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Meningopolyneuritis Bannwarth with Focal Nodular Myositis.

A New Aspect in Lyme Borreliosis

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Summary. A patient with serologically confirmed infection by *Borrelia burgdorferi* presenting with painful paresis and atrophy of the proximal muscles of both upper extremities and bilateral facial paresis is described. Electromyography showed a neurogenic and myopathic pattern, and creatine kinase was raised. Muscle biopsy revealed the typical signs of focal myositis. Treatment with i.v. penicillin led to dramatic clinical and serological improvement. Muscle biopsy was repeated 2 months later; neurogenic changes were still present, but no inflammatory signs could be seen anymore. Thus, the presented case may be the first reported of meningopolyneuritis accompanied by focal nodular myositis, in the second stage of Lyme borreliosis.

Key words: Meningopolyneuritis Bannwarth with focal nodular myositis – Lyme borreliosis, electromyographic and bioptic findings

The neurologic aspects of Lyme disease include meningitis, encephalitis, motor and sensory radiculoneuritis, and myelitis [7, 9, 10, 13, 17, 28, 30]. These manifestations represent part of the second stage of this disease, which most recently has been termed Lyme borreliosis (LB) [3]. Besides these neurologic manifestations, a wide range of extraneural findings is reported [1, 22, 23, 24, 25, 28], involving the skin in the first stage, the heart additionally in the second stage, and, foremost, the joints in its third stage [28]. Ackermann et al. discussed a progressive *Borrelia*-encephalomyelitis [2], a course which seems to be similar to the tertiary Lyme disease of the central nervous system, described by Pachner and Steere [11]. Although the above-mentioned stages may either overlap or occur alone, the illness usually begins in summer with a characteristic skin lesion, erythema chronicum migrans (ECM), that may be accompanied by malaise and fatigue, fever, and myalgia (stage 1). Weeks to months later, some patients develop neurologic or cardiac abnormalities (stage 2), and weeks to years later the patients may develop arthritis (stage 3) [10, 11].

This infection has been found in at least 19 countries on three continents, i.e., Europe, North America, and Australia [15]. Several authors point to the similarity of meningopolyneuritis Bannwarth and Lyme disease. It is now generally accepted that the former represents the neurologic manifestations of LB [7, 12, 14]. Its etiologic agent was identified by Burgdorfer et al. as being a spirochete [5], subsequently named *Borrelia burgdorferi* [8], which is transmitted by bites from thicks or possibly other flying insects [5, 17, 18].

Myalgia, or migratory musculoskeletal pains are frequently observed in the first stage of disease [10, 13, 17]. To our knowledge, no histological or electrophysioligical examinations have been done in patients presenting with this aspect. On the other hand electromyography (EMG) and nerve conduction studies done in patients suffering from the second stage, e.g., radiculoneuritis, either showed a typical neurogenic pattern or were normal [10]. No myopathic changes are described with regard to the the second stage of this disease.

Abkürzungsverzeichnis: *B. burgdorferi* = *Borrelia burgdorferi*; C = Complement; CK = Creatine kinase; CSF = Cerebrospinal fluid; ECM = Erythema chronicum migrans; EMG = Electromyography; ESR = Erythrocyte sedimentation rate; HE = hematoxylin eosin; IgG = Immunoglobulin G; IgM = Immunoglobulin M; IIFT = Indirect immunofluorescence test; LB = Lyme borreliosis; NCV = Nerve conduction velocity; TPHA = Treponema pallidum hemagglutination test

