The rope sign, a typical and yet infrequent clue

Víctor García-Rodríguez[1] MD, Jorge Arandes-Marcocci[1] MD, MT Fernández-Figueras[2] PhD, Montse Salleras-Redonnet[1] PhD

Affiliations: [1]Department of Dermatology, Hospital Universitari Sagrat Cor, Grupo Quirónsalud, Barcelona, Spain, [2]Department of Pathology, Hospital Universitari General de Catalunya, Grupo Quirónsalud, Sant Cugat del Vallés, Barcelona, Spain

Corresponding Author: Victor García-Rodríguez MD, Department of Dermatology, Hospital Universitari Sagrat Cor, Grupo Quirónsalud, Viladomat Street, 288, E-08029 Barcelona, Spain, Tel: 34-933221111, Email: derma.vgr@gmail.com

Abstract

Cutaneous granulomatous reactions are diverse, both from the clinical and the pathological perspective. Most underlying pathophysiological aspects remain elusive. Interstitial granulomatous dermatitis and palisaded neutrophilic and granulomatous dermatitis have been claimed to be reactions to systemic disorders, such as infectious, inflammatory, or neoplastic conditions. Recently, the overarching term "reactive granulomatous dermatitis" has been coined to unify both entities. We herein report two cases of reactive granulomatous dermatitis presenting with the widely known, albeit infrequent "rope sign" and provide clinicopathological correlation. The two patients included a 53-year-old woman with enlarging erythematous plaques and underlying palpable cords on both sides of trunk near axillae (rope sign), and a 51-year-old woman with personal history of rheumatoid arthritis and a palpable cord on the left aspect of the trunk. Pathological findings were compatible with reactive granulomatous dermatitis in both cases. In conclusion, the rope sign represents a strikingly infrequent but decisive diagnostic clue of reactive granulomatous dermatitis.

Keywords: diagnosis, granulomatous dermatitis, interstitial, rope sign

Introduction

Interstitial granulomatous dermatitis (IGD) is a known pathological concept depicting a granulomatous reaction to a plethora of disorders (autoimmune diseases, hematologic and solid malignancies, and infectious diseases), presumably in the setting of immunocomplex deposition on the vessels with subsequent hyperstimulation of the immune system and decreased flux to the dermis, resulting in collagen degeneration. It is clinically heterogeneous, with the "rope sign" being the most specific, yet least commonly seen presentation. As in our cases, it was decisive for clinical suspicion. For the purpose of this manuscript, the recently coined term reactive granulomatous dermatitis (reactive granulomatous dermatitis) will be used in lieu of IGD.

Case Synopsis

A 53-year-old woman presented to our dermatology department with progressively enlarging symmetric inflammatory plaques on both sides of the trunk and the posterolateral aspects of arms and thighs (**Figure 1**). There was also a symmetric palpable cord on both lateral aspects of the trunk. She denied systemic symptoms. The patient's medical history consisted of diabetes mellitus type 1, two episodes of myocardial infarction, intermittent claudication, anxiety, depressive disorder, polyarthralgia, and monophasic Raynaud phenomenon. The patient denied recent intake of new medications, vaccinations or alternative therapeutic agents.

A blood test, chest X-ray and a skin biopsy from the axillary region were performed. Chest X-ray revealed no abnormalities. Blood test results yielded mild anemia (hemoglobin 11.7g/dl, normal 12-16g/dl), leukopenia (3400/µl normal 4000-11000//µl), and

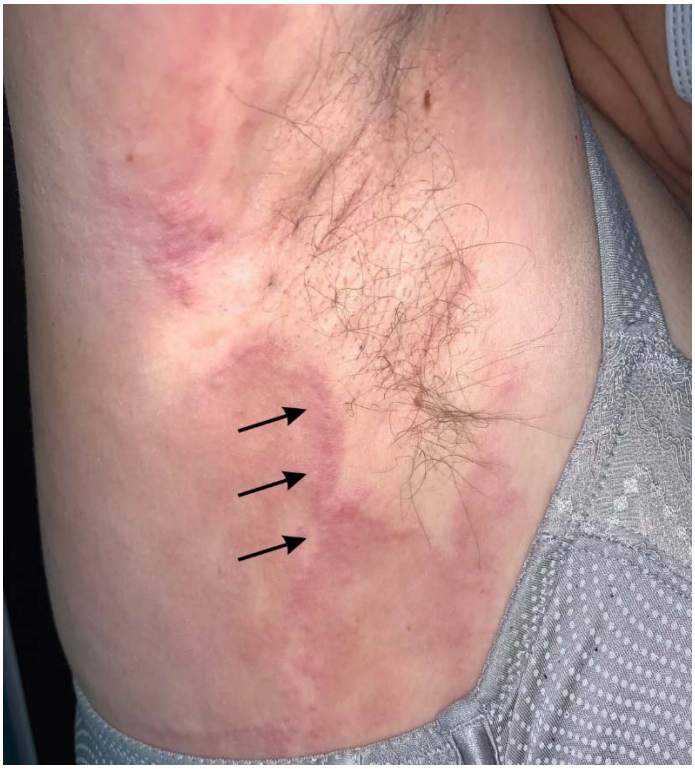

Figure 1. *Erythematous annular plaques in the axillary area. Arrows points toward the underlying palpable cord (rope sign). The patient presented similar lesions on both thighs in a symmetric fashion.*

