LYME DISEASE, ATYPICAL SKIN MANIFESTATIONS

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SUMMARY

Lyme borreliosis is a multisystemic infection associated with a variety of clinical manifestations. Rather often it causes largely incomplete, hidden clinical findings or quite atypical variants. In the present paper less common skin variants of Lyme borreliosis are reviewed including localized alopecia at the site of erythema migrans, urticaria, erythematous papules, nodular panniculitis (Pfeifer-Weber-Christian), scleroatrophic skin conditions, Raynaud's syndrome, benign lymphocytic infiltrate of Jessner-Kanoff, cutaneous B-cell lymphoma, sarcoidosis, granulomatous thrombophlebitis, generalized exanthema, granuloma annulare, pityriasis rosea and purpura. Different species of *Borrelia burgdorferi* have been associated with different clinical manifestations. This may explain the rarity of some clinical variants. The agent of Lyme disease may be responsible for some cases, but further observations are necessary to differentiate atypical Lyme variants and casual associations.

KEY WORDS

Lyme borreliosis, atypical manifestations, Borrelia burgdorferi

INTRODUCTION

Lyme borreliosis is a multisystem infectious disease capable of producing a wide variety of clinical pathologic conditions. Complications of this infection can involve many organ systems, especially skin, joints, nervous system, eyes and heart. These manifestations may be acute, or evolve slowly over months or years. *Borrelia burgdorferi (Bb)* infection rather often causes olygosymptomatic manifestations or quite atypical variants. Diagnostic confirmation of Lyme disease may be difficult, because isolation of *Bb* is usually problematic. Therefore numerous clinical variants have been associated with Lyme disease on the basis of a positive tick bite history, stay in an endemic area, positive serologic results or response to antibiotic therapy. It must also be considered that in endemic areas the presence of an incriminating parameter e.g. seropositivity may lead to overdiagnosis.

In the present paper less common skin variants of Lyme borreliosis are reported.

ATYPICAL VARIANTS

Skin manifestations and histopathological findings depend on the stage of infection and vary from local inflammatory infiltrates to chronic atrophic skin diseases.

Erythema migrans (EM) is the dermatological hallmark of early Lyme borreliosis. There is a considerable variation in the appearance of EM. Particularly its central portion may show equal or greater erythema than the periphery, blue discoloration, purpura, induration, necrosis or ulceration (1,2,3). A low rate (8%) of patients with EM may have a lesion with vesicles (4). Lesions may also have different shapes or textures (1,2). Localized alopecia at the site of EM is also reported (5). Scaling has been occasionally observed on some lesions (1). Recently cases of Lyme borreliosis with erythematous papules or irregular erythema, accompanied by mild burning and itching were observed in patients in whom EM was absent (6). Besides cases of Lyme disease disclosed as urticaria (7) and also cases of urticarial vasculitis (8) were reported.

Involvement of subcutaneous tissue has been observed only very rarely. Hassler et al. (9) reported two patients suffering from nodular panniculitis (Pfeifer-Weber-Christian) with the evidence that the disease was caused by *Bb*. In fact in one of the cases *Bb* was repeatedly isolated from skin and subcutaneous tissue biopsies. A septal panniculitis (10) as a manifestation of Lyme disease was observed in a 22-year-old woman who presented fever, chills, photophobia, and headache, followed by a centrally clearing erythematous skin eruption, migratory polyarthralgias, conjunctivitis, and subsequently, tender, nodular skin lesions. Antibodies to *Bb* were present and skin biopsy revealed an acute septal panniculitis.

Many scleroatrophic skin conditions have been reported as possible late manifestations of Lyme disease. These include: lichen sclerosus et atrophicus (11,12) morphea (11,12,13,14,15,16,17), linear scleroderma (14), disseminated localized scleroderma (18), generalized scleroderma (19), morphea profunda (20), atrophodermia Pasini-Pierini (21), Shulman syndrome (or eosinophilic fasciitis) (22,23), progressive facial hemiatrophy of Parry-Romberg (24), erythema chronicum migrans et atrophicans (25) and porphyria cutanea tarda with sclerodermic alterations (26). Clinical, immunological and microbiological data seem to indicate a clear relationship between infection with *Bb* and scleroatrophic lesions, however many other published studies do not support these findings and have cast doubt on an etiological role for this spirochete in these diseases (27,28,29,30,31,32).