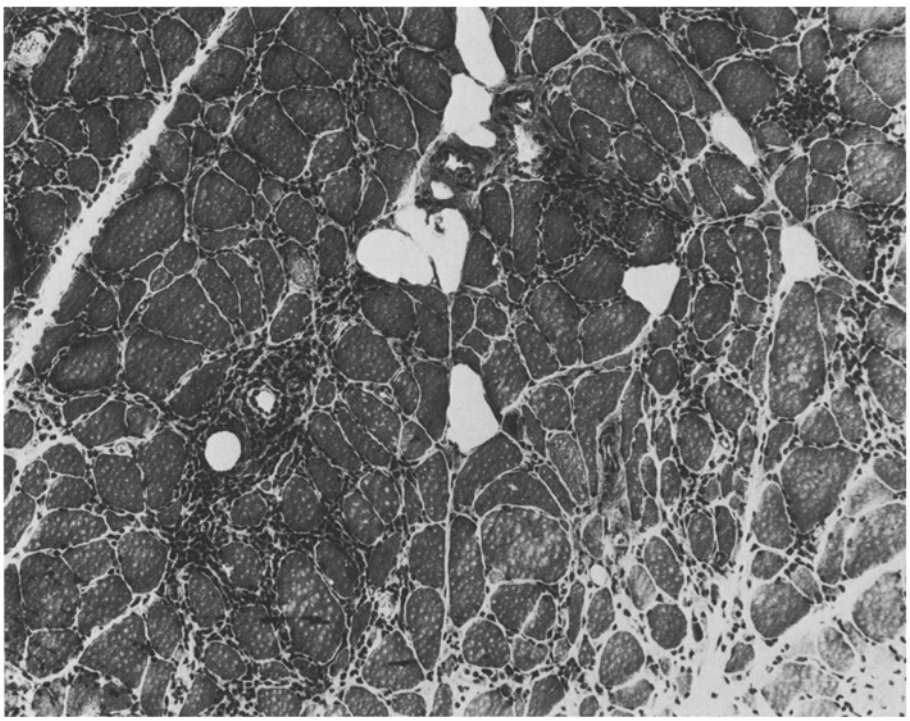

Fig. 1. Cryostat section of right biceps brachii muscle (HE stain, ×80); variation in muscle fiber size, few angulated fibers, interstitial fibrosis with numerous mononuclear infiltrations

We would like to report on a patient with the typical history and clinical signs and symptoms of meningopolyneuritis Bannwarth – the second stage of LB – in whom neurogenic changes in addition to myopathic changes were observed in EMG. Muscle biopsy revealed cellular infiltration, i.e., myositis, as well as signs of neuropathy.

Case report

A previously healthy 52-year-old woman was admitted with a 4-month history of pains and progressive weakness in the proximal muscles of both upper extremities and bilateral peripheral facial paresis. Four weeks prior to the onset of symptoms she was bitten by several horseflies on both shoulders, but she did not recall any thick bite. She had developed an itching erythema around the site of an insect bite measuring some 15 cm in diameter and subsiding without treatment within 2 weeks. No medical advice was sought for it.

On examination she revealed bilateral peripheral facial paresis, marked paresis and atrophy of both serratus anterior, deltoid, biceps and – to a lesser extent – triceps muscles. Mild dysesthesia was present in C5, C6 dermatomata bilaterally. The deep tendon reflexes of the upper extremities were not elicitable. The patient complained about tenderness of all muscles, mainly of the upper extremities, but also mildly of the lower extremities. There were no other motor or sensory symptoms, Babinski's phenomenon being plantar bilaterally.

Laboratory examination showed raised ESR (40 mm in the first hour), raised alpha-2-globulin in electrophoresis (13.3%), and elevated creatine kinase (CK) with 183 U/l. Rheumatoid factor (latex) was negative, as were antinuclear, antimitochondrial, and smooth muscle antibodies and cryoglobulins. Immunoelectrophoresis, C3 and C4 were normal. Red and white blood cell counts were normal and, in particular, no eosinophilia was detectable. All other routine laboratory parameters were within normal limits. The treponema pallidum hemagglutination test (TPHA) was nonreactive. Electrocardiogram and chest roentgenogram were normal. Cerebrospinal fluid analysis, including electrophoresis, did not reveal any abnormality. The indirect immunofluorescence test (IIFT) for antibodies against *B. burgdorferi* [20] showed elevated titers in the serum (IgM, 1:64, IgG, 1:256), suggestive of a recent infection with this organism. In the CSF, no antibodies could be detected. Electromyogram (EMG) or left biceps, right deltoid, and both orbiculares oris and oculi muscles showed positive sharp waves and fibrillations as signs of denervation. Motor unit patterns showed a mixture of two types of units. There were long-duration, high-amplitude units, which were often polyphasic and associated with a single oscillation pattern, but there were also polyphasic units of