lymphopenia (800/µl, normal 1500-4000/µl). Inflammatory parameters were slightly raised, namely rheumatoid factor (17IU/ml, normal <14IU/ml) and C-reactive protein (2.2mg/dl normal <0.3mg/dl). Autoimmunity tests showed elevated titers of antinuclear antibodies: ANA 1:1280, nuclear homogenous pattern, anti-ssDNA 51, and moderate positivity in anti-nucleosome immunoblot. The remaining parameters all tested negative. The histopathology showed an interstitial infiltrate of epithelioid histiocytes involving mainly the mid and deep dermis, with scattered neutrophils and eosinophils and formation of cutaneous extravascular necrotizing granulomas, referred to as Churg-Strauss granulomas (**Figure 2**).

A second case, a 50-year-old woman with personal history of rheumatoid arthritis and chronic spontaneous urticaria, presented with infiltrated papules and also a palpable cord on the left axilla (**Figure 3**). Mondor disease, another condition in the differential diagnosis, was ruled out by high-frequency ultrasound and histopathological study, the latter compatible with reactive granulomatous dermatitis (**Figure 4**). Clinical, laboratory, and histopathological findings were consistent in both cases with reactive granulomatous dermatitis.

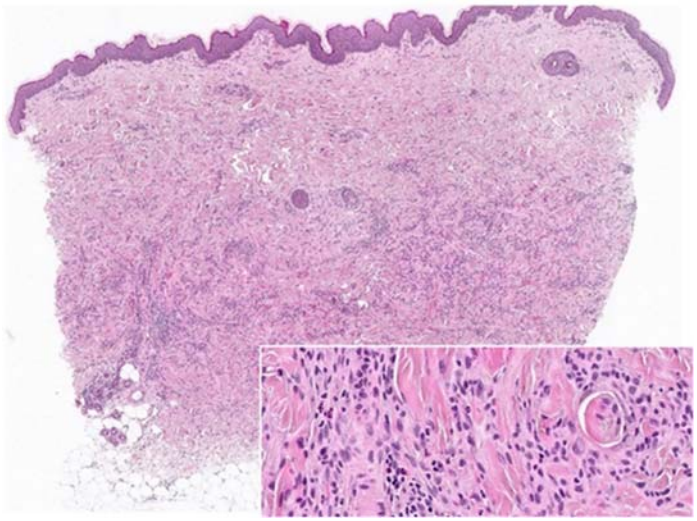

Figure 2. *H&E histopathology. A 4mm punch biopsy from the axillary area showed an interstitial histiocytic infiltrate with some neutrophils and eosinophils. No vasculitic changes, mucin deposition, or interface changes were noted. The inset showed a Churg-Strauss granuloma with a degenerated collagen bundle surrounded by and empty space ("floating sign") and a pseudo-rosette of epithelioid histocytes, 10×; inset 40×.*

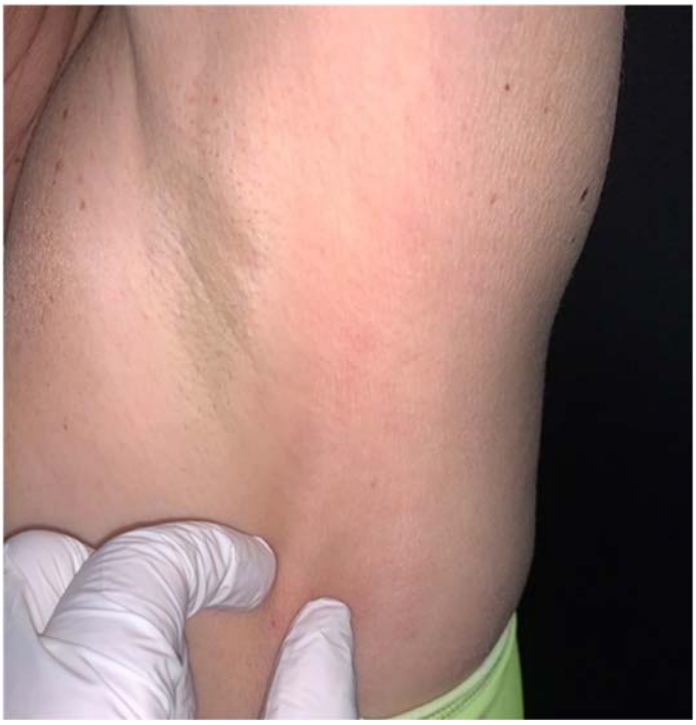

Figure 3. *More palpable than visible erythematous linear lesion beneath the left axilla (rope sign).*