Kristof et al. (33) suggested the association between Lyme borreliosis and Raynaud's syndrome.

The hypothesis of a borrelian etiology has been suggested in the benign lymphocytic infiltrate of Jessner and Kanoff (22,34) and later in one case it has been possible to provide evidence of *Bb* by polymerase chain reaction (35). Cutaneous B cell lymphoma may also be associated with Bb infection. The occurrence of acrodermatitis chronica atrophicans and malignant lymphomas in the same patient was frequently reported in literature before *Bb* was recognized. Garbe et al. (36) presented four patients with low-grade malignant B cell lymphoma of the skin in association with chronic *Bb* infection. Plaque-shaped or nodular erythematous lesions with ill-defined borders were observed. Clinical progression was slow, up to 7 to 15 years. Extracutaneous involvement was found in only one case. In three cases no clinical signs of *Bb* were found; in one patient acrodermatitis chronica atrophicans was present.

Hua et al (37) suggested that *Bb* infection may be a cause of sarcoidosis. They measured antibodies to *Bb* in 33 patients with sarcoidosis confirmed clinically and histopathologically. The results showed that 82 % of the patients were positive for anti-Borrelia antibodies. Besides *Bb* was isolated from a patient's blood. The antibody titers and serum angiotensin converting enzyme rapidly decreased to nearly normal levels after antibiotic treatment. According to these findings they considered that *Bb* may be a cause of sarcoidosis and this last may be a specific type of Lyme disease.

A granulomatous thrombophlebitis in Lyme borreliosis has been reported (38). A patient with Lyme disease developed a thrombophlebitis saltans. Histopathologically there was a granulomatous perivasculitis with deposits of IgG, IgA, IgM, C3 and C4 in the vessels. Antibody titers against *Bb* were elevated, but no anti-cardiolipin antibodies were found.

As *Bb* is capable of eliciting numerous clinical manifestations based on serological criteria also granuloma annulare (39) and pityriasis rosea (40) were reported as manifestations of Lyme borreliosis.

Prinz et al. (41) observed another possible clinical manifestation characterized by a generalized exanthema, acute hepatitis with porphyrinuria and eosinophilia.

Purpura was described as a skin manifestation in Lyme borreliosis. Thrombocytopenic purpura (42) caused by *Bb* was suspected in an old woman with a platelet count of 14.000/microliter. Some years later Acrodermatitis chronica atrophicans appeared

and the high IgG antibody titre against Borrelia suggested a causal relationship with the previous thrombocytopenic purpura.

Schonlein-Henoch purpura seems to be also a possible manifestation in Bb infection (43, 44).

CONCLUSIONS

The Borrelia etiology of the above mentioned skin manifestations may often be only suspected and, owing to the paucity of these observations, it is still under discussion whether they are casually associated pathologies or atypical variants of Lyme borreliosis.

Recently three separate genospecies have been identified: *Borrelia burgdorferi sensu stricto*, *Borrelia garini* and *Borrelia afzelii* VS461 (45). Different strains of *Bb* have been associated with different clinical manifestations. Therefore it is possible that infection with a certain strains of *Bb* will lead to the development of a distinct skin lesion, which fact may explain the rarity of some clinical variants.

At present it seems premature to enlarge the spectrum of Lyme borreliosis skin manifestations in an exaggerated fashion. The agent of Lyme disease may be responsible for some cases, but to differentiate atypical Lyme variants and casual associations further observations with diagnostic proofs of *Bb* in the affected tissues are necessary.

REFERENCES

1. Berger BW. Dermatologic manifestations of Lyme disease. Rev Infect Dis 1989; 11 (Suppl 6): S1475-81.

2. Åsbrink E, Olsson I. Clinical manifestations of erythema chronicum migrans Afzelius in 161 patients: a comparison with Lyme disease. Acta Derm Venereol (Stockh) 1985; 65: 43-52.

3. Gross GP, Cooper PH, Nolan C. Erythema chronicum migrans with purpura and polymorphonuclear infiltrates. Arch Dermatol 1979; 115: 873-4.

