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Multidisciplinary management of patients presenting with Lyme disease suspicion

Prise en charge multidisciplinaire des patients suspects de borréliose de Lyme

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Abstract

Objective. – The teaching hospital of Nancy, France, implemented a specific multidisciplinary care pathway (French acronym AMDPL) to improve the management of patients presenting with Lyme borreliosis (LB) suspicion. We aimed to assess the first year of activity of this care pathway.

Patients and methods. – We included all patients managed in the AMDPL pathway from November 1, 2016 to October 31, 2017. The first step was a dedicated Lyme disease consultation with an infectious disease specialist. Following this consultation, the LB diagnosis was either confirmed and adequate treatment was prescribed, or a differential diagnosis was established and patients received adequate management, or further investigations were required and patients were offered multidisciplinary management as part of a day hospitalization.

Results. – A total of 468 patients were included. LB diagnosis was confirmed in 15% of patients (69/468), 49% of patients received a differential diagnosis, and 26% (122/468) of patients had the LB diagnosis ruled out without receiving any other diagnosis.

Conclusions. – This is to our knowledge the first multidisciplinary center implemented in France for the management of patients presenting with LB suspicion related to polymorphous signs and symptoms. Several diagnoses could be confirmed or corrected, although some symptoms and complaints could not be explained. This cohort could improve our knowledge of LB and its differential diagnoses.

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Keywords: Lyme disease; Borreliosis

Résumé

Objectifs. – Pour améliorer la prise en charge de patients « suspects » de borréliose de Lyme (BL), le CHRU de Nancy a organisé une filière spécifique de soins multidisciplinaire (AMDPL). L'objectif de ce travail était de dresser un bilan de sa première année de fonctionnement.

Patients et méthodes. – Tous les patients pris en charge dans la filière AMDPL à compter du 01/11/2016 ont été inclus. La 1^{re} étape consistait en une consultation d'infectiologie dédiée. À l'issue de cette consultation, soit le diagnostic de BL était établi et un traitement adéquat était prescrit, soit un diagnostic différentiel était retenu et justifiait d'une prise en charge adaptée, soit il apparaissait nécessaire de pousser le bilan et une hospitalisation de jour multidisciplinaire était alors proposée.

Résultats. – Quarante cent soixante-huit patients ont été inclus. Dans 15 % des cas (69/468) le diagnostic de BL a été confirmé, dans 49 % un diagnostic différentiel a été proposé et dans 26 % (122/468) le diagnostic de BL a été exclu sans qu'un autre diagnostic n'ait pu être arrêté.

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Conclusions. – Il s’agit à notre connaissance du 1^{er} centre multidisciplinaire mis en place en France pour la prise en charge de patients présentant une symptomatologie polymorphe « suspecte » d’être en lien avec une BL. Plusieurs diagnostics ont pu être confortés ou redressés. Certaines situations restent néanmoins inexplicables. Cette cohorte devrait nous permettre d’améliorer nos connaissances sur la BL et ses diagnostics alternatifs. © 2018 Elsevier Masson SAS. Tous droits réservés.

Mots clés : Maladie de Lyme ; Borréliose

1. Introduction

Lyme borreliosis (LB) is currently the subject of many debates and controversies in France and in Europe. In 2016 the French Ministry of Health decided to launch a national plan to address Lyme disease and other tick-borne diseases. One of the objectives of this national plan is to improve and standardize management so as to address doctor-shopping and to implement a national protocol for the diagnosis and treatment of LB [1,2].

In France, the estimated 2016 incidence rate of LB was 84 cases per 100,000 inhabitants (all presentations; primary presentations or erythema chronicum migrans accounting for >95% of all presentations). A wide regional and departmental discrepancy can be observed with higher incidence rates in Eastern France (>300 cases/100,000 inhabitants) [16].

