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CASE REPORT

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Isolated neuritis of the sciatic nerve in a case of Lyme disease

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Abstract Lyme disease is an infectious disease caused by the spirochete *Borrelia burgdorferi*. The course of the disease is divided into three stages, the second of which may include various types of peripheral nervous system disturbances. We report the case of a patient with persistent deficits caused by the prevalent involvement of the sciatic nerve, confirmed by electrophysiological and neuropathological findings. The most significant bioptic results were axonal degeneration and perivascular inflammation. Damage to a single peripheral nerve as the dominant clinical expression during the course of Lyme disease is an unusual finding that has been rarely described in the literature.

Key words Lyme disease • Peripheral neuropathy • Sciatic nerve • Nerve biopsy • Vasculitis

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Introduction

Lyme disease, an infectious disease caused by the spirochete *Borrelia burgdorferi,* is transmitted by a tick belonging to the genus *Ixodes* and by other hematophagous parasites. There are many neurological manifestations of Lyme disease that may affect both the central nervous system (CNS) and the peripheral nervous system (PNS), the latter of which include cranial mononeuritis and multineuritis, polyradiculoneuritis, diseases of the plexus, a syndrome similar to Guillain-Barré disease, neuropathies due to trapped nerves, and vasculitic mononeuritis. The mononeuritic forms are usually multiplex [1], and frequently affect not only the area close to the tick bite, but also many other districts. Only a few cases of isolated involvement of a peripheral nerve have been described in the literature [2, 3]. We report the case of a patient whose clinical, electrophysiological and neuropathological signs suggest the presence of prevalent vasculitic mononeuritis of the sciatic nerve.

Case report

A 72-year-old woman was admitted to the Insitute of Neurology at the end of October 1995 because of right foot paralysis and painful right leg paresthesias. Two months previously, the patient had noticed the appearance of a painful erythematous lesion on her right ankle following an insect bite, which remained for a few days and then disappeared without therapy. One month later, painful paresthesias appeared in the middle and distal third of the right leg, which were followed by distal hyposthenia after a period of three weeks. Upon admission, the patient presented an absence of dorsal flexion movement and marked impairment of right foot plantar flexion. In particular, neurological examination revealed hypotrophy of the anterolateral leg muscles: the muscle strength (scale 0-5) of the peroneal muscles, tibialis

anterior, extensor digitorum longus, extensor digitorum brevis and extensor hallucis proprius was 0/5; that of the musculus triceps surae and flexor digitorum brevis was 1/5. There were no knee or Achilles reflexes in the right leg; there was tactile, heat and pain anesthesia in the right foot; hypoesthesia extended laterally to the knee in a proximal direction, and medially to the distal third. No changes were found in the trophism, strength or sensitivity of the left leg, and the ROT were normally excitable. Abdominal reflexes were symmetrical; Babinski's sign was bilateral. Cognitive functions were normal; there were no clinical signs of meningitis; the cranial nerves were intact; there were no sphincter disturbances. The patient lived near a rural area, where the three known species of *Borrelia (B. burgdorferi stricto sensu, B. azeli* and *B. garinii*) are found.

Laboratory examinations

The following laboratory values were within the norm: thyroid and hepatic function indices, VDRL, hemachromocytometric examination, electrolytes, serum protein cataphoresis, ESR, CRP, TAS, R.A.-test, plasma immunoglobulins, circulating immune complexes, CEA and alpha-fetoprotein. Searches for HIV, anti-HBV and HCV antibodies, and for autoantibodies (ANA, anti-DNA, anti-ENA, ANCA) were negative. C3 and C4 complement fractions were also within the norm, with increased C1-inhibitor and decreased C3-activator.

