

Short report

Myositis during *Borrelia burgdorferi* infection (Lyme disease)

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SUMMARY During the second stage of an illness caused by *Borrelia burgdorferi*, a young woman developed a myopathic syndrome characterised by severe muscular pains, incapacitating weakness of the proximal limb and the neck, as well as the bulbar muscles and elevated serum CK levels. Muscle biopsy revealed a non-inflammatory necrotising myopathy. *B burgdorferi* infection was confirmed by a considerable rise of specific IgG antibodies. A course of high dose steroids alleviated the myalgias, but paresis began to improve only after treatment with antibiotics. Our observations confirm that *B burgdorferi* can cause, through an undertermined mechanism, a necrotising myopathy, in addition to the wide spectrum of already known neurological complications.

The spirochete *Borrelia burgdorferi*¹ is known to cause a wide spectrum of clinical manifestations affecting multiple organ systems.² Neurological complications are frequent, though extremely variable (see review, Finkel 1988³). They occur in at least 10% of cases of Lyme disease,⁴⁻⁶ usually during the second stage between the dermatological (erythema chronicum migrans) and the rheumatological stages. The Garin-Bujadoux-Bannwarth syndrome, first described in Europe,⁷⁻¹⁰ is mainly characterised by neurological manifestations.¹¹

The following neurologic syndromes, occurring separately or in combination, have been recognised in the literature:³ cranial neuropathies, radiculopathies, demyelinating polyneuropathies, mononeuritis multiplex, aseptic meningitis, encephalitis, myelitis, pseudotumour cerebri, chorea, and fatigue. Muscular involvement is not a well documented feature of *B burgdorferi* infection, although muscular pains¹² and myocarditis¹³⁻¹⁵ are common during the course of the disease. Recently, an inflammatory necrotising myopathy was shown on muscle biopsy 8 years after a patient had experienced a tick-borne meningoradiculitis.

There were elevated cerebrospinal fluid levels of *B burgdorferi* antibodies.¹⁶

We describe a patient with muscular pain and weakness as the first systemic manifestations of *B burgdorferi* infection, non inflammatory necrosis on muscle biopsy and a dramatic response to antibiotic therapy.

Case report

History and clinical presentation

In July 1987, a 22 year old white female noticed an insect bite on her right leg and, during the next few days, an erythema at the same site. For six months after this she remained asymptomatic. In mid February 1988, she progressively developed malaise, slight fever, anorexia, nausea, headache and muscular pains. Because of increasing weakness and myalgias she was admitted to our department on 2 March 1988.

On neurological examination, there was a marked reduction of proximal muscle strength in upper and lower extremities. Weakness was also prominent in the neck flexors and the bulbar musculature, causing dysphagia and dysphonia. Voluntary movements, as well as passive mobilisation and muscle palpation, were very painful. Tendon reflexes were reduced, particularly in the lower extremities, and there was no left knee jerk. The idiomuscular responses appeared normal. No sensory deficit was detected, nor were there any signs of meningeal irritation or cortical dysfunction. There were a few cervical and axillary microadenopathies, but no other somatic abnormality was found.

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Paraclinical investigations

An electromyogram suggested myositis, and showed numerous, small, brief, polyphasic motor unit potentials, mainly in the proximal muscles, and some fibrillation potentials at rest. Motor and sensory nerve conduction velocities, F waves and somesthetic evoked potentials were normal, as was the EEG.

Laboratory investigations disclosed elevated serum CK levels on admission, which increased dramatically after 30 days (fig 1). These corresponded to the MB isoenzyme. LDH levels were also high (592 U) and myoglobin could be detected in the serum. ESR and several immunological tests were normal.

IgG antibodies against *B burgdorferi*, detected by the indirect fluorescent antibody (IFA) technique, were found at border-line levels on admission, but then progressively rose to reach a high titre of 1/1024 two months later (fig 1). IgM antibodies remained undetectable throughout the course of the disease. Serological tests were negative for the following infectious agents: Epstein Barr virus, rubeola, influenza, cytomegalus virus, mumps, brucella abortus, rickettsia, herpes, herpes zoster, HIV, toxoplasmosis, syphilis.

CSF investigations (cell count and composition; protein content and pattern on agarose gel electrophoresis) were normal, but immunological tests were not performed.

