

# UC Davis

## Dermatology Online Journal

### Title

Localized interstitial granuloma annulare induced by subcutaneous injections for desensitization

### Permalink

<https://escholarship.org/uc/item/3v68m4j7>

### Journal

Dermatology Online Journal, 19(6)

### Authors

Spring, Philipp  
Vernez, Maxime  
Maniu, Christa-Maria  
et al.

### Publication Date

2013

### DOI

10.5070/D3196018572

### Copyright Information

Copyright 2013 by the author(s). This work is made available under the terms of a Creative Commons Attribution-NonCommercial-NoDerivatives License, available at <https://creativecommons.org/licenses/by-nc-nd/4.0/>

Peer reviewed

**Case Presentation**

**Localized interstitial granuloma annulare induced by subcutaneous injections for desensitization**

**Philipp Spring MD<sup>1</sup>, Maxime Vernez MD<sup>1</sup>, Christa-Maria Maniu MD<sup>2</sup>, and Daniel Hohl MD<sup>1</sup>,**

**Dermatology Online Journal 19 (6): 15**

**<sup>1</sup>Dermatology Unit, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland <sup>2</sup>Immunology and Allergy Unit, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland**

**Correspondence**

Philipp Spring, MD: Philipp.spring@chuv.ch

**Abstract**

We describe a patient with interstitial granuloma annulare associated with subcutaneous injection therapy (SIT) for desensitization to type I allergy. Asymptomatic, erythematous, violaceous annular patches were located at the injection sites on both her arms. Medical history revealed perennial rhinoconjunctivitis treated with SIT (Phostal Stallergen® cat 100% and D. pteronyssinus/D.farinae 50%:50%).

**Case Synopsis**

*Interstitial* granuloma annulare (IGA) is a benign dermatological condition associated with diabetes mellitus or drugs such as pegylated interferon alpha (Peg-IFN $\alpha$ ) [1,2]. A few case reports highlight its occurrence with Sjögren's syndrome [3] or cutaneous borreliosis [4]. Herein the authors describe a case of IGA after subcutaneous injection therapy (SIT) for desensitization to a type I allergy.

Our unit saw a 37-year-old woman for asymptomatic, erythematous, violaceous annular patches, located at injection sites on both her arms. Medical history revealed perennial rhinoconjunctivitis treated with SIT (Phostal Stallergen® cat 100% and D. pteronyssinus/D.farinae 50%:50%). The lesions appeared at 1 IR/ml concentration (1 month after treatment initiation). No other skin diseases were reported at the time. Her daughter suffers from asthma and gluten intolerance. Medical treatment consists in desloratadine, topical nasal appliance of mometasone fuorate, and the antidepressant drug venlafaxine. The brownish patchy lesions appeared annular, well demarcated, and symmetrical. They were strictly located at the injection sites. There was no scaling (Figure 1). A skin biopsy revealed an interstitial lympho-histiocytic inflammation in the superficial and deep dermis, with a diffuse interstitial infiltrate of giant multinucleated cells (Figure 2). With alcian blue stain at a pH of 2.5, the collagen bundles appeared eosinophilic and mucin deposits were exhibited (Figure 3). Birefringence analysis excluded a reaction to a foreign body. A diagnosis of IGA was confirmed, ruling out bilateral erythema chronicum migrans or fixed drug eruption. SIT was interrupted and a sublingual immunotherapy (SLIT) modality was proposed. After 4 weeks the lesions were resolved.



Figure 1.

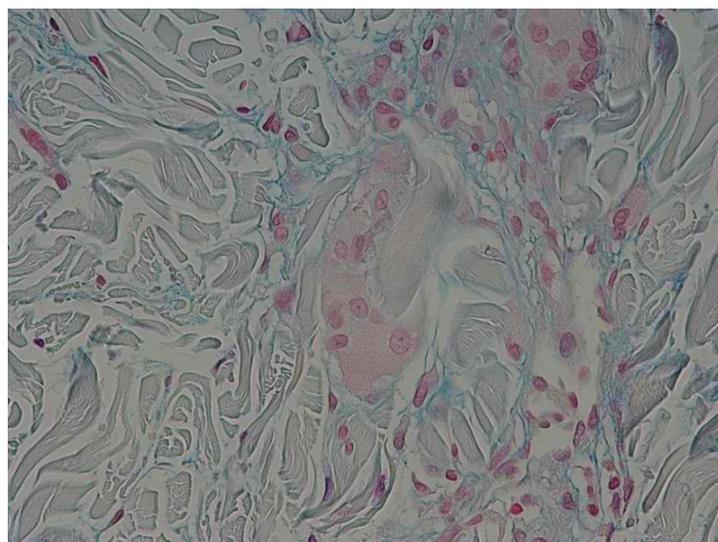
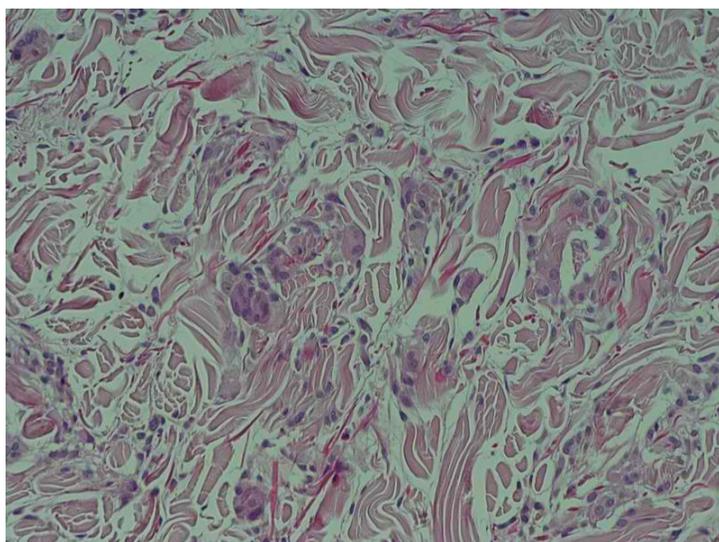