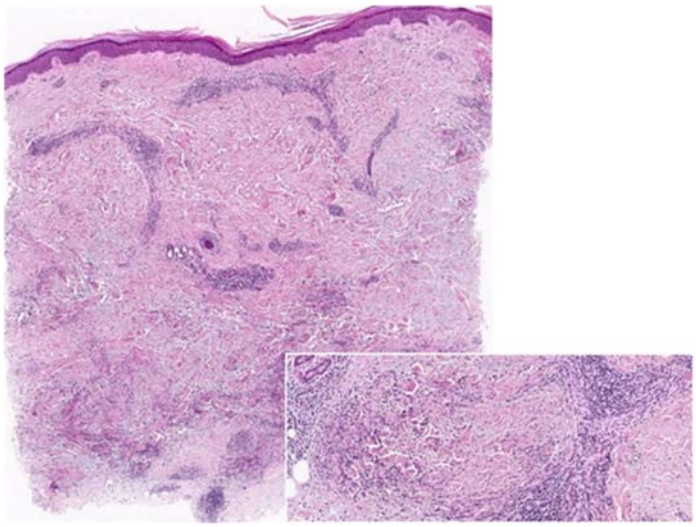

Figure 4. *H&E histopathology. A 4mm punch biopsy shows a dense granulomatous infiltrate localized mainly in the deep dermis. At higher magnification, ring granulomas with degenerated collagen bundles, interstitial infiltrate, and scattered eosinophils were noted, 10×; inset 40×.*

Case Discussion

Reactive granulomatous dermatitis can be the dermatological hint to a myriad of infectious, autoimmune, or neoplastic disorders. With a heterogenous clinical presentation, the "rope sign" accounts for the most specific presentation. Mondor disease (thromboflebitis of a superficial vein in the chest wall resulting in a palpable cord) is in the differential diagnosis and distinguishing between them is sometimes difficult and must be ruled out by skin biopsy and/or ultrasonography [1].

Regarding terminology, scientific literature is confusing since IGD, IGD-arthritis, palisaded neutrophilic and granulomatous dermatitis, and other terms are commonly considered within the same spectrum, or completely separate entities. The overarching term "reactive granulomatous dermatitis" has recently been proposed to encompass this group of disorders [2,3].

Diagnosis is made considering clinicopathological correlation. Other conditions in the differential diagnosis include other granulomatous disorders such as the interstitial variant of granuloma annulare, sarcoidosis, or necrobiosis lipoidica [4]. Treatment evidence is sparse (no randomized trials) and consists of corticosteroids, methotrexate, phototherapy, and colchicine as the most common options. A proper screening of underlying potentially fatal conditions is key to success in the management of this entity. The first of our cases was seemingly related to an autoimmune process (probably lupus erythematosus), but follow-up was lost after performing the blood test and skin biopsy. Whereas the second case was allegedly associated with rheumatoid arthritis. Nonetheless, we deem this clinical presentation and the histopathological picture to be of academic interest in the context of a rare condition where the dermatologist plays a crucial role.

Conclusion

In conclusion, we herein report two cases of interstitial granulomatous dermatitis presenting with the characteristic, yet infrequent rope sign. Clinicians should be aware of this presentation and evaluate screening for systemic disease at the time of the cutaneous onset. Lastly, we highlight the accuracy of the term reactive granulomatous dermatitis over interstitial granulomatous dermatitis, or palisaded neutrophilic and granulomatous dermatitis.

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. Worsnop FS, Ostlere L. Interstitial granulomatous dermatitis with arthritis presenting with the rope sign. *Clin Exp Dermatol*. 2013;38:564–5. [PMID: 23531209].
2. Rosenbach M, English JC. Reactive Granulomatous Dermatitis: A review of palisaded neutrophilic and granulomatous dermatitis, interstitial granulomatous dermatitis, interstitial granulomatous drug reaction, and a proposed reclassification. *Dermatologic Clinics*. 2015;33:373–87. [PMID: 26143420].
3. Rodríguez-Garijo N, Bielsa I, Mascaró JM, et al. Reactive granulomatous dermatitis as a histological pattern including manifestations of interstitial granulomatous dermatitis and palisaded neutrophilic and granulomatous dermatitis: a study of 52 patients. *J Eur Acad Dermatol Venereol*. 2021;35:988–94. [PMID: 33098595].

4. Terziroli Beretta-Piccoli B, Mainetti C, Peeters M-A, Laffitte E. Cutaneous Granulomatosis: a Comprehensive Review. *Clin Rev Allergy Immunol*. 2018;54:131–46. [PMID: 29352388].