V. Preac-Mursic, K. Weber, H. W. Pfister, B. Wilske, B. Gross, A. Baumann, J. Prokop

Survival of Borrelia burgdorferi in Antibiotically Treated Patients with Lyme borreliosis

Summary: The persistence of *Borrelia burgdorferi* in patients treated with antibiotics is described. The diagnosis of Lyme disease is based on clinical symptoms, epidemiology and specific IgG and IgM antibody titers to *B. burgdorferi* in serum. Antibiotic therapy may abrogate the antibody response to the infection as shown in our patients. *B. burgdorferi* may persist as shown by positive culture in MKP-medium; patients may have subclinical or clinical disease without diagnostic antibody titers to *B. burgdorferi*. We conclude that early stage of the disease as well as chronic Lyme disease with persistence of *B. burgdorferi* after antibiotic therapy cannot be excluded when the serum is negative for antibodies against *B. burgdorferi*.

Zusammenfassung: *Persistenz der Borrelia burgdorferi bei negativer Serologie und Behandlung mit Antibiotika.* Es wird über die Persistenz von *Borrelia burgdorferi* bei sechs Patienten berichtet. Nach dem Zecken- bzw. Insektenstich und Erythema migrans konnte *B. burgdorferi* noch Wochen nach der Antibiotikatherapie nachgewiesen werden. Serologische Befunde waren außer bei einem Patienten negativ. Diese Ergebnisse bestätigen unsere früheren Beobachtungen und sprechen dafür, daß die Antibiotikabehandlung die Antikörperbildung gegen *B. burgdorferi* beeinflussen kann. Ferner zeigen diese Ergebnisse und Beobachtungen, daß nicht nur im Frühstadium der Lyme Borreliose, sondern auch in chronischen Stadien bzw. bei Persistenz des Erregers der Nachweis von Antikörpern negativ bleiben kann.

Introduction

Lyme borreliosis (LB), a multisystem disorder with skin, neurological, cardiac and arthritic symptoms caused by *Borrelia burgdorferi* and predominantly transmitted in Europe by infected ticks, *Ixodes ricinus*, can be diagnosed by the detection of antibodies to *B. burgdorferi* and isolation of the borreliae. The therapy of Lyme borreliosis, especially in the late chronic stage seems to be problematic. Antimicrobial therapy with penicillin G and tetracycline has been recommended. Various treatments especially with penicillin G have been proposed and practiced but none of them has been uniformly effective [1–6]. The last time the cephalosporins, cefotaxime and ceftriaxone have been used with success. We report here about survival of *B. burgdorferi* in patients with Lyme borreliosis after therapy with antibiotics.

Patients and Methods

Patients: Clinical data of our patients are listed in Table 1.
Serological tests: Antibodies to the *B. burgdorferi* in blood and cerebrospinal fluid (CSF) were determined by indirect immunofluorescence test (IFT) as described previously [7]. To avoid unspecific false positive reactions, the test samples were absorbed with *Treponema phagedenis*. Antibody titers ≥ 1:64 are regarded as significantly elevated, titers of 1:32 as borderline.
Bacteriological examinations: The samples of CSF and skin biopsies were examined for *B. burgdorferi* by darkfield microscopy and by culture in MKP-medium as previously described [8]. The cultures were incubated at 33 °C for 5 weeks and examined weekly by darkfield microscopy and subcultures.

Results

Spirochetes were isolated from the culture of CSF and skin biopsy specimens from six patients. The isolates showed typical protein pattern of *B. burgdorferi* in SDS-page. The results concerning the relapse of the disease and reinfection with *B. burgdorferi* after penicillin G and tetracycline therapy in the first case are presented in Figure 1.
Case 1: On July 7, 1985, a five-year-old boy had erythema migrans behind the left ear that faded after three days. A tick bite had never been seen by the parents. Beginning July 25, he had fever of up to 39.4 °C, was more tired than usually and had an erythema in the face, on his upper back and on the upper arms. On August 8 he was admitted to a community hospital with a temperature of 37.9 °C and meningism. CSF analysis showed a lymphocytic pleocytosis (480 cells/µl) and an increase in total protein (86 mg/dl); the electroencephalogram (EEG) was abnormal. Serum IgG and IgM antibody titers against *B. burgdorferi* were 1:64 and 1:128, respectively. Borrelia antibodies were not detected in CSF; culture for *B. burgdorferi* isolation from CSF was not done. The patient was treated with penicillin V orally in a dose of 100,000 U/kg daily for 14 days. On September 2 the CSF contained 26 cells/µl, the protein concentration was 40 mg/dl.
Beginning September 7, a paresis of the left facial nerve appeared that faded almost completely after two weeks. In the CSF, cells increased to 285/µl and protein concentration to 111mg/dl. He then received doxycycline orally in a

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Originalia

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Antibody titers against *B. burgdorferi* in serum were IgG 1:32, IgM 1:64 and in CSF negative (<1:2) The patient was free of complaints. However, when CSF was cultivated in MKP-medium, *B. burgdorferi* could be isolated.

