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## Parsonage-Turner and Lyme disease. Absence of evidence is not evidence of absence

We have read and appreciate the letter of Verbanaz et al[1], who observe the current recommendations of the Centers for Disease Control and Prevention (CDC) and exclude Lyme disease (LD) presence in Argentina. In addition, we thank the authors for the opportunity to add further information omitted from the original article for space reasons[2].

To discard other etiologies, we also performed: serum antibodies made against CMV

(IgM, IgG), toxoplasmosis IgG, hepatitis A IgG, Hepatitis B virus (HBsAg, HBcAb, HBs Ab), Hepatitis C virus, and HIV were negative. Serum Leptospira antibodies (IgM, IgG) and VDRL were negative. ELISA and HAI for Chagas were negative. Immunofluorescence indirect (IIF) for Lyme borreliosis in serum: 5$^{th}$ day: IgM (+weak), IgG 1/160; 29$^{th}$ day: IgM (-) IgG 1/640, 45$^{th}$ day IgM (-), IgG 1/1280, day 95$^{th}$ IgM (-), IgG 1/1280, 10 years later IgG 1/160. The cerebrospinal fluid (CSF) revealed pleocytosis (90 nucleated cells) with 90% of lymphocytes, glucose (0.65 g/L), and protein 0.27 g/L were normal, antibodies against *Borrelia burgdorferi* (B.b) IgM and IgG were negative. VHS 1, VHS 2, VZV, and CMV in CSF were negative.

The B.b infection LD is a rare but potentially treatable cause of neuralgic amyotrophy (NA). Efforts must be made to diagnose, considering that we are not in an endemic area and the report is not mandatory. LD should be considered in patients from endemic regions with unexplained diaphragm paralysis[3]. There is general agreement that a positive epidemiological history could be a mainstay for the diagnosis, although it has been suggested that this might not be exclusive. Schmitt et al. believe that patients with Parsonage-Turner should be screened for borreliosis, including those who do not live in an endemic area and do not have erythema migrans, as reported[4]. We were only able to collect the travel history of our patient in the province of Misiones five years before her presentation[2].

As Verbanaz et al[1] stated that there are two-tiered conditional strategies typically used to support the diagnosis of LD. However, Western blot (WB) testing can be challenging to perform and interpret, and IgM measurement is prone to false-positive results. Furthermore, serologic testing alone can neither establish nor exclude the diagnosis of LD. Thus, clinicians must take into account the stage of disease when interpreting the WB results. Accordingly, the indications for public health practice are nowadays different. Clinicians and laboratories should consider serologic tests cleared by Food and Drug Administration (FDA) as well as CDC-recommended procedures for LD serodiagnosis[5].

Picazo et al[6] are emphatic and accept the lack of standardization. The recommendations for interpreting a WB should always be adapted to the environment where this technique is performed using the circulating genospecies**.** For these reasons, it is difficult to define international criteria for interpretation. Interlaboratory variability has been considerable and remains a problem in LD testing[7]. Thus, serological tests used to diagnose domestic LD may not reliably identify internationally acquired infections. CDC recommends using tests specifically validated to detect antibodies to B.b.sensu.lato (s.l) species found in other countries[8].

In our patient, the serologic diagnosis was made by IIF, verifying seroconversion and discarding other conditions. Unfortunately, it has been problematic to perform WB due to the lack of availability of the technique in Argentina. This limitation has already been mentioned[9]. Treatment decisions should not be primarily based on laboratory findings. Though arbitrarily chosen, these criteria have been used as rigid diagnostic benchmarks that have prevented people with LD from getting treatment[10]. The national document for Adaptation of Clinical Practice Guidelines claims that Guidelines must consider the local needs, the context in which it is desired to implement, and the local requirements of the health system, health priorities, legislation, policies, and resources[11].

The issue related to determining the extension of novel B.b.s.l. species infections in ticks, reservoirs, and humans in Latin America are an open result. Recently, new B.b.s.l. strains or new related species have been described in Brazil, Uruguay, and Chile. This could explain the lack of confirmatory tests, such as indeterminate WB and polymerase chain reactions, detecting suspected LD cases in this region[12].The existence of those new Borrelia genomic species should prompt the development of innovative diagnostic and clinical approaches. We can mention here a report of B.b.s.l. infecting ticks of the *Ixodes ricinus* complex in Uruguay[13]. A recent paper suggests that the haplotypes of B.b.s.l. complex found in the three species of the I. ricinus complex distributed found in the Southern Cone of America are related and widely distributed[14].

The changes in the recommendations on serological tests and their limitations would not have prevented us from doing them out if we had had access to them. However, our case report shows an evolution of the IIF

compatible with LD diagnosis, while other conditions could be ruled out with some degree of certainty. An epidemiological record (recognized endemic area) may not be required. With these clinical and serological elements, we decided on a specific treatment with doxycycline. After ten years of follow-up, there was no manifestation of any other related disease. Although the diagnosis of NA is obvious, its etiology should be viewed with caution by current standards. We must point out, so far, we don`t discern any fundament for proclaiming "*overwhelming evidence*" concerning infected people in our country.

In complex situations like this one, we prefer to recall the inspired considerations of Phil Alderson[15], who in turn were inspired by the classical paper by Altman and Bland from the 1990s. When we are told that "there is no evidence that A causes B", we should first ask whether the absence of evidence means simply that there is no information at all. *Absence of evidence is not evidence of absence.* This fallacy is committed when the truth or falsehood is inferred from existing ignorance. Therefore, we need to report uncertain results and do so clearly. Journals must be willing to publish uncertain results, thereby relieving the pressure on researchers to report their results as definitive. We have to create a culture in which it is good to assess and discuss uncertainty.

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