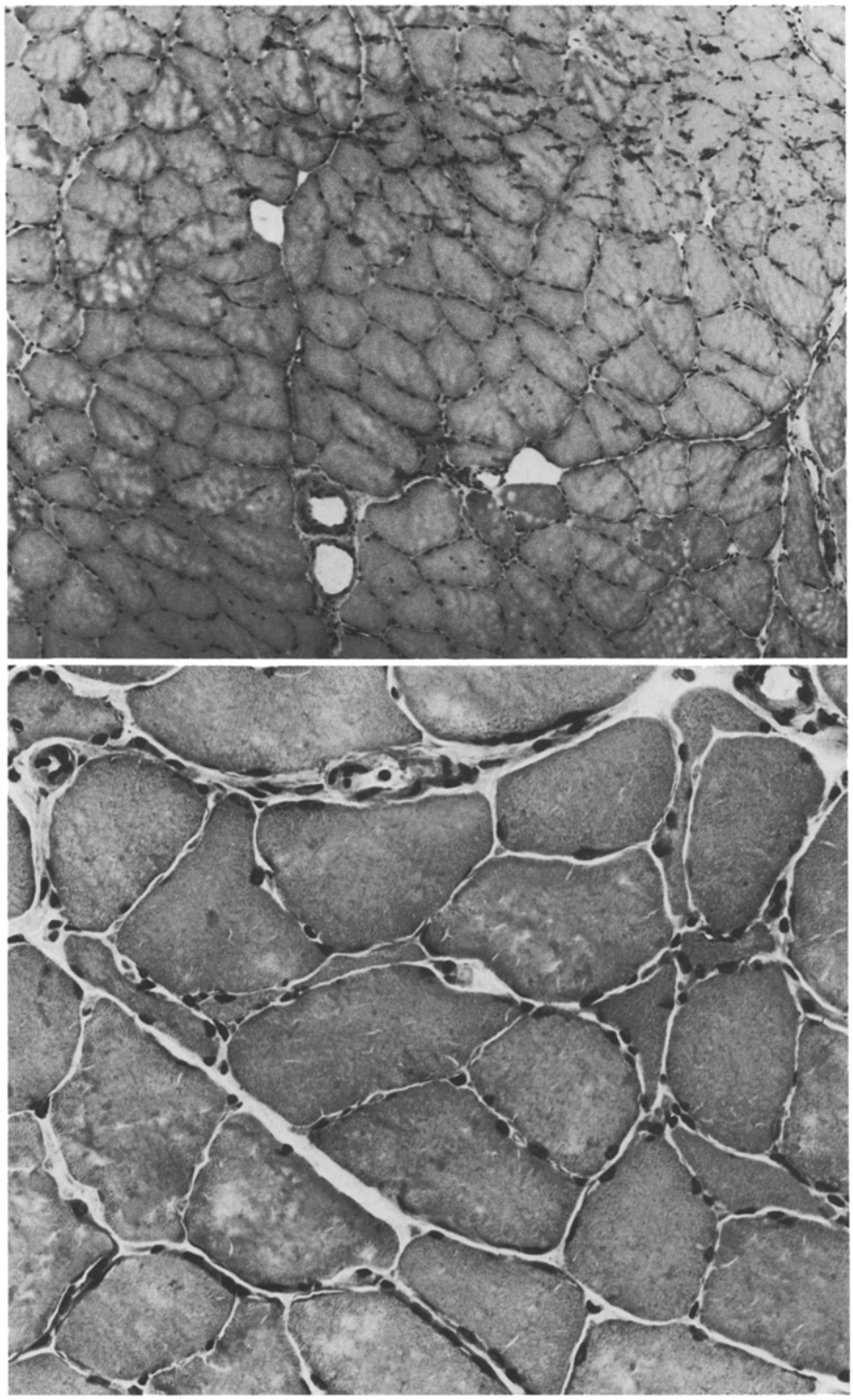

Fig. 2a, b. Cryostat section of left biceps brachii muscle (HE stain ×80, ×300). Two months after treatment, scattered small angulated fibers in small groups as sign of denervation; no inflammatory infiltration

very short duration and low amplitude. EMG of quadriceps muscles was normal on both sides. Motor nerve conduction velocity (NCV) in both ulnar and median nerves was slightly delayed (35 m/s). Terminal motor latency was normal (4.0 m/s – 5 cm – for both ulnar nerves and 3.8 m/s – 5 cm – for both median nerves). Sensory conduction velocities were within normal range.

Muscle biopsy of right biceps was performed. One specimen was processed for cryostat sections

and a routine battery of histochemical reactions [6]. A second specimen, removed in an isometric device, was fixed in 3% glutaraldehyde in 0.1 *M* cacodylate buffer for electron microscopy. By light microscopy the specimen showed moderate variation in the fiber diameter, fibers with central nuclei, and few small angular fibers. A mild endomysial fibrosis was noted with perivascular and interstitial mononuclear infiltration (Fig. 1). On histochemical staining, fiber-type grouping was present, but neither specific fiber atrophy nor predominance could be seen. Electron-microscopic examination did not add any further aspect.

Summarizing all these findings, a diagnosis of meningopolyneuritis Bannwarth accompanied by focal nodular myositis due to infection with *B. burgdorferi* had to be considered. Antibiotic therapy with intravenous penicillin G 5 Mill. unit q.i.d. was given for a period of 14 days [29]. Muscle tenderness subsided within 3 days and the patient regained a marked strength of all affected muscles within 6 weeks; bilateral facial paresis, however, improved only partially. The ESR (12 mm first hour), CK (38 U/l), and electrophoresis had returned to normal within 2 weeks. Twenty days after onset