NCBI Bookshelf. A service of the National Library of Medicine, National Institutes of Health.

StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-.

Acrodermatitis Chronica Atrophicans

Authors

Anita Gade[1]; Taraneh Matin; Richard Rubenstein[2]; Carolyn A. Hardin[3].

Affiliations

[1] Stamford Hospital
[2] Medical College of Virginia, Richmond, VA
[3] San Antonio Uniformed Services Health Education Consortium

Last Update: December 2, 2020.

Introduction

Acrodermatitis chronica atrophicans (ACA) is a late and chronic manifestation of Lyme borreliosis (LB). ACA predominantly involves the distal portions of extremities and is characterized by chronic cutaneous atrophy.[1] Unlike other skin manifestations of Lyme disease, including erythema migrans (EM) and borrelial lymphocytoma (BL), ACA does not spontaneously resolve. If untreated, ACA may progress from bluish-red discoloration and inflammation to chronic atrophy and fibrosis, with the late-stage being more treatment-resistant.

ACA was first described in 1883 by Buchwald in Germany, and cases were later reported in 1895 in North America.[2] The diagnosis of ACA is based on clinical presentation, as well as serologic testing and histopathologic confirmation. Recognizing ACA is often challenging due to variable latency in disease onset following the primary borrelial infection, and lack of symptoms leading to delay in seeking treatment.

Lyme borreliosis is the most common vector-borne disease in the northeastern United States. It is a multisystem disease caused by the spirochete *Borrelia burgdorferi.*[3][4][5] It is transmitted to humans via an *Ixodes* tick bite. There are 3 skin manifestations of LB: Erythema migrans (stage 1) with a characteristic “bull’s eye rash,” which, if untreated, can be followed by early disseminated infection, borrelial lymphocytoma (stage 2) along with neurologic and cardiac abnormalities, and late infection, especially arthritis in North America or acrodermatitis chronica atrophicans (stage 3) in Europe.[6][7][8][9] Acrodermatitis chronica atrophicans is the most common late and chronic manifestation of LB. Approximately 20% of patients with ACA have a history of spontaneously healed EM, usually on an extremity where the ACA lesion developed 6 months to 8 years later.[1]

Etiology

Borrelia is a member of the *Spirochaetacea* family. There are approximately 20 different genospecies, but only five pose a significant pathogenic risk to humans: *B. afzelii, B. garinii, B. bavariensis, B. burgdorferi* sensu stricto, *and B. spielmanii.*[10] Acrodermatitis chronica atrophicans results predominantly from bacterial infection with *B. afzelii.* However, it can also be caused by European *B. burgdorferi* sensu stricto or *B. garinii.*

Epidemiology

Acrodermatitis chronica atrophicans predominantly affects women who are 40-70 years of age. ACA is rare in the pediatric population, with few cases reported in children.[11] It is more commonly seen in Europe due to untreated infection with *Borrelia afzelii* and is rarely found in the United States. The overall prevalence of ACA in patients with Lyme disease in Europe is approximately 10%.

Pathophysiology

The pathogenesis of Lyme disease involves the *Ixodes* tick feeding on an infected animal reservoir. The *Borrelia* spirochetes replicate, and some penetrate out of the tick’s midgut and migrate to the salivary glands.[12] When the tick bites a human, it releases spirochetes into the dermis via saliva. This results in an innate immune response with neutrophil migration and macrophage activation, causing the release of pro-inflammatory cytokines. Increased blood flow to the capillaries leads to erythema migrans at the bite site approximately 1 to 2 weeks later.[13] If untreated,

there is hematogenous spread and development of systemic symptoms.