Case 3: A 26-year-old patient was admitted to our hospital because of headache and intense radicular pain. The radicular pain was most severe at night and located bilaterally in the region of the dermatoma S1 and C7. She reported multiple bites by horseflies a few weeks prior to the admission. Neurological examination was completely normal. Lumbar puncture revealed a lymphocytic pleocytosis with 451 cells/µl. Both total protein (77 mg/dl) and the CSF/serum albumin ratio (10.7) were elevated. Oligoclonal IgG bands were not detected in the CSF. The diagnosis of Bannwarth's syndrome was made although antibodies to *B. burgdorferi* were not detected in serum or CSF. She received ceftriaxone, 2 g/day i.v. for 10 days. During antibiotic therapy, radicular pain and headache improved. Lumbar puncture for the determination of the CSF ceftriaxone concentration was made on the 10th day of therapy 3½ h after antibiotic infusion. The CSF ceftriaxone concentration as measured by HPLC was 1.45 mg/l. At follow-up examination, 7.5 months after antibiotic therapy, the patient reported recurrent episodes of radicular pain, headache, arthralgias and fever. Neurological examination was normal. Antibodies to *B. burgdorferi* were not detected. Repeated lumbar puncture revealed normal values for cell counts (1 cell/µl), total protein (24 mg/dl) and CSF/serum albumin ratio (1.9). Oligoclonal IgG bands were not detected. However, *B. burgdorferi* was isolated from the CSF after 6 weeks incubation in MKP-medium. Erythrocyte sedimentation rate (10/30) and leucocyte counts (7,100/mm³) were normal; C reactive protein, rheumatoid factor and antinuclear antibodies were negative. The patient was treated with cefotaxime 3 × 2 g/day i.v. for 14 days.

Case 4: This, 44-year-old man noticed an erythema migrans of 2 months' duration on the right thigh on June 1, 1988. He had no complaints. His IgG and IgM antibody titers against *B. burgdorferi* were 1:128 and < 1:16, respectively; *B. burgdorferi* could be isolated from skin biopsy taken from the border of the erythema migrans. Treatment carried out with phenoxymethyl-penicillin, 1 million U/3 times daily for 12 days. Erythema migrans disappeared within 2 weeks after the penicillin therapy. Three months later the IgG and IgM antibody titers against *B. burgdorferi* had normalized but *B. burgdorferi* was again isolated from skin biopsy adjacent to the scar of the first biopsy. There were no later manifestations in this otherwise healthy man who could be observed for 7 months. He then received ceftriaxone. Three months after retreatment with ceftriaxone (2 g daily/21 days) a second control culture from a skin biopsy performed adjacent of the first scars was negative.

Case 5: A 40-year-old man developed erythema migrans 24 days after a tick bite, which was slightly pruritic and located on the right arm. Besides a mild itching in the area of the lesion, fatigue and headache, the patient was asymptomatic. The patient received 1 × 10 million U penicilli for 10 days starting 5 weeks after the tick bite. The ery ma migrans faded about 12 days later. Serum IgG and I antibody titers against *B. burgdorferi* were negative, tures for borrelia isolation were not done. Suffering fi headache and fatigue 2 months after the disappearanc erythema migrans and 4 months after the tick bite, the tient went to see a doctor. At that time low titre (IgG 1 IgM < 1:32) antibodies to *B. burgdorferi* were detected. our recommendation a skin biopsy of the tick bite a showing no sign of erythema migrans, was taken. The p ence of *B. burgdorferi*, was demonstrated by culturing organisms in MKP-medium 2 months and 2 weeks a the therapy.

Case 6: On October 20, 1987, a 60 year-old-wor claimed to have had a slowly expanding asymptomatic eruption for at least 6 months. There was no history tick bite. She had been taking methylprednisolone 4 daily for asthma bronchiale for years. In September 1 she received doxycycline, 200 mg daily for 10 days from family physician because of a common cold. Physical amination on October 20, 1987, revealed an erythema grans 32 by 20 cm around both groins. She experienced easional attacks of palpitations and dizziness, but been suffering from angina pectoris for years. IgM IgG antibody titers against *B. burgdorferi* were negative *burgdorferi* could be isolated from skin biopsied from edge of the erythema migrans on October 20, 1987. E and immunoglobulins were normal. The patient refuse take another antibiotic.

Discussion

It is well known that erythema migrans, the most cha teristic sign of Lyme borreliosis, tends to disappear w out therapy. Nevertheless, antibiotic treatment with p cillin or tetracycline has been recommended in orde prevent subsequent clinical manifestations of Lyme bo liosis [1–6, 20].

