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THE MANY FACES OF LYME BORRELIOSIS: A RETROSPECTIVE STUDY COVERING AN 18-YEAR PERIOD

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ABSTRACT: Lyme borreliosis is a bacterial infection caused by *Borrelia burgdorferi* transferred by the bite of the tick *Ixodes.* The disease Lyme borreliosis can affect many organs and therefor has many different clinical manifestations. In order to describe the many clinical manifestations and prescribed treatments in a real-life setting, a retrospective chart review of Lyme borreliosis cases covering an 18-year period was conducted at a large Scandinavian dermatological university department. A total of 69 patients were included. Patients' mean age of time of diagnosis was 45 years, with a mean duration of symptoms of 9 months at time of diagnosis. Most patients presented with erythema migrans (56%), but acrodermatitis chronica atrophicans was also common and found in 41% of cases. All parts of the skin integument were affected, the most common being the lower extremity (57% of cases). On serological testing, most patients were IgG positive (41%), and the majority of patients were treated with penicillin V (82%). Lyme borreliosis and its many appearences should be known by all clinicians, since it has potentially severe multisystems manifestations, which can easily be avoided if a sufficient early curative treatment with antibiotics is prescribed.

KEYWORDS: Acrodermatitis Chronica Atrophicans, Erythema Migrans, Lymphadenosis Benigna Cutis, Lyme Borreliosis, Retrospective Chart Review

INTRODUCTION

Lyme borreliosis is a potential fatal bacterial infection presenting patterns of cutaneous, musculoskeletal, neurologic, and cardiac involvement [1-2]. In Denmark, the incidence is 0.8 per 100000 of the population [3].

The disease has been known since the early 1970s, when numerous cases of juvenile rheumatoid arthritis were observed in Old Lyme in Connecticut in North America, which later became known as the illness Lyme disease [4]. The cases were connected to tick bites *Ixodes*, in North America including *I. pacificus* and *I. scapularis* and in Europe *I. Ricinus*, which transmitted the disease [5]. However, the illness had been described for many years, but not fully understood until the 1980s [6-12]. Furthermore, in 1982 Burgdorf et al. discovered the causative organism, a treponema which was named *Borrelia burgdorferi* [4]. The disease has since commonly been known as Lyme borreliosis.

Like syphilis, another wide-spread treponemal infection, the course of Lyme borreliosis runs in three stages: stage 1, early localized infection; stage 2, early disseminated infection; and stage 3, late stage [13-14]. Depending on type of pathogenic genospecies, Lyme borreliosis can present with different affections in organs (**Table 1**). Further, the diagnosis still rely on the clinical presentation rather than serological testing [15-16].

Despite the widespread occurrence of Lyme borreliosis, to date only few systematic retrospective medical chart reviews of Lyme borreliosis have been conducted, why an overview of the different manifestations of the disease in real-life is missing. Therefore, the aims of this study were to report patient characteristics, clinical presentation, laboratory testing and prescribed treatment of a cohort of patients diagnosed with Lyme borreliosis at a large Nordic dermatology outpatient clinic.

METHOD

In January 2012, a retrospective patient chart review was conducted of patients diagnosed with Lyme borreliosis at the Department of Dermatology at Odense University hospital, serving a population of 1.3 million patients at the Region of Southern Denmark. Patients with Lyme borreliosis were included, encompassing International Cluster of Differentiation 10 (ICD-10) [17] codes for diagnosis for Lyme borreliosis (ICD L90.4, A69.2, A69.2F and L98.8A) in the period from January 1st, 1994 (when the ICD10-codes were introduced at the hospital) until January 2012. All patient charts were carefully and independently consulted, and data extracted according to a predefined data extraction table. Inconsistencies were solved by checking the patient charts. Relevant permissions to look up in the patient charts were given before the study was conducted.

RESULTS

A total of 69 patients were included. Mean age of time of diagnosis was 45 years (s.d. 21 years, range from 3-82 years of age), the majority (58%) being female (**Table 2**). Mean duration of symptoms was 9 months (s.d. 18 months, range from 0 to 120 months) with most of the patients (41%) having a duration of 1-3 months of skin symptoms at the time of first consultation. The majority (56%) of patients were diagnosed with erythema migrans, the common skin symptom was erythema (59%), the lower extremity was most often affected (57%), and the majority (80%) had symptoms restricted to the skin (**Table 3**). In serological analyses, 41% were IgG positive (**Table 4**). However, a histological examination was not conducted for the majority (48%) (**Table 4**). When treatment was prescribed, penicillin was the treatment of choice for 82% of the patients (**Table 5**).