Except for the early localized presentation, LB is a polymorphous and complex infection with early and late presentations and various clinical manifestations that may sometimes be subjective [3,4]. Although LB serological test is not always accurate in early presentations, the reliability of antibody detection using the Elisa method is close to 100% in late presentations. This method is, however, not specific for detecting progressive LB [5].

LB diagnosis in patients presenting with subjective symptoms and a history of tick bites and/or with anti-*Borrelia burgdorferi sensu lato* antibodies, especially if they have received prior treatments, is extremely tricky. Wrongly diagnosing LB may lead to prescribing multiple ineffective antibiotic treatments, with potential adverse events (both at the individual and collective levels with an unnecessary deterioration of the selection pressure of antibiotics and an increased antibiotic resistance) and a risk of delaying the patient’s management because of differential diagnoses [6]. On the contrary, missed diagnoses are associated with disease progression and the associated morbidity.

A survey was conducted in 2016 with family physicians (FPs) of the Lorraine region. Findings revealed that FPs did not have trouble managing patients presenting with a tick bite or with early localized Lyme disease (erythema chronicum migrans = ECM), but 98% of them had difficulties in managing patients presenting with LB suspicions at later stages. Confronted with symptom persistence, 87% of FPs mentioned being uncomfortable with suggesting a treatment strategy [7].

On November 2016 the Teaching Hospital of Nancy, with the support of the Regional Health Agency (French acronym ARS) of Eastern France, decided to set up a dedicated care pathway for these patients to improve their management and to satisfy the

expectations of FPs. This dedicated care pathway was called “Multidisciplinary management of patients presenting with Lyme disease suspicion” (French acronym AMDPL). Several specialist physicians (infectious disease specialists, internists, rheumatologists, neurologists, dermatologists, microbiologists, psychiatrists, and psychologists) are working together to provide a multidisciplinary and coordinated management in a dedicated place and within a restricted period of time so as to establish diagnosis: confirmation of LB diagnosis or differential diagnosis leading to adequate management.

We aimed to describe the characteristics of patients managed as part of the AMDPL pathway between November 1, 2016 and October 31, 2017, i.e. during the first year following the implementation of this care pathway.

2. Patients and methods

We performed a retrospective, monocentric, and observational study at the Teaching Hospital of Nancy.

2.1. Description of the AMDPL pathway

Patients enter the AMDPL pathway upon request of their FP:

- either because the FP has identified clinical signs and symptoms that he believes to be consistent with progressive LB;
- or because the patient himself believes to have progressive LB and has convinced his FP to ask for his inclusion into the AMDPL pathway – even when the LB serology is negative.

The first step is a consultation with an infectious disease specialist, i.e. the dedicated “Lyme disease consultation 1st time”. Patients must fill in a “pre-Lyme disease consultation” questionnaire prior to the consultation (sociodemographic data, tick bites and frequency, ECM, list of possible symptoms, symptom onset following tick bite, prior treatments, treatment effectiveness).

Various care pathways may be suggested at the end of this consultation according to the initial conclusions of the infectious disease specialist:

- LB diagnosis seems probable and does not require further examination: the infectious disease specialist recommends an antibiotic treatment as per the 2006 consensus conference, as well as a dedicated follow-up;
- LB diagnosis is ruled out right away and a differential diagnosis is established or suspected. The following strategies may be considered:

- a differential diagnosis seems probable and the patient is directly referred to another specialist or to the psychologist for confirmation and dedicated management,
- no differential diagnosis can be established at that time, but the observed clinical signs and symptoms are objective and worrying, thus justifying further examination. The patient is included in a specific AMDPL pathway in our multidisciplinary ambulatory care unit (day hospitalization),
- the LB diagnosis is ruled out right away without any complaint or abnormality observed at clinical examination. The patient is informed that the LB diagnosis has been ruled out and is thus reassured and newly referred to his FP.

