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LETTER TO THE EDITOR

Probable early Lyme neuroborreliosis in a non-endemic area: first reported case in Sardinia

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Dear Editor,

Lyme neuroborreliosis (LNB) affects nervous system in a widespread fashion and without clinical suspicion, the diagnosis can be easily overlooked [1], especially in geographic areas not known as endemic for Lyme disease.

We describe the case of a 70-year-old man living in Sardinia found to be affected by early LNB, previously unreported in this region.

He was admitted to our Neurology Department in March 2018 for abrupt onset of bilateral peripheral seventh cranial nerve palsy. He was affected by ischemic heart disease and atrial fibrillation. He regularly spent time in the countryside and he has never left Sardinia for the last 10 years. In January 2018, he noticed an erythematous, flat lesion on his back but he did not seek any medical attention.

At admission, his neurological examination was normal except for bilateral peripheral seventh cranial nerve palsy, and his tendon reflexes were fully normal and symmetric. Routine blood examination was unremarkable. He presented a flat, large, erythematous skin lesion on his back with central clearing (Fig. 1).

During the following days, he developed lower limbs paresthesia and weakness with gait impairment; tendon reflexes became asymmetrically reduced. A nerve conduction study of both upper and lower limbs revealed diffuse reduced amplitude of evoked compound action potentials more pronounced on left tibial, left sural, and right ulnar nerves, consistent with overlapping mononeuropathy multiplex.

Cerebrospinal fluid (CSF) was xanthochromic with 19 cells/μl (lymphocytes) and marked increase in protein concentration (572 mg/dl). Isoelectric focusing of CSF showed IgG oligoclonal bands. CSF culture and PCR for viral DNA were negative. Therapy with ceftriaxone IV 2 g/day was started.

HIV and Syphilis serology was negative and MRI of brain and spine was normal; serum protein electrophoresis was normal.

Testing for antibodies anti-Borrelia in serum with ELISA was positive and confirmatory Western blot was positive with no reactive IgM bands and 5/10 reactive IgG bands.

After 7 days of therapy, bilateral facial palsy and sensory motor impairment gradually improved.

On day 14 from onset, CSF was clear and colorless, with 10 cells/μl (lymphocytes); protein concentration was 320 mg/dl. Testing for antibodies anti-Borrelia in CSF with ELISA demonstrated presence of IgG and absence of IgM. At the same time, a new two-tier serological test was positive for anti-Borrelia IgG with increased titer (7/10 IgG bands in confirmatory Western Blot); IgM were again absent. PCR assay for Borrelia DNA in CSF and serum was negative.

After 4-week treatment with Ceftriaxone, bilateral facial palsy had almost completely recovered, and the patient was able to walk without assistance.

Lyme borreliosis is an infectious disease caused by tick-borne spirochetes of *Borrelia burgdorferi (Bb)* sensu *lato complex*, transmitted by specific *Ixodes* spp. ticks [2, 3].

Lyme disease usually arises with the characteristic skin lesion, erythema migrans, at the site of tick's bite. Following hematogenous dissemination, neurologic, cardiac, and/or rheumatologic involvement may occur [1, 4].

Neurological symptoms (LNB) usually occur after 1–12 weeks (mostly 4–6) after tick's bite (early LNB) [4]. At this stage, most common manifestations involve peripheral nervous system [1, 4]: cranial neuropathy (mostly seventh cranial nerve palsy, bilateral in up to 25% of patients), radiculoneuropathy, brachial plexopathy, and mononeuropathy multiplex (that can be confluent and mimic diffuse axonal polyneuropathy) [1, 4].

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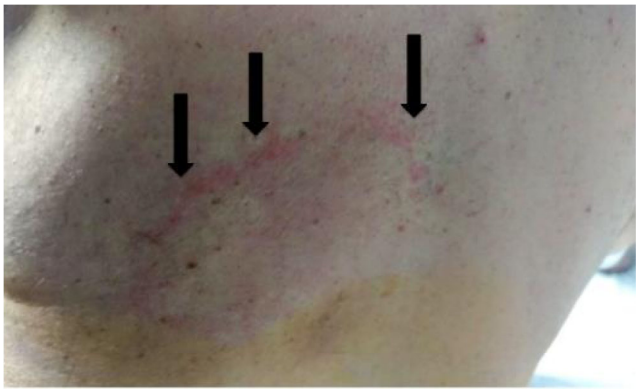

Fig. 1 Erythematous lesion with central clearing (arrows) developed on the back about 8 weeks before hospitalization

Lyme disease is endemic in north-eastern Italy (Friuli-Venezia Giulia and Trentino-Alto Adige) and in some areas near the coasts of Liguria and Emilia-Romagna [5].

In central and southern regions, only sporadic cases are reported [6], but real evidence of borreliosis is unknown.

We present a case of bilateral peripheral facial palsy and overlapping mononeuropathy multiplex with onset 8 weeks after the appearance of a skin lesion consistent with erythema migrans. IgG antibodies against Borrelia were found in serum and CSF. A complete recovery was achieved with a 4-week course of IV ceftriaxone. According to EFNS Guidelines [4], the diagnosis of possible early LNB is supported by neurological manifestations and CSF pleocytosis. Antibody Index was not performed, thus demonstration of intrathecal anti-Borrelia antibodies production is lacking, but the preceding skin lesion with timing and morphology consistent with erythema migrans [7] and rise in anti-Borrelia IgG titer (indicating an ongoing immune response) strongly point to a correct diagnosis of Lyme disease.

Sardinia is not considered endemic for Lyme disease and, to date, only one case of late LNB [8] is reported but the diagnosis was not supported by the presence of anti-Borrelia antibodies in CSF [8].

However, LNB could be not uncommon in Sardinia, considering the presence of large wild and rural areas ecologically compatible with tick's diffusion [3, 6].

Scarce attention towards a disease considered rare, together with the non-pathognomonic features of its manifestations, may have led to under-recognition of LNB.

Our report draws attention to a pathology that may be present even in geographical areas considered at low risk. A misdiagnosis delays specific antibiotic treatment that can lead to resolution of an otherwise serious disease.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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