DISCUSSION

Although Lyme borreliosis is widespread in mainly the Western world, no standard serological or histological test has been introduced to diagnose the cutaneous findings, as demonstrated in this study [15-16]. This study showed that the disease affects all age groups and body sites, in

alignment with previous studies [14]. The treatment of choice was penicillin, in accordance with the recommended treatment for the disease [15].

The study is limited by its retrospective design, often limited descriptions in the medical charts, and a possibility of coding errors [17], why some cases might have been missed. Furthermore, the study was conducted several years ago, limiting its generalizability.

A quality of the study is its real-life setting, reporting the wide-spread and polymorphous clinical presentation. The study findings high-lights the importance of all physicians considering Lyme borrelioses when patients presents with a rash.

Recommendations for researchers and policy-makers

Researchers are encouraged to further research in both reporting the clinical presentations of Lyme borrelioses and to report illustrative case reports to educate physicians and health-care personnel. Further, serological testing and pathological investigations need to be refined, in order to validate the cutaneous findings and detect Lyme borreliosis, in cases when clinic is vague.

Recommendations for clinicians

Clinicians need to consider Lyme borreliosis when patients present with a rash. If suspicion of Lyme borreliosis, either systemic antibiotics with penicillin V should be prescribed or referral to specialist dermatology care, as undeteched Lyme borreliosis can result in debilitating neurological symptoms. Further, as the climate changes, the occurrence of Lyme borreliosis will increase in countries with milder climate [3], while all clinicians are encouraged to be aware of the disease and its many ways of presenting in the skin.

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APPENDIX

Table 1. The pathogenic genospecies of *Borrelia burgdorferi*

Species	Geographical location	Diseases	Clinical presentation*
Borrelia burgdorferi sensu stricto	Europe, North America	Erythema migrans Arthritis	Homogenous erythematous cutaneous patch that that spreads peripherally from the bite. Swelling of joints.
Borrelia afzelii	Europe, Asia	Erythema migrans Lymphadenosis benigna cutis Acrodermatitis chronica atrophicans	- Pseudolymphoma Presents in four stages: Inflammatory-edematous stage; atrophic stage; sclerotic stage; and fibrous nodulus
Borrelia garinii	Europe, Asia	Erythema migrans Neuroborreliosis	- Diffuse neurological symptoms with potential impaired functions
Borrelia valaisiana	Europe	Erythema migrans	-
Borrelia spielmanii	Europe	Erythema migrans	-

**In cases where the same disease entity is mentioned several times, its clinical presentation is only described the first time the disease is mentioned.*

Table 2. Socio-demographic data

Variables	N (%)
Total number of participants	69 (100)
Sex	
Male	29 (42)
Female	**40 (58)**
Age (years)	
0-10	3 (4)
11-17	7 (10)
18-40	9 (13)
41-50	7 (10)
51-60	13 (19)
61-75	**26 (38)**
>75	4 (6)

Data describing the majority of patients is highlighted in bold.

Table 3. Diagnosis and symptoms

Variables	N (%)
Type of borrelia diagnosis	
Acrodermatitis chronica atrophicans	28 (41)
Erythema migrans	**39 (56)**
Lymphadenosis benigna cutis	2 (3)
Cutaneous symptoms	
Erythema	**59 (81)**
Atrophy	15 (22)
Hyperpigmentation	10 (15)
Anatomical region affected	
Upper extremity	19 (28)
Lower extremity	**39 (57)**
Truncus	11 (16)
Face and neck	6 (9)
Duration of symptoms (months)	
<1	11 (16)
1-3	**28 (41)**
4-6	12 (17)
7-9	3 (4)
10-20	9 (13)
21-30	1 (1.5)
31-40	1 (1.5)
41-50	2 (3)
51-60	1 (1.5)
>60	1 (1.5)
Non-cutaneous symptoms	
None	**55 (80)**
Neurological	4 (6)
Cardiac	1 (1)
Arthralgia	5 (7)
Arthritis	3 (4)
Lymphadenitis	2 (3)

Data describing the majority of patients is highlighted in bold. Nb. A patient may have several symptoms and regions affected.

Table 4. Laboratory analyses

Variables	N (%)
Serology	
Negative	8 (12)
IgM positive	22 (32)
IgG positive	**28 (41)**
Not examined	23 (33)
Histological examination	

Detected	20 (29)
Not detected	16 (23)
Not examined	**33 (48)**

Data describing the majority of patients is highlighted in bold. Nb. A patient may be both IGM and IgG positive.

Table 5. Prescribed treatment

Variables	N (%)
Antibiotic treatment	
Penicillin V	**57 (82)**
Amoxicillin	1 (1.5)
Tetracycline	10 (15)
No treatment	1 (1.5)

Data describing the majority of patients is highlighted in bold.