of treatment, the IIFT showed that antibodies against *B. burgdorferi* in the serum had declined, IgM being negative, IgG 1:64. Two months later the muscle biopsy was repeated from the left biceps muscle. Scattered small angulated fibers suggesting denervation were still present, but inflammatory signs could not be seen anymore (Fig. 2a and b).

Discussion

Several authors describe myalgia as a common feature of LB in its first stage [10, 13, 17]. So far it has not yet been shown that this myalgia represents a myositis. On the other hand, myositis has never been described as being part of the second stage of this disease, either. Pachner and Steere report on eight patients in whom EMG and NCV were done [10]. In six of them, EMG showed typical neuropathic abnormalities and in two EMG studies were normal. One showed marked slowing of nerve conduction velocity, five had near-normal NCV, and in two they were normal. None showed an EMG pattern suggestive of myopathy. No histological examination of muscle tissue was performed. Our patient's history, the clinical course with ECM, and signs of radiculitis and peripheral facial paresis, the significantly elevated IIFT titer for antibodies against *B. burgdorferi*, and the prompt clinical and serological response to treatment with i.v. penicillin, suggested the diagnosis of LB. Muscle tenderness and raised CK level were suggestive of myositis. EMG showed a mixture of neurogenic and myopathic pattern. Muscle biopsy specimens revealed the combination of inflammatory myopathy and neurogenic atrophy. These features were consistent with polyneuritis and nodular myositis associated with infection by *B. burgdorferi*. Myositis due to connective tissue disease or malignancies could be excluded. The disappearing of the cellular infiltration in the control biopsy, taken 6 weeks after antibiotic treatment, supported the consideration that *B. burgdorferi* was the causative agent.