In ACA, there is a chronic T-cell mediated immune reaction against *Borrelia* with the presence of CD3+ and CD4+ cells in the dermal infiltrate.[14][15] *Borrelia* bind to extracellular matrix proteins, including glycosaminoglycan-binding protein, fibronectin-binding protein, and decorin proteoglycan.[16][17][18] They activate metalloproteases and cause degradation of the extracellular matrix. *Borrelia* also have a high affinity for collagen fibers, which has been demonstrated on electron microscopy.[19][20] Damage to connective tissues, with the destruction of collagen, leads to fibrosis and dermal atrophy.[21][22][23][24]

Histopathology

In the early inflammatory stage, biopsy specimens of active lesions show perivascular lymphocytic infiltrate with plasma cells in the dermis, telangiectatic endothelial-lined spaces, and mild atrophy of the epidermis. Histological examination of late lesions demonstrates an atrophic epidermis, and interstitial lymphocytic infiltrate with plasma cells and occasional histiocytes or mast cells.[7][25]

History and Physical

Most patients may not recall a tick bite due to the delayed progression of ACA. Furthermore, diagnosis is quite challenging due to varying clinical manifestations. Acrodermatitis chronica atrophicans is considered to be biphasic; it initially presents as bluish-red lesions overlying doughy and swollen skin. It later progresses to extensive skin atrophy with a prominence of underlying blood vessels and a shiny appearance or “cigarette paper skin.” Lesions are primarily located on the bilateral extensor surfaces of the limbs. Fibroid nodules may develop over bony prominences, especially in the ulnar or tibial regions.[26]

In 15% of the patients with ACA, a localized increase of collagen leads to band-like induration with decreased movement of the joints.[27] Peripheral neuropathy can occur in approximately half of the patients, with associated numbness, tingling, or allodynia.[28] Enlargement of the limb with tenosynovitis and dactylitis is a rare occurrence.[29][30][31]

Evaluation

The diagnosis of ACA is based on clinical findings and supported by serologic tests (high level of specific *Borrelia* IgG antibodies).[32] In the majority of the chronic Lyme disease patients, serology is positive for *Borrelia* IgG antibodies. IgM antibodies against *Borrelia* are often a false positive in late-stage and thus not useful in diagnosing ACA.[33] A negative serologic test excludes ACA. When the clinical picture is uncertain, further diagnosis is made with a skin biopsy and histological examination. Detection of *B. burgdorferi* DNA by culture or PCR helps in confirming the diagnosis.[5]

Treatment / Management

The standard management is based on the administration of 1 of the following antibiotics:

1. Oral amoxicillin 500 to 1000 mg three times daily for 14 to 28 days
2. Oral doxycycline 100 mg twice daily or 200 mg once daily for 14 to 28 days
3. Intravenous ceftriaxone 2000 mg every 24 hours for 14 to 28 days
4. Intravenous cefotaxime 2000 mg every 8 hours for 14 to 28 days
5. Intravenous penicillin G 3 to 4 MU every 4 hours for 14 to 28 days[34][35]

Differential Diagnosis

The differential diagnosis of ACA depends on the clinical presentation and disease stage. Lesions on the lower extremities are often mistaken as vascular insufficiency (i.e., chronic venous or arterial insufficiency, superficial thrombophlebitis), cold injury, livedo reticularis, localized scleroderma, erysipelas, lymphedema, related to chronic use of potent topical corticosteroids or aging. Nodules may be confused with rheumatoid disease, gout, or erythema nodosum.[5]

Prognosis

The clinical outcome is positive if the acute inflammatory stage is treated appropriately. The clinical outcome is difficult to predict for the chronic atrophic phase, as changes are only partially reversible. One study showed that third-generation cephalosporin therapy for 28 days resulted in partial dissolving to complete fading of the skin lesion.[1][36] If the skin lesion is left untreated, it does not typically resolve spontaneously, and fibrosis and atrophy can occur. Moreover, antibiotic therapy may not reverse neurologic symptoms, such as polyneuropathy (i.e., pain, paresthesia).

Complications

Acrodermatitis chronica atrophicans skin lesions may lead to bacterial superinfections. ACA is also considered a risk factor for malignancies, including B-cell lymphoma, basal cell carcinoma, and squamous cell carcinoma.[37]

Deterrence and Patient Education

The diagnosis of ACA is often delayed as patients do not report significant symptoms or seek medical attention, and due to the natural history of the disease developing months to years after a tick bite.