Cerebral spinal fluid (CSF) examination showed: glycorrhachia and proteinorrhachia within the norm, pleocytosis (26 cells/mm^3, prevalently mononucleates), an increased Link index (0.85; normal range < 0.75) with oligoclonal bands at isoelectofocusing. The search for anti-*Borrelia* antibodies using enzyme-linked immunosorbent assay (ELISA) and western blotting was positive for serum (titre ≥1:256 of the IgG anti-*Borrelia burgdorferi stricto sensu*) but not for CSF. The virological investigations were negative.

Neurophysiological data

Electromyography (EMG) and electroneurography (ENG) – first performed on 19 October 1995 – revealed signs of right sciatic nerve neuropathy. EMG of the tibialis anterior, gastrocnemius, extensor digitorum brevis and tibialis posterior of the lower right limb revealed fibrillation potentials and positive sharp waves with a marked reduction in the recruitment of motor unit potentials during voluntary contraction. The external sciatic popliteal (ESP) and internal sciatic popliteal (ISP) nerves showed a marked reduction in motor conduction velocity (right ESP, 34.7 m/s in the "head of fibula-neck of foot" tract; right ISP, 36.4 m/s, normal range >43 m/s) and in the amplitude of the motor action potential (right ESP, 2.0 mV; right ISP, 2.0 mV, normal range >3 mV). These low motor potential values did not permit any evaluation of the F wave. There was no sensitive action potential in the right sural nerve. The ENG findings for the left ESP, left ISP, right and left median and ulnar nerves were within the norm. The bilateral EMG recording of the lumbar paraspinal muscles did not reveal any spontaneous pathological activity indicative of acute neurogenic suffering. Furthermore, the EMG data obtained from the quadriceps only showed signs of neurogenic suffering during the phase of stable reinnervation, and was therefore probably from an earlier date. On the basis of the clinical findings, we did not consider it necessary to make an EMG recording of the gluteal muscles or the muscles in the posterior compartment of the thigh.

A control EMG evaluation revealed greater signs of denervation, with a further reduction in motor conduction velocity (right ESP, 28.8 m/s in the "popliteal fossa-head of the fibula" tract, and 21.5 m/s in the "head of the fibula-neck of the foot" tract; left ISP, 25.3 m/s), as well as in the amplitude of the motor action potential (right ESP, 0.71 mV; right ISP, 0.21 mV) upon both proximal and distal stimulation. The ENG data showed signs of marked axonal damage to both the peroneal and tibial branches of the sciatic nerve.

Neuroradiological data

In order to exclude possible root compressions, the following investigations were carried out:

- Pelvic CT: no expansive processes or adenomegaly.
- L2-S1 computed tomography (CT) of the L2-S1 tract: severe osteophytic osteoarthrosis. In L4-L5, median and right medio-lateral disc projection, in the absence of any real disc protrusions. Vertebral channel of regular width.
- NMR (without contrast) of the dorsal and dorso-lumbar (D4-L3) regions: the morphology, size and signal of the medulla spinalis and conus medullaris were normal; free perimedullary fluid spaces. Absence of any signs of root swelling.

Neuropathological data

A right sural nerve biopsy was carried out on 7 December 1995. In the semi-thin sections, the eight examined nerve bundles showed a marked loss of myelinic fibres of all calibres, as well as degenerating fibres. There were consistent perivasal, peri- and epineural areas of inflammatory infiltrate (Fig. 1). No necrosis of the vascular walls was detected. Analysis of the individual teased fibres revealed signs of axonal degeneration in 60% of the fibres. Ultrastructural analysis revealed signs of severe axonal damage, a significant loss of amyelinic fibres and infiltrates in the vessels of the microcirculation. No spirochetes were detected.