Use of penicillin for treatment of Lyme borreliosis initiated in Europe on the basis of empiric evidence. Tl apy today is founded on experiences and studies conc ing the favorable effect of penicillin and tetracycline ducted by *Steere* et al. and *Weber* [1–4].

However, some patients later developed symptoms of disease despite antibiotic treatment [9–11]. Because these observations it has become questionable if a defi eradication of *B. burgdorferi* with antibiotics is possible this context some results of our *in vitro* and *in vivo* stu concerning the susceptibility of *B. burgdorferi* to antibic may be of interest [12, 13]. Testing 20 strains of *B. burg feri* the MIC_{90} for penicillin G was found to be 4 mg/l. corresponding result for tetracycline was 0.5 mg/l. Th results confirm findings of other researchers [14, 15].

To kill 50% of *B. burgdorferi* with 1.0 µg of antimicrob we required 48 h using penicillin G and 6–18 h using te cycline. These differences should be taken into consid

V. Preac-Mursic et al.: Lyme borreliosis – Persistence of Borrelia burgdor

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References

1. Steere, A. C., Malawista, S. E., Newman, J. H., Spieler P. N., Bartenhagen, N. H.: Antibiotic therapy in Lyme disease. Ann. Intern. Med. 93 (1980) 1–8.
2. Steere, A. C., Hutchinson, G. J., Rahn, D. W., Sigal, L. H., Craft, J. E., De Sanna, E. T., Malawista, S. E.: Treatment of the early manifestations of Lyme disease. Ann. Intern. Med. 99 (1983) 22–26.
3. Steere, A. C., Pachner, A. R., Malawista, S. E.: Neurological abnormalities of Lyme disease: successful treatment with high-dose intravenous penicillin. Ann. Intern. Med. 99 (1983) 767–772.
4. Weber, K.: Treatment of Lyme disease. Ann. Intern. Med. 94 (1981) 137.
5. Kristoferitsch, W., Baumhackl, U., Sluga, E., Stanek, G., Zeller, K.: High dose penicillin in meningopolyneuritis Garin-Bujadoux-Bannwarth. Zentralbl. Bakteriol. Mikrobiol. Hyg. A 263 (1986) 357–364.
6. Weber, K., Neubert, U., Thurmayr, R.: Antibiotic therapy in early erythema migrans disease and related disorders. Zentralbl. Bakteriol. Mikrobiol. Hyg. A 263 (1986) 377–388.
7. Wilske, B., Schierz, G., Preac-Mursic, V., Weber, K., Pfister, H. W., Einhäupl, K.: Serological diagnosis of erythema migrans disease and related disorders. Infection 12 (1984) 331–337.
8. Preac-Mursic, V., Wilske, B., Schierz, G.: European *Borrelia burgdorferi* isolated from humans and ticks – culture conditions and antibiotic susceptibility. Zentralbl. Bakteriol. Mikrobiol. Hyg. A 263 (1986) 112–118.
9. Diringer, M. N., Halperin, J. J., Dattwyler, R. J.: Lyme meningoencephalitis – report of a severe, penicillin resistant case. Arthritis Rheum. 30 (1987) 705–708.
10. Dattwyler, R. J., Halperin, J. J.: Failure of tetracycline therapy in early Lyme disease. Arthritis Rheum. 30 (1987) 448–450.
11. Pal, G. S., Baker, J. T., Wright, D. J. M.: Penicillin-resistant borrelia encephalitis responding to cefotaxime. Lancet i (1988) 50–51.
12. Preac-Mursic, V., Wilske, B., Schierz, G., Holoburger, M., Süß, E.: *In vitro* and *in vivo* susceptibility of *Borrelia burgdorferi*. Eur. J. Clin. Microbiol. 4 (1987) 424–426.
13. Preac-Mursic, V., Wilske, B., Schierz, G., Süß, E., Groß, B: parative antimicrobial activity of the new macrolides against *burgdorferi*. Eur. J. Clin. Microbiol. 8 (1989) 651–653.
14. Johnson, R. C., Kodner, C., Russel, M.: *In vitro* and *in vivo* s bility of the Lyme disease spirochete, *Borrelia burgdorferi*, antimicrobial agents. Antimicrob. Agents and Chemot (1987) 164–167.
15. Johnson S. E., Klein, G. C., Schmidt, G. P., Feeley, J. C.: Susc ty of Lyme disease spirochete to seven antimicrobial agents. Biol. Med. 57 (1984) 99–103.
16. Dattwyler, R. J., Halperin, J. J., Pass, H., Luft, B. J.: Ceftria effective therapy in refractory Lyme disease. J. Infect. I (1987) 1322–1325.
17. Dattwyler, R. J., Halperin, J. J., Volkman, D. J., Luft, B. J. ment of late lyme borreliosis – randomised comparison o axone and penicillin. Lancet ii (1988) 1191–1194.
18. Pfister, H. W., Preac-Mursic, V., Wilske, B., Einhäupl, K. M.: xime versus penicillin G for acute neurological manifesta Lyme borreliosis: A prospective randomised study. In press
19. Preac-Mursic, V., Wilske, B., Schierz, G., Pfister, H. W., Einh M.: Repeated isolation of spirochetes from the cerebrospina a patient with meningoradiculitis Bannwarth. Eur. J. Clin. M 3 (1984) 564–565.
20. Weber, K., Preac-Mursic, V., Neubert, U., Thurmayr, R., He Wilske, B., Schierz, G., Marget, W.: Antibiotic therapy of ear pean Lyme borreliosis and acrodermatitis chronica atro Ann. NY Acad. Sci. 539 (1988) 324–345.
21. Weber, K., Preac-Mursic, V., Wilske, B., Thurmayr, R., Neu Scherwitz, C.: Ceftriaxone and oral penicillin for therapy Lyme borreliosis. In press.
22. Tramont, E. C.: Persistence of *Treponema pallidum* following lin G therapy. JAMA 236 (1976) 2206–2207.
23. Greene, B. M., Miller, N. R., Bunnem, T. E.: Failure of pen benzathin in the treatment of neurosyphilis. Arch. Intern. M (1980) 1117–1118.