Cutaneous lesions in ACA mostly present on the extremities but may be located in other areas, including the abdomen or face, necessitating serologic and histopathologic confirmation. Treatment should be implemented as early as possible to prevent irreversible skin damage.

Lyme borreliosis can be primarily prevented by avoidance of tick bites. When walking in wooded areas, individuals should use personal protective measures to keep safe. These include applying repellents, wearing long sleeves, tucking pant legs into socks or long boots, and wearing light-colored clothing to allow ticks to be more readily visible.[38] When returning from the outdoors, it is crucial to change clothing and examine the body for ticks. If a tick is found, individuals should use fine-tipped tweezers to grasp the organism as close to the surface of their skin, pull upwards to remove the tick, dispose of it appropriately, and clean the bite area with soap and water. If an individual develops a rash or fever, it is recommended to seek medical care immediately to prevent further sequelae.

Enhancing Healthcare Team Outcomes

Lack of familiarity with acrodermatitis chronica atrophicans is a major contributor to delay in proper diagnosis and treatment. Thus, ACA should be kept on the differential when evaluating skin lesions on the extremities in elderly patients, and especially for those with a history of a tick bite. In patients with multiorgan involvement, a collaboration between an interprofessional team (dermatologist, rheumatologist, neurologist, cardiologist) is beneficial.

Continuing Education / Review Questions

- Access free multiple choice questions on this topic.
- Earn continuing education credits (CME/CE) on this topic.
- Comment on this article.

References

1. Moniuszko-Malinowska A, Czupryna P, Dunaj J, Pancewicz S, Garkowski A, Kondrusik M, Grygorczuk S, Zajkowska J. Acrodermatitis chronica atrophicans: various faces of the late form of Lyme borreliosis. Postepy Dermatol Alergol. 2018 Oct;35(5):490-494. [PMC free article: PMC6232541] [PubMed: 30429707]
2. Scott JD. Presentation of Acrodermatitis Chronica Atrophicans Rashes on Lyme Disease Patients in Canada. Healthcare (Basel). 2020 Jun 04;8(2) [PMC free article: PMC7349802] [PubMed: 32512846]
3. Sigal LH. Current recommendations for the treatment of Lyme disease. Drugs. 1992 May;43(5):683-99. [PubMed: 1379147]
4. Stanek G, Strle F. Lyme borreliosis-from tick bite to diagnosis and treatment. FEMS Microbiol Rev. 2018 May 01;42(3):233-258. [PubMed: 29893904]
5. Stanek G, Fingerle V, Hunfeld KP, Jaulhac B, Kaiser R, Krause A, Kristoferitsch W, O'Connell S, Ornstein K, Strle F, Gray J. Lyme borreliosis: clinical case definitions for diagnosis and management in Europe. Clin Microbiol