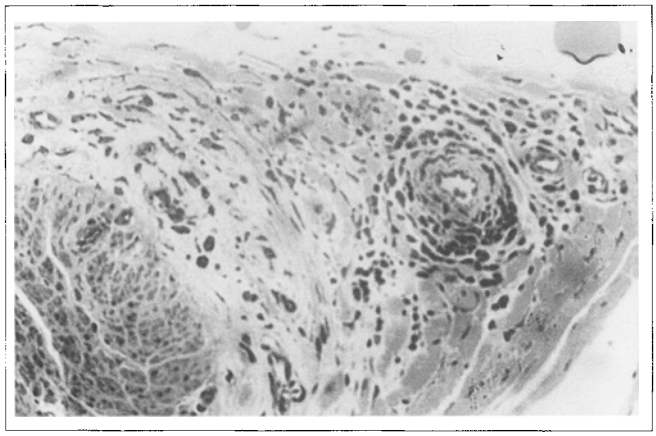

Fig. 1. Sural nerve biopsy. Marked perineural and epineural mononucleate cell infiltration. Semi-thin sections, toluedine blue, x250

Immunohistochemical analysis (cryostated sections of nerve and muscle) showed a marked response to the reaction for HLA-Dr in the epi-, peri- and endoneural sites. There were numerous T lymphocytes (CD3) in the areas of infiltrate and in the perivasal site of the nerve bundles; there were some T lymphocytes in the endomysium of the muscle. There were numerous T lymphocytes (CD4 and CD8) in the perivasal, peri- and epineural sites. A biopsy of the right musculus peroneus brevis revealed marked signs of denervation.

Therapy

Treatment with ceftriaxone was begun immediately (2 g twice daily i.v. and then 2 g/day i.v. for two weeks) without any clinical improvement in the neurological deficits, except for a partial remission of the painful paresthesias. However, there was a reduction in the CSF indices: from 26 to 5 cells/mm^3 and the Link index from 0.85 to 0.56 (within the norm).

Discussion

The course of Lyme disease can be divided into three stages. Stage 1 takes place during the first month and is characterised by chronic migrating erythema and associated manifestations. Stage 2 may show classic meningoradiculitis (Garin-Bujadoux-Bannwarth syndrome) [4] or other less specific neurological pictures, such as isolated acute or even remittent lymphocytic meningitis, encephalitis, an apparently idiopathic paralysis of the facial nerve, neuritis of other cranial nerves, Argyll-Robertson's sign, acute transverse myelitis, PNS involvement and myositis. In the cases described in Europe, the distribution of the painful radiculitis usually corresponds to the area of the tick bite [5]. During stage 3 (between three and five, or more months after the onset of the disease), chronic arthritis, acrodermatitis chronica atrophicans and various neurological syndromes (chronic neuropathies and chronic CNS involvement) may be observed.

PNS involvement during stage 2, widely described in the literature [6-9] and demonstrated by nerve biopsy findings [8, 10], may give rise to polyneuropathies or multiple mononeuritis. Recent papers have demonstrated a wide spectrum of manifestations involving the PNS, including diffuse neuropathies [5, 11] with paresthesias of the limbs as the predominant symptom [5], plexitis [3], a picture similar to Guillain-Barré syndrome [12] and neuropathies due to nerve entrapment [13].

The atypical forms of PNS involvement include electromyographically-confirmed isolated neuritis as documented in three case reports: one case of mononeuritis of the right suprascapular nerve and signs of denervation of the ipsolateral infraspinatus muscle [3]; one case of paralysis of the serratus anterior muscle due to a lesion of the long thoracic nerve [2]; and one case of the isolated involvement of the phrenic nerve [14]. Some other less detailed cases involving the nerves of the upper limbs have also been reported [7, 10, 15, 16].

The case described by us fulfils the following criteria [17] justifying a diagnosis of Lyme disease: possible exposure to a tick bite, given that the patient lived in an endemic area; erythema; subsequent asymptomatic lymphocytic meningeal reaction (with the intrathecal synthesis of IgG and oligoclonal bands) and concomitant painful sensorymotor neuritis; and immunological evidence of exposure to *Borrelia burgdorferi*.

