

### Multiple granuloma annulare lesions presenting simultaneously with herpes zoster infection: Wolf's isotopic response



*To the Editor:* We read with great interest the case reported by Storer et al<sup>1</sup> in the November 2016 issue of *JAAD Case Reports* that described a 56-year-old white woman with a 20-year history of systemic lupus erythematosus who had non-photo-exposed initial cutaneous manifestation of lupus within a dermatome previously affected by zoster. In this patient, the cutaneous lupus lesions appeared 1 year after herpes zoster infection. The occurrence of new distinct skin disease within a dermatome previously affected by zoster infection supported the interesting phenomenon of Wolf's isotopic reaction in this case.

All reported cases with Wolf's isotopic reaction occurred after resolution of the primary skin dermatosis, mainly herpes zoster infection. Here we share an interesting case we evaluated in our dermatology clinic, and we still believe it fits under Wolf's isotopic reaction, although the occurrence of both dermatosis occurred simultaneously, which makes it a rare presentation.

Our patient was a 54-year-old woman with a history of right breast cancer treated with mastectomy and chemotherapy. She presented with progressive multiple slightly pruritic annular lesions on the left side of the abdominal wall. Painful grouped vesicles developed in the center of the initial annular lesions within a few days. Some vesicles were hemorrhagic (Fig 1, A and B). The patient had a history of herpes zoster at the site of right breast mastectomy scar a year ago. It resolved with a 7-day course of valacyclovir without scarring. On the latest presentation, her annular lesions were diagnosed as granuloma annulare (GA). The patient's concern and the reason for presentation to our clinic was the evolution of the vesicular eruption that was restricted to the center of some of the annular lesions. Based on clinical and laboratory evaluation with Tzanck smear with features suggestive of herpes-type virus infection

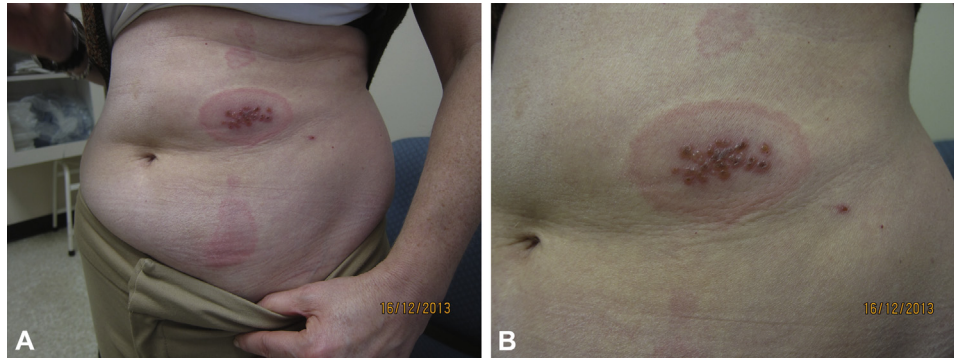
(Fig 2) and positive direct fluorescent antibody for varicella zoster virus, atypical presentation of herpes zoster infection restricted to the center of GA lesions was diagnosed. She responded well to a course of valacyclovir with complete resolution of vesicles within 7 to 10 days. GA lesions healed with no residual scarring within 3 to 4 weeks without additional treatment.

Development of a skin disease at the site of another distinctly different and healed skin disease is known as *Wolf's isotopic response*.<sup>2</sup> This phenomenon was first described by Wolf et al<sup>3</sup> in 1995. Most reported cases of Wolf's isotopic response have occurred after herpes zoster or herpes simplex infection.<sup>4</sup> Various skin diseases have developed after herpes zoster infection was reported, with the granulomatous reactions being the largest category—within this group, GA was the most common.<sup>4</sup> Other skin diseases reported include leukemic infiltrate, lymphoma, lichen planus, morphea, reactive perforating collagenosis, infections, and others.<sup>4</sup> The exact mechanism of development of an isotopic response is still unknown, but different hypotheses are postulated in the literature. One hypothesis suggested by Ruocco et al<sup>5,6</sup> is that herpes virus targets the sensory nerve fibers, resulting in the release of neuropeptides that modulate the immune and angiogenic responses locally. Another report suggests that the development of granulomatous reactions within healed herpes zoster scars is not caused by the persistence of viral DNA within the lesions, but could represent a delayed-type hypersensitivity reaction to incompletely degraded varicella zoster envelope glycoproteins.<sup>7</sup>

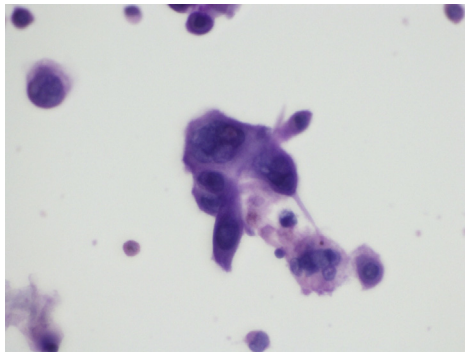
Recognition of Wolf's isotopic response is important for accurate diagnosis and appropriate management of patients presenting with this phenomenon. To our knowledge, our case is the first report of a multiple GA lesions presenting with simultaneous active herpes zoster infection. This case also highlights the importance of simple and rapid bedside diagnostic tests such as Tzanck smear, which is easy to perform and non invasive in confirming the suspected diagnosis.

We thank the authors for giving us the chance to discuss this unique and interesting topic.

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**Fig 1.** A, Unilateral annular plaques with grouped vesicles in the center of one of the lesions. B, Closer view.



**Fig 2.** Tzanck smear shows multinucleate giant cells.

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Funding sources: None.

Conflicts of interest: None disclosed.

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#### REFERENCES

1. Storer M, Nazarian RM, Kourosch AS. Nonphoto-exposed initial cutaneous manifestation of lupus after zoster: A case of Wolf's isotopic reaction. *JAAD Case Rep.* 2016;2(6):425-427.
2. Wolf R, Brenner S, Ruocco V, Filioli FG. Isotopic response. *Int J Dermatol.* 1995;34(5):341-348.
3. Wolf R, Wolf D, Ruocco E, Brunetti G, Ruocco V. Wolf's isotopic response. *Clin Dermatol.* 2011;29:161-168.
4. Ruocco V, Brunetti G, Puca RV, Ruocco E. The immunocompromised district: a unifying concept for lymphoedematous, herpes-infected and otherwise damaged sites. *J Eur Acad Dermatol Venereol.* 2009;23:1364-1373.
5. Ruocco V, Ruocco E, Ghersetich I, Bianchi B, Lotti T. Isotopic response after herpesvirus infection: an update. *J Am Acad Dermatol.* 2002;46:90-94.
6. Ruocco E. Genital warts at the site of healed herpes genitalis: the isotopic response. *Int J Dermatol.* 2000;39:705-706.
7. Nikkels AF, Pierard GE. Are granulomatous reactions in old zoster lesions due to an immune response to varicella zoster virus envelope glycoproteins? *Clin Exp Dermatol* 1998;23(5):237-238.

<https://doi.org/10.1016/j.jdc.2018.03.006>