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Interstitial granuloma annulare triggered by Lyme disease

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Abstract

Granuloma annulare is a non-infectious granulomatous skin condition with multiple different associations. We present a case of a man in his 60s with a three-week history of progressive targetoid plaques on his arms, legs, and trunk. Skin biopsy demonstrated interstitial granuloma annulare. Additional testing revealed IgM antibodies to *Borrelia burgdorferi* on western blot suggesting interstitial granuloma annulare was precipitated by the recent infection. Lyme disease is an uncommonly reported association with interstitial granuloma annulare.

Keywords: *Borrelia burgdorferi*, borreliosis, granuloma annulare, granulomatous dermatitis, interstitial, Lyme disease

Introduction

Lyme disease, or borreliosis, is a bacterial infection caused by the spirochete *Borrelia burgdorferi*. It is transmitted by certain ticks in the genus *Ixodes*, most notably the deer ticks *Ixodes scapularis*, *Ixodes pacificus*, and *Ixodes ricinus* in various regions of the United States and Europe [1]. Lyme disease is classically associated with erythema migrans, but a variety of additional cutaneous manifestations including granuloma annulare (GA) have also been reported [2]. Granuloma annulare typically presents as one or more erythematous papules or plaques with central clearing most often located on the distal extremities, which occasionally are pruritic. Although the epidemiology, etiology, and pathogenesis of GA remain poorly understood, it has

been associated with a variety of systemic diseases including diabetes mellitus, malignancy, thyroid disease, dyslipidemia, and infection [3,4].

There are multiple histological variants of GA, including interstitial GA. The histopathology of classic GA demonstrates a focal degeneration of collagen surrounded by an inflammatory infiltrate composed of lymphocytes and histiocytes. In a less common variant, interstitial GA, scattered histiocytes are seen between the surrounding collagen bundles in the upper and mid-dermis [3,5].

Case Synopsis

A man in his 60s with past medical history of psoriasis and dyslipidemia presented with a 3-week history of a painful left ankle joint as well as non-pruritic, non-painful lesions on his abdomen, flanks, back, axilla, and arms. When the rash first appeared the patient indicated he had a few days of fever, myalgia, and night sweats which had since resolved. He endorsed a recent camping trip in Ohio two weeks prior to the onset of symptoms but did not recall any tick exposure. Skin examination revealed targetoid plaques on his abdomen, back, legs, and arms (**Figure 1**). Skin biopsy of the right upper back was performed and demonstrated interstitial histiocytic dermatitis. In the superficial and reticular dermis, there were scattered interstitial histiocytes with minimal mucin deposition. In addition, there was a perivascular lymphoid infiltrate and rare eosinophils (**Figure 2**). Lyme IgM and IgG antibodies were both positive on western blot consistent with recent *B. burgdorferi* infection. He was started on doxycycline



Figure 1. Multiple erythematous plaques with central clearing are exhibited most notably on the abdomen in a patient diagnosed with interstitial granuloma annulare.

100mg twice daily for one month. Upon follow-up he noted complete resolution of his rash and arthralgias after two weeks of treatment and continued to deny any systemic symptoms.

Case Discussion

Our patient presented with the interstitial variant of generalized GA. Interstitial GA has an uncommon association with Lyme disease with only one other case, to the best of our knowledge, previously described in the literature [6]. Although also rarely reported, classic GA has also been linked to *B. burgdorferi*. A retrospective study of 73 skin biopsies of GA from patients with a suspected tick bite detected *Borrelia* DNA by PCR in 9.6% (7/73) of biopsies. Chlamydiales DNA, which is also known to be present in *Ixodes* ticks, was isolated in 72.6% (53/73) in the same study, thereby suggesting tick exposure in these patients with GA [7]. Additionally, another study investigating a total of 157 biopsies of GA using a stain containing polyclonal *Borrelia* antibodies and focus-floating microscopy detected *Borrelia* in 80.9% (127/157) of biopsies of GA [8].

