Dear Editors,

The characteristic primary lesion in Lyme borreliosis (LB) is erythema migrans (EM) which can be diagnosed clinically in the majority of cases [1]. However, different patterns have been described with various clinical, microbiological or serologic findings [2]. The predominant histologic picture is a superficial and deep perivascular and interstitial infiltrate composed mostly of lymphocytes, plasma cells and eosinophils [3].

Case 1

A 52-year-old Caucasian male presented with an asymptomatic, erythematous and livid-colored infiltrated erythema on the lateral aspect of the left lower leg, with a central homogenous scale measuring about 1 cm in diameter. An excoriation extended 4 cm downward on the leg. The patient had previously worked in the garden with potential contact to ticks. Within one month the lesion grew in size to 8 cm and was accompanied by small irregular protrusions (Figure 1a–c). The center of the lesion became livid, hemorrhagic, indurated, and shiny; its margins were erythematous. Clinically an unspecific arthropod reaction, malignant lymphoma, deep vasculitis, or unusual EM were suspected. The patient reported no pruritus, pain or general symptoms.

Histological investigation revealed a perivascular, perianexal and interstitial infiltrate of lymphocytes, macrophages, plasma cells, eosinophils and erythrocytes in the entire dermis, extending into the fatty tissue (Figure 2a). Connective tissue was destroyed in some areas (Figure 2b), and fat lobules were slightly widened. These unexpected findings presented a pattern that can also be seen in the inflammatory stage of circumscribed scleroderma. Fungal scrapings were negative. IgM antibodies to Borrelia (B.) burgdorferi were positive on ELISA (1.13 U/ml; positive > 1.09) and confirmed by immunoblot, showing positive OspC antibodies. The ELISA test for IgG was negative, but the IgG immunoblot was positive with reaction to early antigens of B. burgdorferi OspC, VlsE, and p18. PCR of the skin biopsy with OspA primers was negative. Although Borrelia DNA could not be shown by molecular investigation, serological examination indicated an acute B. burgdorferi infection. The patient received doxycycline 200 mg/d for 20 days. The skin lesion resolved completely during this period (Figure 1d, e).

Case 2

A 41-year-old male presented with a classical EM lesion, 25 cm in diameter, arising in the right popliteal fossa. Antibodies to B. burgdorferi IgM and IgG were negative. The patient was given doxycycline 200 mg for 20 days. Eight days after starting treatment the patient presented with tiny red papules in the resolving EM lesion in conjunction with severe arthralgia (Figure 3a). At this time B. burgdorferi IgM

---

**Figure 1** Livid erythematous plaque on the left leg of patient 1, with a central homogenous scale, on day 7 (a). Livid erythematous plaque with erythematous elevations, on day 14 (b). Livid erythematous plaque on day 30 (c). Livid plaque one week after starting antibiotic treatment (d). Minimal livid erythema three weeks after the start of antibiotic treatment (e).
antibodies were positive with 16.74 U/ml with a 23-kD band against OspC on the immunoblot. Treatment with doxycycline was continued. All the lesions resolved within two weeks and the patient reported improvement of arthralgia. Histological investigation of a papule showed a dense perivascular and interstitial inflammatory infiltrate with destruction of collagen fibers (Figure 3b). PCR of the skin biopsy specimen with OspA primers was negative.

**Discussion**

In the first case we observed a rapidly progressing skin lesion with a histological tissue reaction resembling the inflammatory stage of morphea. This lesion responded promptly to antibiotic treatment with doxycycline. Rapid peripheral growth of a skin lesion with an erythematous border was clinically indicative of EM. In contrast, in the second patient we observed pinhead papules in a resolving EM lesion, which revealed a reaction pattern histologically very similar to early morphea.

In the two patients reported here, an early lesion of LB was suspected clinically and proven serologically [2]. *Borrelia burgdorferi* PCR was negative. In EM the detection rate of *B. burgdorferi* in skin biopsies is positive by PCR in approximately 50 % [4], the patients’ prompt response to antibiotic treatment confirmed the infectious origin of the lesions.

Our clinical and histological differential diagnosis was “lymphoplasmacytic plaques” with a band-like or mixed infiltrate and granulomas [5]. No palisaded granulomas and mucin deposition as seen in granuloma annulare nor sclerotic necrobiotic collagen areas like in necrobiosis lipoidica were seen in our case [6].

Collagen degeneration as seen in the two cases reported here has not been previously described in early LB. *B. burgdorferi* has a predilection for collagenous tissue, interacts with plasmin, fibronectin, and possesses endogenous collagenase that degrades extracellular matrices [7, 8]. Doxycycline therapy was effective in both patients.

Collagen alterations have been described in the late stage of LB, in acrodermatitis chronica atrophicans, with a dense inflammatory infiltrate leading to collagen atrophy or pseudosclerodermatous changes [9] sometimes similar to morphea and also lichen sclerosus. Edematous swelling of collagen bundles was observed in early morphea and destruction of collagen bundles by electron microscopy [10].

We summarize that a tissue reaction with perivascular, periadnexal and interstitial mononuclear infiltrates and foci of collagen degradation resembling the inflammatory stage of circumscribed scleroderma is a hitherto undetected reaction pattern in LB.

**Conflict of interest**

None.
Elisabeth Aberer, Bernd Leinweber, Werner Aberer
Department of Dermatology, Medical University of Graz, Graz, Austria

Correspondence to
Elisabeth Aberer, MD
Department of Dermatology and Venereology
Medical University of Graz
Auenbrugger Platz 8
8036 Graz, Austria
E-mail: eaberer@gmx.at

References
1 Strle F, Stanek G. Clinical manifestations and diagnosis of Lyme borreliosis. Curr Probl Dermatol 2009; 37: 51–110.
2 Hofmann H, Fingerle V, Hunfeld KP et al. Cutaneous Lyme borreliosis: Guideline of the German Dermatology Society. AWMF-Register Nr. 013/044. Available from: https://www.awmf.org/leitlinien/detail/ll/013-044.html [Last accessed September 17, 2020].
3 Berger B, Clemmensen OJ, Ackerman AB. Lyme disease is a spirochetosis: A review of the disease and evidence for its cause. Am J Dermatopathol 1983; 5: 111–24.
4 Cerar T, Ruzič-Sabljić E, Glinsek U et al. Comparison of PCR methods and culture for the detection of Borrelia spp. in patients with erythema migrans. Clin Microbiol Infect 2008; 14: 653–8.
5 Mitteldorf C, Palmedo G, Kutzner H et al. Diagnostic approach in lymphoplasmacytic plaque. J Eur Acad Dermatol Venereol 2015; 29: 2206–15.
6 Weidenthaler-Barth B. Clinical and histological spectrum of palisaded granulomatous dermatitides: Granuloma annulare, necrobiosis lipoidica, rheumatoid nodules, and necrobiotic xanthogranuloma. Hautarzt. 2017; 68: 536–41.
7 Coleman JL, Sellati TJ, Testa JE et al. Borrelia burgdorferi binds plasminogen, resulting in enhanced penetration of endothelial monolayers. Infect Immun 1995; 63: 2478–84.
8 Grab DJ, Kennedy R, Philipp MT. Borrelia burgdorferi possesses a collagenolytic activity. FEMS Microbiol Lett 1996; 144: 39–45.
9 Aberer E, Klade H, Hobisch G. A clinical, histological, and immunohistochemical comparison of acrodermatitis chronica atrophicans and morphea. Am J Dermatopathol 1991; 13: 334–41.
10 Badakov S. Elastoid transformation of the collagen fibrils in scleroderma skin. Folia Med (Plovdiv) 1992; 34: 17–21.