Infect. 2011 Jan;17(1):69-79. [PubMed: 20132258]
6. Hofmann H, Fingerle V, Hunfeld KP, Huppertz HI, Krause A, Rauer S, Ruf B., Consensus group. Cutaneous Lyme borreliosis: Guideline of the German Dermatology Society. Ger Med Sci. 2017;15:Doc14. [PMC free article: PMC5588623] [PubMed: 28943834]
7. Vasudevan B, Chatterjee M. Lyme borreliosis and skin. Indian J Dermatol. 2013 May;58(3):167-74. [PMC free article: PMC3667275] [PubMed: 23723463]
8. McGinley-Smith DE, Tsao SS. Dermatoses from ticks. J Am Acad Dermatol. 2003 Sep;49(3):363-92; quiz 393-6. [PubMed: 12963900]
9. Bhate C, Schwartz RA. Lyme disease: Part I. Advances and perspectives. J Am Acad Dermatol. 2011 Apr;64(4):619-36; quiz 637-8. [PubMed: 21414493]
10. Hubálek Z, Halouzka J. Distribution of Borrelia burgdorferi sensu lato genomic groups in Europe, a review. Eur J Epidemiol. 1997 Dec;13(8):951-7. [PubMed: 9476827]
11. Glatz M, Resinger A, Semmelweis K, Ambros-Rudolph CM, Müllegger RR. Clinical spectrum of skin manifestations of Lyme borreliosis in 204 children in Austria. Acta Derm Venereol. 2015 May;95(5):565-71. [PubMed: 25366035]
12. Wolgemuth CW. Flagellar motility of the pathogenic spirochetes. Semin Cell Dev Biol. 2015 Oct;46:104-12. [PMC free article: PMC4994469] [PubMed: 26481969]
13. Vig DK, Wolgemuth CW. Spatiotemporal evolution of erythema migrans, the hallmark rash of Lyme disease. Biophys J. 2014 Feb 04;106(3):763-8. [PMC free article: PMC3944903] [PubMed: 24507617]
14. Tee SI, Martínez-Escanamé M, Zuriel D, Fried I, Wolf I, Massone C, Cerroni L. Acrodermatitis chronica atrophicans with pseudolymphomatous infiltrates. Am J Dermatopathol. 2013 May;35(3):338-42. [PubMed: 23147352]
15. Buechner SA, Rufli T, Erb P. Acrodermatitis chronic atrophicans: a chronic T-cell-mediated immune reaction against Borrelia burgdorferi? Clinical, histologic, and immunohistochemical study of five cases. J Am Acad Dermatol. 1993 Mar;28(3):399-405. [PubMed: 8095272]
16. Parveen N, Leong JM. Identification of a candidate glycosaminoglycan-binding adhesin of the Lyme disease spirochete Borrelia burgdorferi. Mol Microbiol. 2000 Mar;35(5):1220-34. [PubMed: 10712702]
17. Brissette CA, Bykowski T, Cooley AE, Bowman A, Stevenson B. Borrelia burgdorferi RevA antigen binds host fibronectin. Infect Immun. 2009 Jul;77(7):2802-12. [PMC free article: PMC2708576] [PubMed: 19398540]
18. Guo BP, Norris SJ, Rosenberg LC, Höök M. Adherence of Borrelia burgdorferi to the proteoglycan decorin. Infect Immun. 1995 Sep;63(9):3467-72. [PMC free article: PMC173478] [PubMed: 7642279]
19. de Koning J, Tazelaar DJ, Hoogkamp-Korstanje JA, Elema JD. Acrodermatitis chronica atrophicans: a light and electron microscopic study. J Cutan Pathol. 1995 Feb;22(1):23-32. [PubMed: 7751475]
20. Müller KE. Damage of collagen and elastic fibres by borrelia burgdorferi - known and new clinical and histopathological aspects. Open Neurol J. 2012;6:179-86. [PMC free article: PMC3751012] [PubMed: 23986790]
21. Kempf W, Kazakov DV, Hübscher E, Gugerli O, Gerbig AW, Schmid R, Palmedo G, Kutzner H. Cutaneous borreliosis associated with T cell-predominant infiltrates: a diagnostic challenge. J Am Acad Dermatol. 2015 Apr;72(4):683-9. [PubMed: 25617014]
22. Zambrano MC, Beklemisheva AA, Bryksin AV, Newman SA, Cabello FC. Borrelia burgdorferi binds to, invades, and colonizes native type I collagen lattices. Infect Immun. 2004 Jun;72(6):3138-46. [PMC free article: PMC415685] [PubMed: 15155615]
23. Yssel H, Shanafelt MC, Soderberg C, Schneider PV, Anzola J, Peltz G. Borrelia burgdorferi activates a T helper type 1-like T cell subset in Lyme arthritis. J Exp Med. 1991 Sep 01;174(3):593-601. [PMC free article: PMC2118948] [PubMed: 1831490]
24. Grab DJ, Kennedy R, Philipp MT. Borrelia burgdorferi possesses a collagenolytic activity. FEMS Microbiol Lett. 1996 Oct 15;144(1):39-45. [PubMed: 8870250]
25. Leslie TA, Levell NJ, Cutler SJ, Cann KJ, Smith ME, Wright DJ, Gilkes JJ, Robinson TW. Acrodermatitis chronica atrophicans: a case report and review of the literature. Br J Dermatol. 1994 Nov;131(5):687-93. [PubMed: 7999602]
26. Zajkowska J, Czupryna P, Pancewicz SA, Kondrusik M, Moniuszko A. Acrodermatitis chronica atrophicans. Lancet Infect Dis. 2011 Oct;11(10):800. [PubMed: 21958583]
27. Müller DE, Itin PH, Büchner SA, Rufli T. Acrodermatitis chronica atrophicans involving the face. Evidence for Borrelia burgdorferi infection confirmed by DNA amplification. Dermatology. 1994;189(4):430-1. [PubMed:

7873838]
28. Kristoferitsch W, Sluga E, Graf M, Partsch H, Neumann R, Stanek G, Budka H. Neuropathy associated with acrodermatitis chronica atrophicans. Clinical and morphological features. Ann N Y Acad Sci. 1988;539:35-45. [PubMed: 2847621]
29. Molka A, Jachiet M, Lepelletier C, de Masson A, Bagot M, Bouaziz JD. Asymetric red-blue hypertrophic hand and tenosynovitis due to acrodermatitis chronica atrophicans. Rheumatology (Oxford). 2019 Apr 01;58(4):655. [PubMed: 30239931]
30. Levy E, Morruzzi C, Barbarini A, Sordet C, Cribier B, Jaulhac B, Lipsker D. Clinical images: toe dactylitis revealing late Lyme borreliosis. Arthritis Rheum. 2012 Apr;64(4):1293. [PubMed: 22275216]
31. Kaufman LD, Gruber BL, Phillips ME, Benach JL. Late cutaneous Lyme disease: acrodermatitis chronica atrophicans. Am J Med. 1989 Jun;86(6 Pt 2):828-30. [PubMed: 2729343]
32. Steere AC, Strle F, Wormser GP, Hu LT, Branda JA, Hovius JW, Li X, Mead PS. Lyme borreliosis. Nat Rev Dis Primers. 2016 Dec 15;2:16090. [PMC free article: PMC5539539] [PubMed: 27976670]
33. Ljøstad U, Mygland Å. Chronic Lyme; diagnostic and therapeutic challenges. Acta Neurol Scand Suppl. 2013;(196):38-47. [PubMed: 23190290]
34. Flisiak R, Pancewicz S., Polish Society of Epidemiology and Infectious Diseases. [Diagnostics and treatment of Lyme borreliosis. Recommendations of Polish Society of Epidemiology and Infectious Diseases]. Przegl Epidemiol. 2008;62(1):193-9. [PubMed: 18536243]
35. Pancewicz SA, Garlicki AM, Moniuszko-Malinowska A, Zajkowska J, Kondrusik M, Grygorczuk S, Czupryna P, Dunaj J., Polish Society of Epidemiology and Infectious Diseases. Diagnosis and treatment of tick-borne diseases recommendations of the Polish Society of Epidemiology and Infectious Diseases. Przegl Epidemiol. 2015;69(2):309-16, 421-8. [PubMed: 26233093]
36. Asbrink E, Brehmer-Andersson E, Hovmark A. Acrodermatitis chronica atrophicans--a spirochetosis. Clinical and histopathological picture based on 32 patients; course and relationship to erythema chronicum migrans Afzelius. Am J Dermatopathol. 1986 Jun;8(3):209-19. [PubMed: 3728879]
37. Leverkus M, Finner AM, Pokrywka A, Franke I, Gollnick H. Metastatic squamous cell carcinoma of the ankle in long-standing untreated acrodermatitis chronica atrophicans. Dermatology. 2008;217(3):215-8. [PubMed: 18607109]
38. Bhate C, Schwartz RA. Lyme disease: Part II. Management and prevention. J Am Acad Dermatol. 2011 Apr;64(4):639-53; quiz 654, 653. [PubMed: 21414494]

Bookshelf ID: NBK563289 PMID: 33085436