4. Goldberg NS, Forseter G, Nadelman RB, Schwartz I, Jorde U, McKenna D, Holmgren D, Bittker S, Montecalvo M, Wormser GP, Vesicular erythema migrans. Arch Dermatol 1992; 128: 1495-8.

5. Spach DH, Shimada JK, Paauw DS. Localized alopecia at the site of erythema migrans . J Am Acad Dermatol 1992; 27: 1023-4.

6. Yi-Shu W, Wei-Fen Z, Fang-Po F, Bao-Zhen W, Yuan-Jin Z. Atypical cutaneous lesions of Lyme disease. Clin Exper Dermatol 1993; 18: 434-6.

7. Alemanni M, Taillandier J, Manigand G. Maladie de Lyme revelée par une urticaire. Presse Med 1987; 16: 1653.

8. Olson JC, Esterly NB. Urticarial vasculitis and Lyme disease. J Am Acad Dermatol 1990; 22: 1114-1116.

9. Hassler D, Zorn J, Zoller L, Neuss M, Weyand C, Goronzy J, Born IA, Preac-Mursic V. Nodulare Pannikulitis: eine Verlaufsform der Lyme-Borreliose? Hautarzt 1992; 43: 134-8.

10. Kramer N, Rickert RR, Brodkin RH, Rosenstein ED. Septal panniculitis as a manifestation of Lyme disease. Am J Med 1986; 81: 149-52.

11. Aberer E, Stanek G. Histological evidence for spirochetal origin of morphea and lichen sclerosus et atrophicans. Am J Dermopathol 1987; 9: 374-379.

12. Ross SA, Sanchez JL, Taboas JO. Spirochetal forms in the dermal lesions of morphea and lichen sclerosus et atrophicus. Am J Dermatopathol 1990; 12: 357-362.

13. Weber K, Preac-Mursic V, Reimers CD. Spirochetes isolated from two patients with morphea. Infection 1988; 16: 29-30.

14. Aberer E, Neumann R, Stanek G. Is localized scleroderma a Borrelia infection? Lancet 1985; 11: 278.

15. Aberer E, Klade H, Stanek G, Gebhart W. Borrelia burgdorferi and different types of morphea. Dermatologica 1991; 182: 145-154.

16. Ramelet AA. Association of acrodermatitis chronica atrophicans and morphea. Dermatologica 1987; 175: 253-256.

17. Rufli T, Lehner S, Aeschlimann A, Chamot E, Gigon F. Jeanneret JP. Zum erweiterten Spektrum zeckenübertragener Spirochätosen. Hautarzt 1986; 37: 597-602.

18. Maleville J, Baranton G, Klene C, Galand M, Sauciaume C. Hajjer M. Fontan I, Taieb A. Sclerodermie en plaque multiples avec seropositive conversion pour Borrelia burgdorferi. Presse Méd 1987; 36: 1808.

19. Trevisan G, Marinoni S, Briscik E, Magaton Rizzi G. Severe generalized scleroatrophoderma: manifestation of Lyme disease? In Dermatology in Europe. Ed Panconesi, Backwell Scientific Publications, Oxford, 1991; 693-4.

20. Buchner SA, Rufli T. Morphea profunda. Hautarzt 1990; 3: 155-157.

21. Hoffmann H, Martin C, Preac-Mursic V. Atrophodermia Pasini et Pierini. Seronegative Borrelia burgdorferi infection. Abstr IVth Int Conf on Lyme Borreliosis, Stockholm, 1990: 89.

22. Sepp N, Schmutzhard E, Fritsch P. Shulman syndrome associated with Borrelia burgdorferi and complicated by carpal tunnel syndrome. J Am Acad Dermatol 1988; 18: 1361-1362.

23. Stanek G, Konrad K, Jung M, Ehringer H. Shulman Syndrome, a scleroderma subtype caused by Borrelia burgdorferi? Lancet 1987; i, 1490.

24. Abele DC, Anders KH. The many faces and phases of borreliosis II. J Am Acad Dermatol 1990; 23: 401-410.

25. Trevisan G, Agolzer A, Grizzo A. Erythema chronicum migrans et atrophicans of the breast in a baby girl. Eur J Pediat Dermatol 1992; 2: 25-18.