2.1.1. 2nd step: the ambulatory care unit of the AMDPL pathway

Management of patients in the ambulatory care unit as part of the AMDPL pathway relies on a day hospitalization under the responsibility of the Tropical and Infectious Diseases Department and is coordinated by an infectious disease specialist. A weekly slot is allocated to AMDPL patients in the ambulatory care unit of the Teaching Hospital of Nancy. Further examinations, specialists' advice, and the dedicated psychological management performed or given during the patient's stay in the ambulatory care unit are decided based on the findings from the initial consultation.

At the end of this step, the patient's chart is discussed at the multidisciplinary meeting with all healthcare professionals involved and the patient's FP – if he wishes so – to summarize the diagnosis and to suggest adequate management. The patient then has another consultation with the infectious disease specialist with whom he initially met. The psychological management may be continued as external consultations if the patient wishes so.

2.2. Lyme borreliosis diagnosis

LB diagnosis was established based on current guidelines (2006 consensus conference of the French Infectious Diseases Society – SPILF; 2014 recommendations of the High Council for Public Health):

- anamnesis criteria indicating a history of tick bite and/or potential exposure to tick bites and/or a history of ECM;
- clinical signs and symptoms consistent with those reported at the various stages of LB (objective or subjective signs);
- presence of biological markers consistent with LB, especially with late presentations: presence of IgG antibodies detected by immune-enzymatic technique (ELISA) and confirmed by Western-Blot technique. A *Borrelia* PCR test could be performed as part of the analysis of joint fluid samples, cutaneous samples, or cerebrospinal fluid (CSF) sample. As for the lumbar puncture, the detection and titration of antibodies could be performed in the CSF to document an intrathecal synthesis;
- evaluation of the potential effectiveness of any prior and well-conducted anti-infective treatment with reference molecules (amoxicillin, ceftriaxone, cyclins, etc.).

2.3. Conduct of the study

2.3.1. Study population

We included all patients who came to the dedicated “Lyme disease consultation 1st time” between November 1, 2016 and October 31, 2017.

2.3.2. Data collection

Data collection was retrospectively performed using the “pre-consultation” questionnaire as well as consultation and day hospitalization reports. The collected database was then anonymized.

Data collected prior to the consultation included:

- demographic data (age, sex, lifestyle, department of origin, profession);
- exposure to ticks (forest activities, tick bites, tick bite frequency, time interval since tick bite responsible for the symptoms);
- prior and current signs and symptoms (ECM, date of ECM, signs indicative of a late presentation of LB, date of symptom onset, cessation of work due to the described signs and symptoms, etc.);
- biological markers (Lyme serology ± Western-Blot, etc.);
- treatments previously received for LB.

At the end of the consultation, the following was added to the patient's form:

- conclusions of the infectious disease specialist was LB diagnosis retained? Presentation and clinical stage retained in case of LB? Treatment initiated at the end of the consultation? Other diagnosis retained if LB was ruled out? Following the initial consultation, care pathway suggested to the patient (referred to another specialist? Scheduled management in the ambulatory care unit? New consultation scheduled? Etc.);
- when management in the ambulatory care unit was scheduled, the following data was recorded: time interval (months) between the initial consultation and admission to the unit, further examinations performed in the ambulatory care unit, specialists contacted, dedicated psychological support or lack of it. Conclusions drawn at the end of the management in the ambulatory care unit were also recorded: was the LB diagnosis retained? Presentation and clinical stage retained in case of LB? Treatment initiated at the end of the consultation? Other diagnosis retained if LB was ruled out?

2.3.3. Statistical analysis

Quantitative variables were expressed as means ± standard deviation ($m \pm SD$). Qualitative variables were expressed as frequencies (n/N) and percentages (%).

Data was analyzed using the R 3.3.1 statistical software® (<http://www.r-project.org>).

