet A light 3 times per week and clobetasol ointment 0.05% twice daily, with improvement over the course of 2 months, eventually returning to less than 1% affected total body surface area. Of interest, 1 week before worsening psoriasis, he also developed herpes zoster involving the right leg and buttock, which was resolving at the time of his initial presentation to dermatology.

At the 12th World AIDS Conference in Geneva in 1999, French et al[6] reported numerous conditions worsening after starting cART and introduced the term "immune restoration disease," which is now more commonly termed "immune reconstitution inflammatory syndrome." Over 15 years after the first reports, IRIS remains a well-described but poorly understood phenomenon. There is emerging evidence that one of the immunopathogenic mechanisms of IRIS involves the rapid and dysregulated shift from the T helper (Th)2-predominant state of advanced HIV infection to the Th1- and Th17-dominant state of immune recovery. It is intriguing that psoriasis, a Th1- and Th17-mediated inflammatory condition, has not, to our knowledge, until now been reported to undergo an IRIS reaction, despite being a relatively common HIV-associated dermatosis.

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Granulomatous rosacea manifesting after herpes simplex 2 infection: A case of Wolf's isotopic response

To the Editor: We present the case of a 57-year-old man with a 2-year history of a recurrent transient eruption on the mid aspect of his forehead, described as pruritic, erythematous vesicles preceded by a tingling sensation. He had previously been treated with valacyclovir with modest response. On presentation to our clinic, he had a mildly indurated erythematous plaque across the mid aspect of his forehead, with a small yellow crusted plaque in the center (Fig 1). He reported that the crusted plaque appeared approximately 1 year prior, after an episode of vesicular eruptions resolved in the same location. He also endorsed the plaque worsening with heat and exercise. Histologic examination of a punch biopsy specimen of the lesion showed granulomatous dermatitis, consistent with granulomatous rosacea (Fig 2), with negative immunohistochemical staining for herpes simplex virus and varicella zoster virus. He was given a diagnosis of granulomatous rosacea and empirically prescribed oral doxycycline and topical metronidazole for a total of 10 weeks. At 10 weeks he had improved significantly, with near clearance of the erythematous plaque. Within months of the patient's diagnosis of granulomatous rosacea, he presented with another recurrence of the vesicular eruption, at which time culture and direct fluorescent antibody test confirmed herpes simplex virus 2.

To our knowledge and after extensive literature searching in MEDLINE (PubMed), Embase, and the Web of Science databases for published English-language articles, this is the first report of a case of granulomatous rosacea arising at the site of a recurrent herpes simplex eruption, consistent with Wolf's isotopic response.

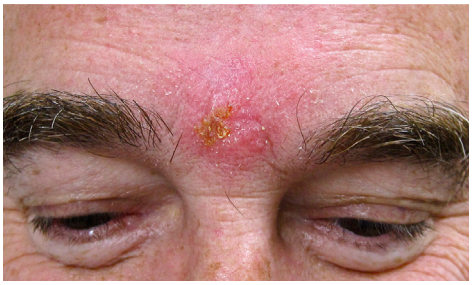

Fig 1. Isotopic response of granulomatous rosacea at a site of prior herpes simplex infection. Primary lesion. Initial presentation of a mildly indurated, erythematous plaque with central yellow crusting located on medial aspect of forehead after a resolved herpes simplex virus infection.

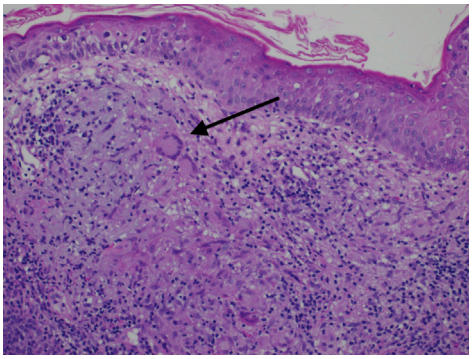

Fig 2. Histopathology of granulomatous rosacea occurring as isotopic response. Punch biopsy specimen of erythematous plaque revealing superficial granulomatous inflammation with giant cells (*arrow*), with a superficial and deep lymphohistiocytic infiltrate. Viral cytopathic effect is not identified. (Hematoxylin-eosin stain; original magnification: ×20.)

When considering the pathogenic mechanism driving the isotopic response, 4 causes have been described: viral, immunologic, vascular, and neural.[1] Although the primary lesion in our patient was viral, there was no evidence of viral infection on histopathology of the secondary lesion. A better explanation may lie in the immunologic, vascular, or neural theories.

Alterations in cutaneous vascular homeostasis have been implicated in the origin of rosacea,[2] and indeed it has been theorized that microcirculation may be altered by local infiltration of primary inflammatory factors such as those seen in viral infection.[3] The neural origin theory proposes that the destruction of nerve fibers may affect the local immune response, sometimes leading to up-regulation of growth factors and resulting in the promotion of