The neurophysiological data and the clinical extension of the sensory deficiency to the knee suggest that the damage to the sciatic nerve was located proximally to the popliteal fossa; however, since this is not a focal but a multifocal lesion, it is not possible to define the true location of the lesion. The clinical finding of an absence of the right rotular reflex does not allow concomitant plexus or radicular involvement to be excluded (however, the EMG data support the absence of denervation in the paraspinal muscles, and the sensitivity of the saphenous territory has been spared), and plexopathy has been described as one of the manifestations of the second stage of Lyme disease [18]. Furthermore, a more widespread involvement is to be expected in the case of meningoradiculoneuritis (the CSF examination revealed a picture of lymphocytic meningeal reaction). Another hypothesis is that the rotular reflex may have been previously absent.

The biopsy of our patient showed histopathological characteristics of significant inflammatory lesions without necrosis of the vessel walls, and axonal degeneration. Despite the absence of spirochetes, the degree of fibre loss and the axonal degeneration can be attributed to vasculitic

alterations to the perineural and epineural vasa nervorum. Together with the predominantly mononeuritic clinical picture, these aspects suggest an angiopathic etiology of nerve damage, in agreement with other authors [19, 20]. The pathogenetic mechanism responsible for the peripheral neuropathies observed during the course of Lyme disease is still unknown. The presence of perivascular cellular infiltrates suggests that in our case, as in those reported by others [7, 21], the neuropathy may have an immunomediated inflammatory basis, with associated angiopathy around the perineural, epineural and endoneural vessels.

The neuropathological aspects described above confirm the observations in the literature [8, 11, 19] concerning the absence of vessel wall destructive lesions in the nerve biopsies of Lyme disease patients. This finding is also important as a further element to be considered in the differential diagnosis of systemic vasculites: the vasculitic alterations involved in the PNS complications of borreliosis can in fact be distinguished from the vasculitis due to nodose polyarteritis or other collagen diseases which cause necrotising vasculitis [19].

Although concomitant radicular or plexus involvement cannot be completely excluded in the case described by us, it is worth pointing out that the clinical picture is dominated by mononeuropathy with painful paresthesias and sensory-motor deficiency limited to the territory of the sciatic nerve. These aspects therefore allow it to be placed among the few cases described in the literature in which PNS involvement during the course of borreliosis has clinical characteristics (documented electrophysiologically and neuropathologically) of the prevalent involvement of a single nerve.

Sommario *La malattia di Lyme è una malattia infettiva causata dalla spirocheta Borrelia burgdorferi. Il decorso della malattia si divide in 3 stadi. Fra i possibili aspetti clinici di interessamento del sistema nervoso, durante lo stadio 2, si possono osservare vari tipi di disfunzione del sistema nervoso periferico. Riportiamo il caso di una paziente con deficit persistenti causati dal prevalente coinvolgimento del nervo sciatico, confermato dai reperti elettrofisiologici e neuropatologici. Gli aspetti piu rilevanti alla biopsia del nervo erano rappresentati da degenerazione assonale e infiammazione perivascolare. Il danno di un singolo nervo periferico come espressione clinica dominante durante il decorso della malattia di Lyme e un rilievo inusuale, raramente descritto in letteratura.*