Thus, the commonly observed clinical signs and symptoms of the second stage of Lyme borreliosis, radiculoneuritis and facial paresis, were confirmed by EMG as well as histologically. In addition, however, myopathic changes and myositis could be demonstrated, an observation which has never been reported in the second stage of LB.

Further prospective investigations appear to be necessary in order to determine whether the myalgia, frequently observed during the first stage of disease is equivalent to the myositis described in our report – since overlapping of symptoms does occur within the various stages of the disease [10]. Neither laboratory tests, such as CK, nor electromyographic or histological examinations have been carried out so far in those patients who complained about this myalgia.

Furthermore, the possibility has to be considered that the observed accompanying nodular myositis is, indeed, a rare but hitherto not-yet-described sign of the second stage of LB.

We propose that in all patients suffering from the second stage of LB and complaining about local muscle tenderness, CK should be examined and EMG done. A higher percentage of myositis might thereby be detected in these patients. Moreover, all patients with myositis or unclear etiology should be asked about thick bites or other insect bites and ECM in their history. Should the patient answer in the affirmative, examination of serum and, if possible, of CSF for antibodies against *B. burgdorferi* should be performed.

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References

1. Ackermann R, Boisten HP, Kabatzki J, Runne U, Krüger K, Hermann WP (1984) Serumantikörper gegen Ixodes-rici-

nus-Spirochäte bei Acrodermatitis chronica atrophicans (Herxheimer) Dtsch Med Wochenschr 109:6–10
2. Ackermann R, Gollmer E, Rehse-Küpper B (1985) Progressive Borrelien-Encephalitis. Dtsch Med Wochenschr 110:1039–1042
3. Barbour AG, Stanek G (1986) Lyme Borreliosis Newsletter 1/1:4
4. Benach JL, Bosler EM, Hanrahan JP, Coleman JL, Habicht GS, Bast TF, Cameron DH, Ziegler JL, Barbour AG, Burgdorfer W, Edelman R, Kaslow RA (1983) Spirochetes isolated from the blood of two patients with Lyme disease. N Engl J Med 308:740–742
5. Burgdorfer W, Barbour AG, Hayes SF, Benach JL, Grundwaldt E, Davis JP (1982) Lyme disease – a thick-borne spirochetosis? Science 216:1317–1319
6. Dubowitz V, Brooke MH (1973) Muscle biopsy: a modern approach. Saunders, London Philadelphia Toronto
7. Hindfeldt B, Jeppson PG, Nilsson B, Olsson JE, Ryberg B, Sörnäs R (1982) Clinical and cerebrospinal-fluid findings in lymphocytic meningo-radiculitis (Bannwarth's syndrome). Acta Neurol Scand 66:444–453
8. Johnson RC, Schmid GP, Hyde FW, Steigerwaldt AG, Brenner DJ (1984) *Borrelia burgdorferi sp.nov.:* etiologic agent of Lyme disease. Int J Syst Bact 34:496–497
9. Klenk W, Heitmann R, Ackermann R (1985) Rezidivierende Erythema-chronicum-migrans-Krankheit des Nervensystems: Querschnittsmyelitis als Rückfall einer Meningopolyneuritis Garin-Bujadoux-Bannwarth. Akt Neurol 12:20–23
10. Pachner AR, Steere AC (1985) The triad of neurologic manifestations of Lyme disease: meningitis, cranial neuritis and radiculoneuritis. Neurology 35:47–53
11. Pachner AR, Steere AC (1985) Tertiary Lyme disease – central nervous system manifestations of longstanding infection with *B. burgdorferi.* Second international symposium on Lyme disease and related disorders. Vienna, Austria, 17–19 September, Compendium of Abstracts, p 38
