

Isomorphic and isotopic phenomenon occurring simultaneously in a case of granuloma annulare

Sir,

A 65-year-old male patient presented to us with generalized annular skin lesions over his body. The patient had no other significant comorbidities except for peripheral neuropathy over the legs for which he was being managed in the Neurology department. Dermatological examination showed well-defined discrete, skin-colored papules and annular plaques in a generalized manner, more so over the extremities. There was no evidence of any sensory loss or thickened nerves. Systemic examination was within normal limits. Clinical diagnoses of granuloma annulare and cutaneous sarcoidosis were considered. The initial skin biopsy showed a non-specific granulomatous inflammation—a possibility of interstitial granuloma

annulare was considered. The patient was extensively investigated to rule out any systemic association, especially diabetes mellitus, sarcoidosis, Hansen's disease, connective tissue diseases and any underlying malignancy. Results of all investigations were within normal limits. The patient was empirically started on a low dose of systemic steroids, following which the skin lesions subsided dramatically. The patient had to be maintained on a dose of 10 mg prednisolone for more than 6 months, with intermittent relapses of the skin lesions on withdrawal of the steroid. Approximately a year later, the patient presented with an episode of herpes zoster over the left lower thoracic dermatomes. The patient was treated appropriately with systemic antiviral medication. A month later, the patient presented with an exacerbation of the skin lesions (similar to his previous lesions a year ago), with significant grouping of the lesions over the healed herpes zoster scars [Figure 1]. The possibility of granuloma annulare presenting as a Wolf's isotopic

response was considered. Interestingly, many areas of the body showed lesions in a linear configuration, suggesting an isomorphic response (Koebner's phenomenon) [Figure 2]. A skin biopsy was repeated from the new lesions. Histopathology was consistent with granuloma annulare [Figures 3 and 4].

The patient was otherwise well with no other significant systemic complaints. He was restarted on a short course of low-dose prednisolone (10 mg), following which the skin lesions showed a good response. The patient is continuing on regular follow-up.

Various cutaneous lesions including granulomatous reactions are known to occur at the site of resolved herpes zoster infection. The term isotopic response refers to the occurrence of a new skin disorder at the site of another, unrelated, and already healed skin disease. It was first described by Wolf *et al.*, in 1985 and is hence referred to as the Wolf's isotopic response.^[1]



Figure 1: Grouped annular lesions on the left side of abdomen (over healed herpes zoster lesions)



Figure 2: Lesions in a linear pattern-isomorphic response

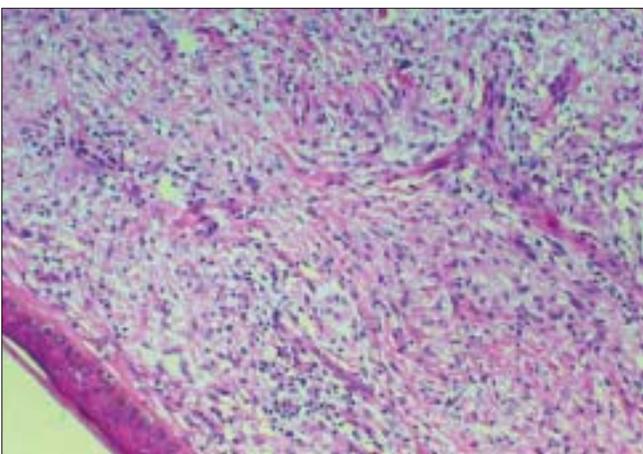


Figure 3: Granulomatous dermal inflammation (H & E, x10)

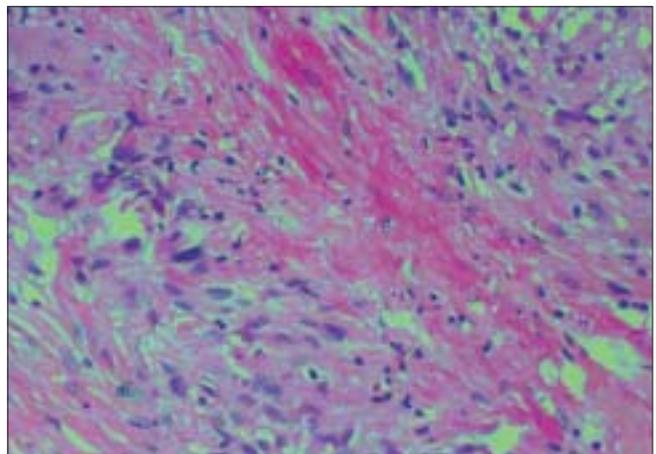


Figure 4: Degenerated collagen with surrounding histiocytes (H & E, x40)