References

1. Dupuis MJM (1988) Les multiples manifestations neurologiques des infections a *Borrelia burgdorferi*. Rev Neurol 144:765-775
2. Monteyne P, Dupuis MJM, Sindic CJM (1994) Névrite du grand dentelé associée à une infection par *Borrelia burgdorferi*. Rev Neurol 150:75-77
3. Pachner AR, Steere AC (1985) The triad of neurologic manifestations of Lyme disease: Meningitis, cranial neuritis, and radiculo-neuritis. Neurology 35:47-53
4. Bannwarth A (1941) Chronische lymphocytäre Meningitis entzündliche Polyneuritis und "Rheumatismus". Ein beitrag zum Problem. Allergie und Nervensystem. Arch Psychiat Nervenkr 113:284-376
5. Halperin J, Luft BJ, Volkman DJ, Dattwyler RJ (1998) Lyme neuroborreliosis: Peripheral nervous system manifestations. Brain 113:1207-1221
6. Wulff CH, Hansen K, Strange P, Trojaborg W (1983) Multiple mononeuritis and radiculitis with erythema, pain, elevated CSF protein and pleocytosis (Bannwarth's syndrome). J Neurol Neurosurg Psychiatry 46:485-490
7. Hirsch E, Sellal F, Christmann D, Steinmetz G, Monteil H, Jesel M, Warter JM, Collard M (1987) Les méningo-radiculites après morsure de tique: étude de 31 cas. Rev Neurol (Paris) 143:182-188
8. Vallat JM, Hugon J, Lubeau M, Lebouet MJ, Dumas M, Desproges-Gotteron (1987) Tick-bite meningoradiculoneuritis: Clinical, electrophysiologic, and histologic findings in 10 cases. Neurology (Cleveland) 37:749-753
9. Kristoferitsch W, Sluga E, Graf M, Partsch H, Neumann R, Stanek G, Budka H (1988) Neuropathy associated with acrodermatitis chronica atrophicans: Clinical and morphological features. Ann N Y Acad Sci 539:35-45
10. Halperin J, Little BW, Coyle PK, Dattwyler RJ (1987) Lyme disease: Cause of a treatable peripheral neuropathy. Neurology 37:1700-1706
11. Camponovo F, Meier C (1986) Neuropathy of vasculitic origin in a case of Garin-Bujadoux-Bannwarth syndrome with positive borrelia antibody response. J Neurol 233:69-72
12. Sterman AB, Neslon S, Barclay P (1982) Demyelinating neuropathy accompanying Lyme disease. Neurology 32: 1302-1305
13. Halperin J,Volkman DJ, Luft BJ, Dattwyler RJ (1989) Carpal tunnel syndrome in Lyme borreliosis. Muscle Nerve 12:397-400
14. Melet M, Gerard A, Voiriot P, Gayet S, May T, Hermann J, Dournon E, Dureux J, Canton PH (1986) Méningoradiculonevrite mortelle au cours d'une maladie de Lyme. Presse Méd 15:2075
15. Midgard R, Hofstad H (1987) Unusual manifestations of nervous system *Borrelia burgdorferi* infection. Arch Neurol 44:781-783
16. Baumhackl U, Kristoferitsch W, Sluga E, Stanek G (1986) Neurological manifestations of *Borrelia burgdorferi* infections: The enlarging clinical spectrum. Zbl Bakt Hyg 263:334-336
17. Halperin J, Logigian EL, Finkel MF, Pearl RA (1996) Practice parameters for the diagnosis of patients with nervous system Lyme borreliosis (Lyme disease). Neurology 46:619-627
18. Garcia-Monco JC, Gomez Beldarrain M, Estrade L (1993) Painful lumbosacral plexitis with increased ESR and Borrelia burgdorferi infection. Neurology 43:1269
19. Meier C, Grahmann F, Engelhart A, Dumas M (1989)

Peripheral nerve disorders in Lyme-Borreliosis. Nerve biopsy studies from eight cases. Acta Neuropathol (Berl) 79:271-278

20. Tezzon F, Corradini C, Huber R, Egarter Vigl E, Simeoni J, Stanek G, Ferrari G (1991) Vasculitic mononeuritis multiplex in patient with Lyme disease. Ital J Neurol Sci 12:229-232

21. Maimone D, Villanova M, Stanta G, Bonin S, Malandrini A, Guazzi GC, Annunziata P (1997) Detection of Borrelia burgdorferi DNA and complement membrane attack complex deposits in the sural nerve of a patient with chronic polyneuropathy and tertiary Lyme disease. Muscle Nerve 20(8): 969-975