A biopsy of the left quadriceps muscle, performed 5 days after admission, showed discrete, parcellar necrosis of some muscle fibres with infiltration by some macrophages (fig 2a). There was almost no detectable inflammatory reaction. At the electron microscopic level, a variable intensity of localised sarcoplasmic necrosis was found in several fibres, while subsarcolemmal nuclei were spared. Myophages but no inflammatory cells were associated with the most intense necrotic areas (fig 2b). A slight proliferation of myoblasts could be seen (fig 2c), indicating a regenerative process. In a

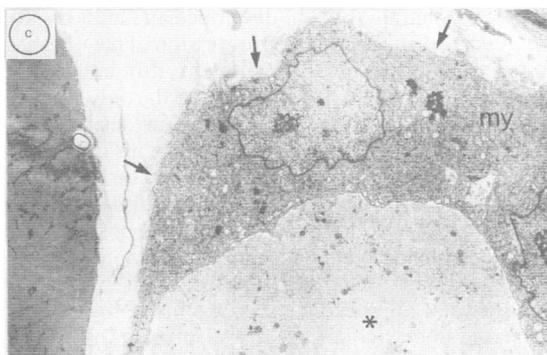
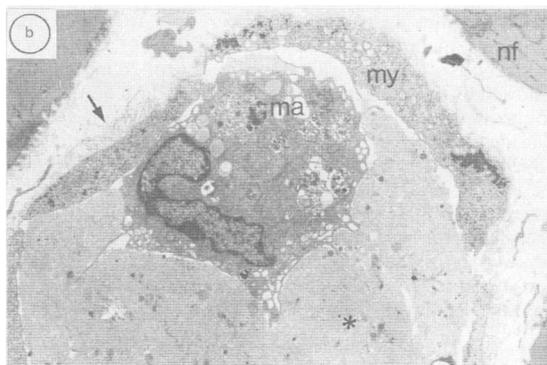
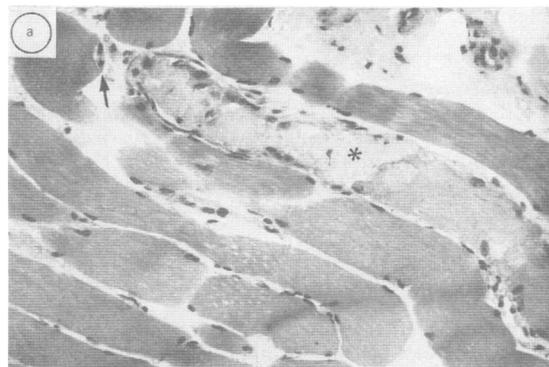
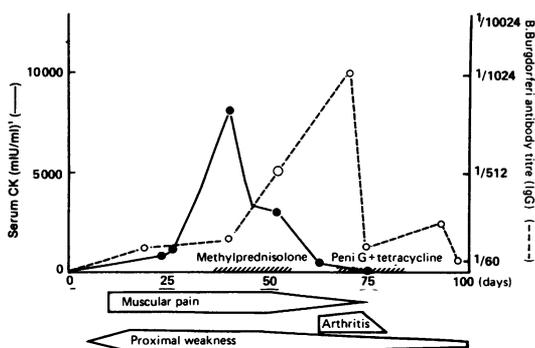


Fig 2a Partial necrosis of a muscle fibre (*). Some rounded macrophages and elongated myoblasts are seen beneath the sarcolemma. Activated satellite cells (arrow) can be seen in an adjacent normal fibre. H and E $\times 120$.

Fig 2b Necrotic muscle fibre (*) containing a rounded macrophage (ma) and portions of a myoblast (my) underneath the convoluted sarcolemma (arrow). Note adjacent, normal appearing fibres (nf). EM $\times 1800$.

Fig 2c Two large myoblasts (my) lying between the necrotic sarcoplasm (*) and the remaining sarcolemma (arrows). EM $\times 1500$.



Key: ●—● CK levels; ○—○ *B burgdorferi* IgG antibody titres.

Fig 1 Diagram illustrating the temporal evolution of neurological symptoms, serum CK levels and *B burgdorferi* IgG antibody titres from day 0 (beginning of systemic symptoms) to 100 days follow up. The timing of successive therapies is indicated.

single spot, a few leucocytes around a venous capillary were seen.

Clinical evolution and therapies

Before the rise of specific antibodies against *B burgdorferi*, a diagnosis of polymyositis was considered and the patient was treated for 10 days with oral methylprednisolone (1.5 mg/kg/day). The dose was progressively reduced over a 2 week period before being stopped. During this treatment period, the muscular pains decreased and finally disappeared. This was accompanied by a decrease in serum CK, but an increase in IgG antibodies against *B burgdorferi* (fig 1). Proximal and bulbar muscle weakness remained severe, but the patient improved and was then discharged.

One week later, she was readmitted because of an arthritic syndrome. The ankle, elbow and, to a lesser degree, knee joints were preferentially affected and swollen. The titre of IgG antibodies against *B burgdorferi* rose to 1/1024 and antibiotic therapy was started. Penicillin G was given intravenously for 8 days at a daily dosage of 20 million IU, followed by oral tetracycline 2 g/day for 10 days. Forty eight hours after starting the antibiotics, the arthralgias decreased considerably and her muscular strength began to improve slowly. The titre of anti-*B burgdorferi* antibodies fell below the cut-off level 5 days later (fig 1). Two weeks later, the patient was free from any articular complaint and the strength in the proximal limb and neck muscles was much improved. A slight dysphonia persisted. The patient's condition continued to improve after the antibiotic therapy, but it was another 4 weeks before she was totally asymptomatic.

