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Médecine et maladies infectieuses

Médecine et maladies infectieuses 44 (2014) 429–432

Short communication

Impact of serodiagnosis on the management of Lyme borreliosis at Angers University Hospital

Impact du sérodiagnostic sur la prise en charge de la borréliose de Lyme au CHU d'Angers

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Received 14 October 2013; received in revised form 22 May 2014; accepted 19 July 2014
Available online 22 August 2014

Abstract

Introduction. – Lyme borreliosis (LB) is an emerging arthropod-borne disease the diagnosis of which is made on clinical and biological data. We assessed the Angers University Hospital physicians' management of LB, in case of positive serology, and estimated their compliance to European recommendations (EUCALB).

Methods. – We retrospectively included 75 cases with positive ELISA serologies confirmed by Western-Blot, performed at the Angers University Hospital between 2008 and 2012.

Results and discussion. – There were 4 cases of early localized phase, 26 of early-disseminated phase (including 17 cases of neuroborreliosis), and one case of late phase. The curative management complied with EUCALB guidelines in 28 cases out of 31.

Conclusion. – Serology remains a reference diagnostic tool for LB, as long as the practitioner is aware of the main clinical and biological criteria.
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Keywords: Lyme borreliosis; Serodiagnosis; EUCALB

Résumé

Introduction. – La borréliose de Lyme (BL) est une maladie vectorielle émergente dont le diagnostic est posé devant un faisceau d'arguments clinico-biologiques. Nous avons évalué les conduites pratiques des médecins du CHU d'Angers en cas de sérologie positive dans la prise en charge de la BL et apprécié leur conformité au vu des recommandations européennes (EUCALB).

Méthodes. – Nous avons recensé rétrospectivement 75 patients ayant présenté des sérologies Elisa positives confirmées par Western-Blot réalisées au CHU d'Angers entre 2008 et 2012 inclus.

Résultats et discussion. – Il y avait quatre cas de phase précoce localisée, 26 cas de phase précoce disséminée, dont 17 cas de neuroborréliose, et un cas de phase tardive. Le traitement curatif était conforme aux recommandations dans 28 cas sur 31.

Conclusion. – La sérologie constitue un bon outil diagnostique de la BL à condition de disposer d'une meilleure connaissance des critères de définition clinico-biologique.
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Mots clés : Borréliose de Lyme ; Sérodiagnostic ; EUCALB

1. Introduction

Lyme borreliosis (LB) is an infection due to bacteria of the *Borrelia* genus transmitted by the bite of a tick of the *Ixodes*

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http://dx.doi.org/10.1016/j.medmal.2014.07.011
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genus [1]. The clinical diagnosis of the disease lacks specificity during the disseminated stage. During that stage, the biological diagnosis is crucial and relies on an indirect serologic diagnosis in two steps: a first screening serological test, using an immunoenzymatic technique (ELISA), and a second confirmation test using an immunolabelling or Western-Blot technique (WB), allowing defining the specificity of identified antibody [2]. Analyzing all the clinical and biological data allows the physician to confirm the infection or not. The diagnosis relies on strict criteria well defined on the national level by the consensus conference issued by the French Infectious Diseases Society (SPILF), and at the European level by the European Concerted Action on Lyme Borreliosis (EUCALB) [3–5]. Ignoring the recommendations may lead to misdiagnosis and inadequate treatment. We assessed the Angers University Hospital physician's management of LB, in case of positive serology, and estimated their compliance to EUCALB.