Figure 2. Figure 3.

## Discussion

IGA is a self-limited condition, also associated with diabetes mellitus. A few reported cases have highlighted the role of interferon (IFN) in drug-induced IGA related to Peg-IFN $\alpha$  [1,2]. Drugs implicated in this pathomechanism include allopurinol [5] or amlodipin [6]. Case reports have proposed the positive role of adalimumab [7], with regard to the possible link between immunological deregulation and the occurrence of interstitial granulomatous disorders [8]. Our patient appeared to suffer from IGA induced by the injected product. The interstitial infiltrate with lymphocytes and histiocytes, along with large multinucleated cells and mucin deposits confirms the diagnosis.

To our knowledge, this is the first case of IGA associated with the injection of house dust mite allergen extracts. The main adjuvants are phosphate, NaCl, Glycerolum, and tricalcii phosphas; Phenolum 4mg is the only preservative. There are cases of deep granuloma annulare (GA), or rheumatoid nodule-like patterns induced by the aluminium contained in vaccines [9]. Yet in our case, the SIT preparation contained no aluminium (thus there was no indication for performing an azurin staining). There is no known association between phosphate and the pathogenesis of IGA or deep GA.

The presence of eosinophils, and the lack of significant necrobiosis, also pointed to the diagnosis of an interstitial granulomatous drug reaction (IGDR), which usually follows drug-intake or appliance. This entity is similar to IGA and lesions can spread in both conditions. Nevertheless, the histopathological features of IGDR are closer to those of an interstitial lymphocyte infiltrate with interface dermatitis, usually seen in lupus erythematosus or erythema annulare centrifugum [10]. Also, the giant cells are usually missing [10]. Furthermore, drug induced IGA must be looked at as separate from IGDR. On a skin biopsy, IGA can show the typical signs of necrobiosis, but this is not systematic. In our case, only mucin deposits were present, but as a rule they are not for IGDR. In conclusion, IGA is self-limited and may be drug induced following SIT, which is considered to be the trigger for the disease.

## References

1. Ahmad U, Li X, Sodeman T, Daboul I: Hepatitis c virus treatment with pegylated interferon-alfa therapy leading to generalized interstitial granuloma annulare and review of the literature. *American journal of therapeutics* 2011. PMID:21317616
2. Kluger N, Moguelet P, Chaslin-Ferbus D, Khosrotherani K, Aractingi S: Generalized interstitial granuloma annulare induced by pegylated interferon-alpha. *Dermatology* 2006;213:248-249. PMID:17033180
3. Sumikawa Y, Ansai S, Kimura T, Nakamura J, Inui S, Katayama I: Interstitial type granuloma annulare associated with sjogren's syndrome. *The Journal of dermatology* 2010;37:493-495. PMID:20536658
4. Gualco F, Zaccaria E, Drago F, Rebora A: Interstitial granuloma annulare and borreliosis: A new case. *Journal of the European Academy of Dermatology and Venereology : JEADV* 2007;21:1117-1118. PMID:17714142
5. Brechtel B, Kolde G: [granuloma annulare disseminatum as a rare side effect of allopurinol]. *Der Hautarzt; Zeitschrift fur Dermatologie, Venerologie, und verwandte Gebiete* 1996;47:143. PMID:8868461
6. Lim AC, Hart K, Murrell D: A granuloma annulare-like eruption associated with the use of amlodipine. *The Australasian journal of dermatology* 2002;43:24-27. PMID:11869204
7. Werchau S, Enk A, Hartmann M: Generalized interstitial granuloma annulare--response to adalimumab. *International journal of dermatology* 2010;49:457-460. PMID:20465706
8. Paul M, Cribier B, Heid E, Grosshans E, Lipsker D: [generalized granuloma annulare and drug-induced immunodeficiency]. *Annales de dermatologie et de venerologie* 2004;131:1051-1054. PMID:15692437
9. McDermott MB, Lind AC, Marley EF, Dehner LP: Deep granuloma annulare (pseudorheumatoid nodule) in children: Clinicopathologic study of 35 cases. *Pediatric and developmental pathology : the official journal of the Society for Pediatric Pathology and the Paediatric Pathology Society* 1998;1:300-308. PMID:10463292
10. Magro CM, Crowson AN, Schapiro BL: The interstitial granulomatous drug reaction: A distinctive clinical and pathological entity. *Journal of cutaneous pathology* 1998;25:72-78. PMID:9521495