Discussion

According to the clinical and serological data, there is little doubt that this patient developed an illness due to *B burgdorferi* infection. The progression of the disease, in three stages, is characteristic of this condition. Erythema chronicum migrans may be the only clinical manifestation in stage 1. This skin lesion was attributed to a bite from a flying insect, but ticks, flies and mosquitoes can also serve as vectors for the spirochete.¹⁷ The second stage of the disease manifested itself 7 months after the initial exposure with general influenza-type symptoms and a neurological syndrome. The latter was characterised by severe myalgias and appreciable weakness in the muscles of the neck, pharyngolaryngeal and proximal limb. It was accompanied by increased CK levels and EMG alterations, both compatible with the suspected diagnosis of (poly)myositis, which was confirmed by the muscle biopsy. As in a typical case of Lyme disease,¹⁸ stage 3 was rheumatological. In this case, it was remarkable that frank arthritis developed only 8 weeks after the start of stage 2.

The immunofluorescence assay, used to detect antibodies against *B burgdorferi* in our patient was clearly positive. We must point out, however, that the first serological test, performed 20 days after the appearance of the stage 2 symptoms, did not reach the cut-off dilution (1/256) considered to indicate a

positive result. A considerable rise in the antibody titre was seen only 1.5 months after the beginning of stage 2. Interestingly, *B burgdorferi* antibodies were shown using two different commercially available IFA kits, one manufactured by an American company (Zeus Scientific, Inc, Raritan, NJ) and using strain B31 of the spirochete, the other made in Germany (DMD GmbH, Gailingen) and based on a European strain. This suggests that both of these strains have a vast common antigenicity, although antigenic differences have been reported between European and North American isolates.¹⁹ Antibodies of the IgM class have not been seen in our patient, possibly because of the long delay between the exposure to *B burgdorferi* and the serological testing. On the other hand, it is a common experience that IgM antibodies are less frequently demonstrated than IgG antibodies.^{11 20 21} Unfortunately, immunodiagnostic tests were not performed on the CSF in our patient. There was, however, no clinical indication for central nervous system involvement which would have been most effectively established by demonstrating the production of *B burgdorferi*-specific antibodies in the spinal fluid.²² Moreover, no cell reaction and no oligoclonal bands on agarose gel electrophoresis, one or both of which are usually found in association with specific antibodies,^{11 16} were detected in the CSF.

Primary muscle involvement during *B burgdorferi* infection has so far been documented¹⁶ in only one other patient. Its prevalence might, however, be underestimated, since muscle pains/discomfort and fatigue are the most frequent clinical features in many patients with Lyme disease.² The histopathological lesion described here, that is, foci of segmental muscle fibre necrosis containing myophages and regenerating fibres, but no inflammatory cells, is considered to be a non-specific reaction to a variety of systemic diseases.^{23 24} The best known of these so-called necrobiotic myopathies²³ is Zenker's degeneration complicating severe infective diseases, such as typhoid fever. In this study, the necrotising myopathy is undoubtedly related to the *B burgdorferi* infection, since no other possible aetiology was detected. A non-specific Zenker-like process seems unlikely because of the absence of a severe systemic infectious state. *B burgdorferi* is thus probably responsible for the necrotising myopathy. Several pathogenetic mechanisms can be considered. A direct invasion of muscles, seen in Lyme myocarditis,¹⁴ could not be confirmed in this case. An immunological mechanism, such as the one thought to mediate *B burgdorferi* associated demyelinating neuropathies,⁵ is unlikely considering the complete absence of local and systemic inflammation. Nonetheless, in the only other published case of muscle involvement during *B burgdorferi* infection,¹⁶ biopsy showed an inflammatory necrotising

myopathy, which would have been compatible with the former pathogenesis. This patient had, in addition, a meningoradiculitis and his myopathy developed slowly over 8 years, contrasting with the acute progression in our case. Another possible mechanism would be a toxin synthesised by the spirochete. This hypothesis seems plausible because of the pathological features of the muscle lesion, but it remains to be proven.

The muscular symptoms of our patient rapidly improved after treatment with parenteral penicillin and oral tetracyclin, as reported elsewhere.^{24,25} A course of high dose steroids, which are known to help relieve some symptoms in Lyme disease,^{15,26} considerably reduced muscular pains and serum CK levels, but not weakness. Whether this was due to a direct steroid effect on muscle membranes or to interference with immunopathologic mechanisms is an open question.

J Schoenen is a senior research associate at the National Fund for Scientific Research, Belgium.

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Addendum: After submission of this manuscript, another published case of muscle involvement during *B burgdorferi* infection came to our attention. This was a patient with meningoradiculitis and focal nodular myositis. (Schmutzhorol E, Willeit J, Gerstenbrand F. Meningopolyneuritis Bannwarth with focal nodular myositis: A new aspect in Lyme borreliosis. *Klin Wochenschr* 1986;44:781–3.)