2. Materials and methods

2.1. Inclusion criteria for cases with positive serological tests

We collected the LB serologies performed by the Angers University Hospital microbiology laboratory between 2008 and 2012, recorded with GLIMS™ (MIPS) software. We then separated the negative ELISA results from the significant (positive or doubtful) confirmed by WB. The patient's clinical data for each positive serology was documented by consulting the electronic medical record on the CROSSWAY™ (CLM) network and classified according to the EUCALB diagnostic criteria [5].IgM and IgG kit (DIASORIN, Italy)

2.2. Kits used for the serology

The ELISA *Liaison Borrelia* IgM and IgG kit (DIASORIN, Italy) was used for the screening test. The test's principle relies on the semi-quantitative chemiluminescent immunoassay of anti-*Borrelia burgdorferi* sansu lato (*Bb*sl) IgM and IgG. The manufacturers defined the significant thresholds of positivity for IgG and IgM according to European recommendations. The confirmation technique, performed only in case of positive or doubtful screening serological test for IgG and/or IgM, relied on the Euroline–WB Anti-*Borrelia* + *VlsE*™ kit (EUROIMMUN, Germany) [6]. The interpretation of WB is based on a combination algorithm between the major antigenic bands (OspC in case of IgM and VlsE in case of IgG) and minor antigenic bands of total *Borrelia afzelii* extract. The bands were scanned and analyzed by an automatic scanning system Euroline Scan™.

2.3. Classification of cases in clinical stages

The seropositive clinical cases were classified according to the EUCALB recommendations [5]: early localized phase, early disseminated phase, and late disseminated phase. The compliance of treatments undertaken to the same recommendations was also assessed [3–5]. We created two other groups that could not be classified according to EUCALB criteria: aspecific clinical presentations and asymptomatic seropositivity. The main objective was to determine the compliance of the clinical diagnosis and of the treatment to EUCALB recommendations for the management of LB.

3. Results and discussion

We collected 2524 requests for LB serologies from 2008 to 2012 included; corresponding to 2369 patients after eliminating redundant requests (6%). Repeating LB serologies is only justified to screen for seroconversion and not to assess therapeutic effectiveness. There were 253 (10%) significant serologies with ELISA for IgG, including 187 positives (74%) and 66 doubtful (26%). There were almost twice less significant serologies for IgM, 134 (5%), including 94 positives (70%) and 40 doubtful (30%). The WB, when performed (only for 80% significant ELISA for IgG), confirmed the results of the ELISA for IgG in 103 cases out of 204 (50%) and for IgM in 24 cases out of 134 (18%).

This retrospective study focusing on all requests for serological tests during 5 years revealed the weak rate of confirmed significant (positive or doubtful) serological results: 4% (103/2524) for IgG and almost 1% (24/2524) for IgM. Fig. 1 illustrates the number of negative and significant ELISA and those confirmed by WB according to various prescribing units. The rate of significant tests ranged at an average of 10% in the units with the greatest number of requests except for the infectious and tropical diseases unit where it reached 25%. The retrospective analysis of all the data proves an overprescription for LB serologies that inevitably exposes to risks of misdiagnosis and overtreatment. This is why the systematic prescription of LB serology is contra-indicated and that the indications for this serology are based on well defined epidemiological, clinical, and biological data [3–5]. The analysis of results allowed us to identify 10 cases for which ELISA serologies were positive both for IgG and IgM, and despite recommendations, 2 WB (IgG and IgM) had been performed. It is recommended to perform only the confirmation test for IgG which is more specific in this case.

Finally, the study of 2524 serologies prescribed between 2008 and 2012 included led us to include only 75 cases.

The diagnosis made for 75 patients (Table 1) were classified by phase. Four cases of single erythema migrans (EM) were observed. Nevertheless, after carefully reading the medical observations, the semiological description of lesions remained weakly informative. An adequate treatment was administered in 75% of the cases. The early disseminated phase presentations were multiple EM (MEM = 2), early neuroborreliosis (NB = 17), Lyme arthritis (LA = 4), and cardioborreliosis (CB = 3). The late disseminated phase presentation was an *acrodermatitis chronica atrophica* (ACA = 1).

The high rate of NB (54.8%) reflects the clinical epidemiology of LB and corresponds to the most frequent disseminated phase of *Bb*sl infections [7,8]. These early NB (most often, facial palsy and meningoradiculitis) were all typical but were not classified as proven diagnosis because of a missing specific intrathecal synthesis index even though CSF samples

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