Granuloma annulare has been a commonly reported “second disease” as part of an isotopic response. Other diseases reported include lichen planus, granulomatous folliculitis, tinea, multiple epidermoid cysts, morphea, rosacea, erythema annulare cetrifugum and sarcoidosis (scar sarcoidosis).^[2-4]

Our case was interesting because it represented a segmental presentation of a preexisting generalized disease. The segmental presentation usually precedes the development of generalized lesions. The other salient feature was the presence of prominent Koebnerization or isomorphic phenomenon, concurrently presenting with an isotopic response. The need for distinguishing isomorphic response as a totally different entity from the isotopic response has been dealt before by Thappa.^[4] The term isotopic response as mentioned earlier refers to the occurrence of a new skin disorder at the site of another, unrelated, and already healed skin disease. The isomorphic response, or Koebner phenomenon, indicates the appearance of typical skin lesions of an existing dermatosis at sites of injury.^[4] However, considering that granuloma annulare has been described commonly in the contexts of both isomorphic and isotopic response, we wonder if there could be an underlying common pathology? Happle^[5] has, in a recent article, suggested that in polygenic disorders, such as granuloma annulare, which sometimes shows segmental or linear patterns, a genetically oriented concept of an isolated or superimposed segmental manifestation may be more meaningful. Happle suggests that this genetic basis possibly involves loss of heterozygosity of one of the genes that predispose to the disorder.^[6] Local neuroimmune dysregulation set off by herpes virus-induced lesions of dermal sensory nerve fibers has been suggested as a possible explanation for the Wolf’s response by Ruocco *et al.*^[3] Psoriasis is another condition, which has been described in the context of both isotopic and isomorphic responses. The role of substance P has been considered in the pathogenesis of psoriasis occurring in herpes zoster scars, as substance P is implicated in the pathogenesis of psoriasis as well as in the pathogenesis of pain associated with herpes zoster.^[5] Through this article we would like to highlight the possibility of both isotopic and isomorphic response occurring simultaneously, thus suggesting the possibility of some common link in the etiopathogenesis. It is possible that neuropeptides are significantly involved in both conditions.

**Feroze Kaliyadan, Siby Gopinath¹,
M. G. Jayasree², Chirag Parmar²**

Departments of Dermatology, ¹Neuro-Medicine, ²Pathology,
Amrita Institute of Medical Sciences and Research Centre, Kochi,
Kerala, India

Address for correspondence: Dr. Feroze Kaliyadan,
Department of Dermatology, Amrita Institute of Medical Sciences
and Research Centre, Elamakkara PO, Kochi - 26, Kerala, India.
E-mail: ferozkal@hotmail.com

DOI: 10.4103/0378-6323.51270 - PMID: 19439892

REFERENCES

1. Wolf R, Brenner S, Ruocco V, Filioli FG. Isotopic response. *Int J Dermatol* 1995;34:341-8.
2. Sanli HE, Koçyiğit P, Arica E, Kurtyüksel M, Heper AO, Ozcan M. Granuloma annulare on herpes zoster scars in a Hodgkin's disease patient following autologous peripheral stem cell transplantation. *J Eur Acad Dermatol Venereol* 2006;20:314-7.
3. Ruocco E, Baroni A, Cutri FT, Filioli FG. Granuloma annulare in a site of healed herpes zoster: Wolf's isotopic response. *J Eur Acad Dermatol Venereol* 2003;17:686-8.
4. Thappa DM. Isotopic response versus isomorphic response. *Indian J Dermatol Venereol Leprol* 2004;70:376.
5. Happle R. Superimposed segmental manifestation of polygenic skin disorders. *J Am Acad Dermatol* 2007;57:690-9.
6. Gupta S. Many faces of Koebner phenomenon in psoriasis. *Indian J Dermatol Venereol Leprol* 2002;68:222-4.