26. Stadler R, Detmar M, Orfanos CE. Akute Porphyria Sclerodermiformis und erhöhter Borrelientiter. In: Gollnick H, Stadler R. eds. Dia-Klinik: Fallvorstellungen anlässlich des 17. Weltkongresses fur Dermatologie Berlin (West), 24, bis 29, Mai 1987. Stuttgart-New York: Schattauer, 1987; 92-95.

27. Hoesly JM, Mertz LE, Winkelmann RK. Localized Scleroderma (morphea) and antibody to Borrelia burgdorferi. J Am Acad Dermatol 1987; 17: 455-458.

28. Hansen K, Serup J, Hoybye S. Antibodies to Borrelia burgdorferi and localized scleroderma. Lancet 1987; i: 682.

29. Tuffanelli DL, Tuffanelli DR, Hoke A. False positive Lyme antibody test in morphea. J Am Acad Dermatol 1993; 1: 112-113.

30. Lecerf V, Bagot M, Revus J. Touraine R, Dournon E. Borrelia burgdorferi and localized scleroderma. Arch Dermatol 1989; 125: 297.

31. Raguin G, Boisnic S, Souteyrand P, Baranton G, Piette JC, Godeau P, Francès C. No evidence for a spirochetal origin of localized scleroderma. Br J Dermatol 1992; 127; 218-220.

32. Vaillant L, Goudeau A. Localized scleroderma is not a Borrelia burgdorferi infection in France. Dermatology 1992; 184: 286.

33. Kristof V, Bozsik BP, Szirtes M. Simony J. Lyme borreliosis and Raynaud's syndrome. Lancet 1990; 975-6.

34. Abele DC, Kenya HA, Chandler FW. Benign lymphocytic infiltration (Jessner-Kanoff): another manifestation of borreliosis. J Am Acad Dermatol 1989; 21: 795-797.

35. Rabb DC, Lesher JL Jr, Chandler FW. Polymerase chain reaction confirmation of Borrelia burgdorferi in benign lymphocytic infiltrate of dermis. J Am Acad Dermatol 1992; 26: 267-268.

36. Garbe C, Stein H, Dienemann D, Orfanos CE. Borrelia burgdorferi-associated cutaneous B cell lymphoma: clinical and immunohistologic characterization of four cases. J Am Acad Dermatol 1991; 24: 584-90.

37. Hua B, Li OD, Wang FM. Ai CX. Luo WC. Borrelia burgdorferi infection may be the cause of sarcoidosis. Chin Med J 1992; 105: 560-563.

38. Lauer M, Stolze K, Hatz HJ, Helmke K, Loffler W. Granulomatose Thrombophlebitis bei Lyme-Borreliose. Fallvorstellung. Immun Infekt 1990; 18: 57-58.

39. Strle F, Preac-Mursic V, Ruzic E, et al. Isolation of Borrelia burgdorferi from a skin lesion in a patient with granuloma annulare. Infection 1991; 19: 351-352.

40. Kuske B, Schmidli J, Hunziker T. Antibodies against Borrelia burgdorferi in patients with pityriasis rosea. Dermatologica 1988; 177: 255.

41. Prinz A, Weiss P, Stanek G. Generalized exanthema, acute hepatitis with porphyrinuria and eosinophilia. Another clinical feature of Lyme disease? Zentrabl Bakteriol Mikrobiol Hyg 1987; 263: 389-91.

42. Schneider T, Lange R, Niederhut D. Thrombozytopenische Purpura durch Borrelia burgdorferi? Dtsch Med Wochenschr 1988; 113(26): 1061-3.

43. Balcarkova H, Konvickova E, Pejcoch M. Borelioza pod obrazem Schonlein-Henochovy purpury. Cesk Pediatr 1990; 45: 495.

44. Schlotfeldt D, Fahrenkrug H. Schoenlein-Henoch-Purpura bei Infection mit Borrelia burgdorferi. Immun Infekt 1988; 16: 15-7.

45. Baranton G, Postic D, Saint Girons I, Boerlin P, Piffaretti JC, Assous M, Grimont PA. Delineation of Borrelia burgdorferi sensu stricto. Borrelia garini sp. nov., and group VS 461 associated with Lyme borreliosis. Int J Syst Bacteriol 1992; 42: 378-83.

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