Erratum

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References

1. Steere, A. C., Malawista, S. E., Newman, J. H., Spieler P. N., Bartenhagen, N. H.: Antibiotic therapy in Lyme disease. Ann. Intern. Med. 93 (1980) 1–8.
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10. Dattwyler, R. J., Halperin, J. J.: Failure of tetracycline therapy in early Lyme disease. Arthritis Rheum. 30 (1987) 448–450.
11. Pal, G. S., Baker, J. T., Wright, D. J. M.: Penicillin-resistant borrelia encephalitis responding to cefotaxime. Lancet i (1988) 50–51.
12. Preac-Mursic, V., Wilske, B., Schierz, G., Hofaburger, M., Süß, E.: *In vitro* and *in vivo* susceptibility of *Borrelia burgdorferi*. Eur. J. Clin. Microbiol. 4 (1987) 424–426.
13. Preac-Mursic, V., Wilske, B., Schierz, G., Süß, E., Groß, B: parative antimicrobial activity of the new macrolides against *burgdorferi*. Eur. J. Clin. Microbiol. 8 (1989) 651–653.
14. Johnson, R. C., Kodner, C., Russel, M.: *In vitro* and *in vivo* s bility of the Lyme disease spirochete, *Borrelia burgdorferi*, antimicrobial agents. Antimicrob. Agents and Chemot (1987) 164–167.
15. Johnson S. E., Klein, G. C., Schmidt, G. P., Feeley, J. C.: Susc ty of Lyme disease spirochete to seven antimicrobial agents. Biol. Med. 57 (1984) 99–103.
16. Dattwyler, R. J., Halperin, J. J., Pass, H., Luft, B. J.: Ceftria effective therapy in refractory Lyme disease. J. Infect. I (1987) 1322–1325.
17. Dattwyler, R. J., Halperin, J. J., Volkman, D. J., Luft, B. J. ment of late lyme borreliosis – randomised comparison o axone and penicillin. Lancet ii (1988) 1191–1194.
18. Pfister, H. W., Preac-Mursic, V., Wilske, B., Einhäupl, K. M.: xime versus penicillin G for acute neurological manifesta Lyme borreliosis: A prospective randomised study. In press
19. Preac-Mursic, V., Wilske, B., Schierz, G., Pfister, H. W., Einh M.: Repeated isolation of spirochetes from the cerebrospina a patient with meningoradiculitis Bannwarth. Eur. J. Clin. M 3 (1984) 564–565.
20. Weber, K., Preac-Mursic, V., Neubert, U., Thurmayr, R., He Wilske, B., Schierz, G., Marget, W.: Antibiotic therapy of ear pean Lyme borreliosis and acrodermatitis chronica atro Ann. NY Acad. Sci. 539 (1988) 324–345.
21. Weber, K., Preac-Mursic, V., Wilske, B., Thurmayr, R., Neu Scherwitz, C.: Ceftriaxone and oral penicillin for therapy Lyme borreliosis. In press.
22. Tramont, E. C.: Persistence of *Treponema pallidum* following lin G therapy. JAMA 236 (1976) 2206–2207.
23. Greene, B. M., Miller, N. R., Bunnem, T. E.: Failure of pen benzathin in the treatment of neurosyphilis. Arch. Intern. M (1980) 1117–1118.

Erratum

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