Like our patient who could not recall a tick bite, it is common for individuals with Lyme disease to not

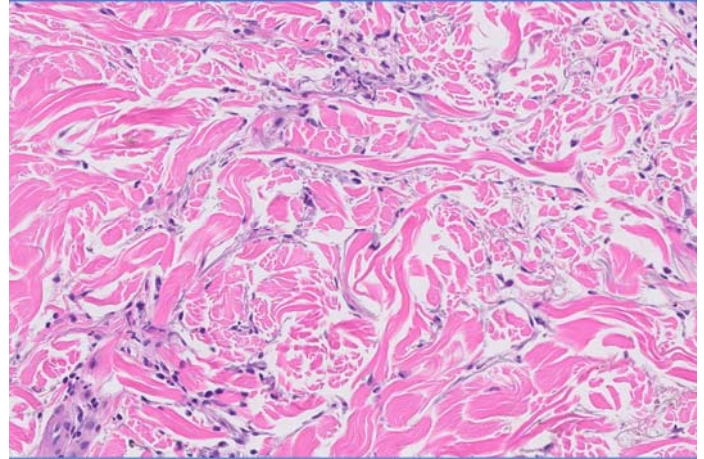


Figure 2. There are scattered interstitial histiocytes with minimal mucin deposition in the superficial and reticular dermis. Additionally, there is a perivascular infiltrate and rare eosinophils. H&E, 10 \times .

recall tick exposure with one study finding only 14% (34/237) of those with Lyme disease remembered being bitten by a tick [2]. Our patient also originally had constitutional symptoms of fever, myalgia, and arthralgias consistent with early Lyme disease. Currently, the recommendation for diagnosis of Lyme disease involves a two-test methodology first utilizing enzyme-linked immunosorbent assay or immunofluorescence, followed by a western blot for positive or equivocal specimens [9]. Although GA can be resistant to therapy, the patient's GA resolved with treatment of the Lyme disease with doxycycline. Therefore, we recommend patients who have viral prodromal symptoms and subsequent interstitial GA should undergo testing for Lyme disease.

Conclusion

Interstitial granuloma annulare precipitated by Lyme disease has only been reported one other time in the literature. Since Lyme disease can progress to cause significant morbidity and even be fatal, is it important that dermatologists are aware of this potential association with GA.

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. Cardenas-de la Garza JA, De la Cruz-Valadez E, Ocampo-Candiani J, Welsh O. Clinical spectrum of Lyme disease. *Eur J Clin Microbiol Infect Dis*. 2019;38:201-208. [PMID: 30456435].
2. Berger BW. Dermatologic manifestations of Lyme disease. *Rev Infect Dis*. 1989;11 Suppl 6:S1475-81. [PMID: 2814169].
3. Prendiville JS. Granuloma Annulare. In: Kang S, Amagai M, Bruckner AL, Enk AH, Margolis DJ, McMichael AJ, Orringer JS, editors. 9th ed. Fitzpatrick's Dermatology. McGraw-Hill; ch. 34.
4. Keimig EL. Granuloma Annulare. *Dermatol Clin*. 2015;33:315-29. [PMID: 26143416].
5. Ronen S, Rothschild M, Suster S. The interstitial variant of granuloma annulare: Clinicopathologic study of 69 cases with a comparison with conventional granuloma annulare. *J Cutan Pathol*. 2019;46:471-478. [PMID: 30883851].
6. Gualco F, Zaccaria E, Drago F, Rebora A. Interstitial granuloma annulare and borreliosis: a new case. *J Eur Acad Dermatol Venereol*. 2007;21:1117-8. [PMID: 17714142].
7. Tolkki L, Hokynar K, Meri S, et al. Granuloma Annulare and Morphea: Correlation with Borrelia burgdorferi Infections and Chlamydia-related Bacteria. *Acta Derm Venereol*. 2018;98:355-360. [PMID: 29110020].
8. Ziemer M, Grabner T, Eisendle K, Baltaci M, Zelger B. Granuloma annulare--a manifestation of infection with Borrelia? *J Cutan Pathol*. 2008;35:1050-7. [PMID: 18616764].
9. Mead P, Petersen J, Hinckley A. Updated CDC Recommendation for Serologic Diagnosis of Lyme Disease. *MMWR Morb Mortal Wkly Rep*. 2019;68:703. [PMID: 31415492].