12. Pfister HW, Einhäupl K, Preac-Mursic V (1984) The spirochetal etiology of lymphocytic meningoradiculitis Bannwarth (Bannwarth's syndrome). J Neurol 231:141–144
13. Reik L, Steere AC, Bartenhagen NH, Shope RE, Malawista SE (1979) Neurologic abnormalities of Lyme disease. Medicine (Baltimore) 58:281–294
14. Ryberg B, Nilsson B, Burgdorfer W, Barbour AG (1983) Antibodies of Lyme disease spirochaete in European lymphocytic meningoradiculitis (Bannwarth's syndrome) Lancet II:519
15. Schmid GP (1985) The global distribution of Lyme disease. Rev Infect Dis 7:41–50
16. Schmutzhard E, Stanek G, Pohl P (1985) Polyneuritis cranialis associated with *B. burgdorferi.* J Neurol Neurosurg Psychiatry 48:1182–1184
17. Smolen JS, Luger TA, Neumann R, Kristoferitsch W, Stanek G, Graniger W (1984) Die Lyme-Krankheit – eine weitere durch Zecken übertragene Erkrankung in Österreich. Wien Klin Wochenschr 96:823–829
18. Stanek G (1984) Zecken als Überträger von Borrelien in Österreich. Hygiene Aktuell 1:1–3
19. Stanek G, Flamm H (1985) Epidemiologie von Borrelia-Infektionen in Österreich. Österr Ärztez 4:19–22
20. Stanek G, Hirschl A (1986) IFA, ELISA and Immunoblot zur Serodiagnostik von Berrelia-Infektion. Mitt Öst Ges Tropenmed Parasitol 8 (in press)
21. Stanek G, Kristoferitsch W, Hirschl A, Wewalka G (1985) Borrelia-Infektionen in Österreich 1984. Mitt Öst Ges Tropenmed Parasitol 7:55–62
22. Steere AC, Malawista SE, Hardin JA, Ruddy S, Askenase PE, Andiman WA (1977) Erythema chronicum migrans and Lyme arthritis. The enlarging clinical spectrum. Ann Int Med 86:685–689
23. Steere AC, Malawista SE, Snydman DR, Shope RE, Andiman WA, Ross MR, Steele FM (1977) Lyme-arthritis: an epidemic of oligo-articular arthritis in children and adults in three Connecticut communities. Arthritis Rheum 20:7–17
24. Steere AC, Batsford WP, Weinberg M, Alexander J, Berger HJ, Wolfson S, Malawista SE (1980) Lyme carditis: cardiac abnormalities of Lyme disease. Ann Intern Med 93:8–16
25. Steere AC, Bartenhagen NH, Craft JE, Hutchinson GJ, Newman JH, Rahn DW, Sigal LH, Spieler PN, Stenn KS, Malawista SE (1983) The early clinical manifestations of Lyme disease. Ann Intern Med 99:76–82
26. Steere AC, Grodzicki RL, Kornblatt AN, Craft JE, Barbour AG, Burgdorfer W, Schmid GP, Jonson E, Malawista SE (1983) The spirochetal etiology of Lyme disease. N Engl J Med 308:733–740
27. Steere AC, Pachner AR, Malawista SE (1983) Neurologic abnormalities as Lyme disease: successful treatment with high-dose intravenous penicillin. Ann Intern Med 99:767–772
28. Steere AC, Bartenhagen NH, Carft JE, Hutchinson GJ, Newmann JH, Pachner AR, Rahn DW, Sigal LH, Spieler PN, Taylor E, Malawista SE (1985) Clinical manifestations of Lyme disease. Second international symposium on Lyme disease and related disorders. Vienna, Austria, 17–19 September, Compendium of Abstracts, p 30
29. Steere AC, Green J, Hutchinson GJ, Rahn DW, Pachner AR, Schoen RT, Sigal LH, Taylor E, Malawista SE (1985) Treatment of Lyme disease and related disorders. Vienna, Austria, 17–19 September. Compendium of Abstracts, p 52
30. Uldry PA, Steck AJ, Regli F (1986) Manifestations neurologiques des infections à *Borrelia burgdorferi.* Schweiz Med Wochenschr 116/5:135–142

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