3. Results

3.1. Dedicated “Lyme disease consultation 1st time” as part of the multidisciplinary management of patients presenting with Lyme disease suspicion (AMDPL)

A total of 468 patients benefited from the dedicated “Lyme disease consultation 1st time” as part of the AMDPL pathway from November 1, 2016 to October 31, 2017 (i.e., one year of activity); 235 (50%) were females and 233 (50%) were males. Mean age of patients was 51.4 years (± 16 years, range: 7–86 years). The sociodemographic characteristics are detailed in

Table 1.

Most patients came from the Meurthe-et-Moselle department (35%), the former Lorraine region (22.4% from Moselle, 16% from the Vosges, and 6.4% from Meuse), the other departments of the Eastern region of France (12.1%), and the rest of France (7.7%). Two patients lived abroad (0.4%).

Patients had been referred by their FP in 85% of cases (289/342 for whom this data had been recorded in the collection form). Despite the initially agreed approach, 15% of patients managed to obtain an appointment for the consultation without first consulting their FP.

The main reason for consultation was the presence of clinical signs that could be partly or entirely consistent with those of the secondary or late presentations of LB (96%).

Table 1
Sociodemographic characteristics, risk factors for exposure to Lyme disease, and anamnesis data of patients admitted to consultation as part of the multidisciplinary management of patients presenting with Lyme disease suspicion and of those referred to the ambulatory care unit.
Caractéristiques sociodémographiques, facteurs d'exposition à la maladie de Lyme et données anamnestiques des patients admis en consultation dans le cadre de l'approche multidisciplinaire des patients suspects de maladie Lyme et ceux adressés en unité de médecine ambulatoire.

	Global population (n = 468)		Patients referred to the ambulatory care unit (n = 121)	
	n (N) or mean, \pm SD	%	n (N) or mean, \pm SD	%
<i>Sociodemographic factors</i>				
Age	51.4 \pm 16	–	50 \pm 13.4	–
Sex				
Male	233	50	61	50
Female	235	50	60	50
<i>Socioprofessional categories</i>				
Farmers	20	4	5	4
Craftsmen, retail traders	11	2	4	3
Senior executives	25	5	7	6
Middle management	62	13	27	22
Employees	64	14	22	18
Workers	32	7	9	7
Retired persons	102	22	25	21
Other unemployed	42	9	10	8
Unknown	110	24	12	10
<i>Lifestyle</i>				
Living in a rural area	217 (315)	69	70 (89)	79
Occupational activity in forests	44 (334)	13	14 (100)	14
Hobbies in forests	269 (319)	84	88 (98)	90
<i>Referral letter from the FP</i>	289 (342)	85	78 (88)	89
<i>Reason for consultation</i>				
For informational purposes	2 (459)	0.4	–	–
Strategy to adopt following tick bite	1 (459)	0.2	–	–
Management of erythema chronicum migrans	2 (459)	0.4	1 (121)	0.8
Other symptoms that may be observed during the secondary phase of the infection	440 (459)	96	120 (121)	99.2
Positive serology only	14 (459)	3	–	–
<i>Clinical history</i>				
Tick bite	296 (378)	78	82 (121)	68
Erythema chronicum migrans	139 (339)	41	50 (121)	41
Signs indicative of the secondary phase	428 (449)	95	121 (121)	100
<i>Lyme serology</i>				
IgG positive	244	52	61	50
IgM positive	62	13	21	17
IgG and IgM negative	144	31	37	31
Unknown status/not informed	18	4	2	2
<i>Prior treatments</i>	373 (440)	85	103 (121)	85

FP: family physician.

3.1.1. Risk factors for exposure to ticks, anamnesis and clinical data

Tick bite was reported as a risk factor for exposure to ticks in 78% of cases (296/378), and skin lesion compatible with ECM diagnosis was reported in 41% of cases (139/339) (Table 1). At the time of consultation, 52% of patients had a positive serology for IgG, 13% a positive serology for IgM, and 31% a negative serology overall; 4% of patients had an unknown serological status or unreported on the day of consultation.

The clinical signs observed were multiple and diverse (Fig. 1). The three main signs reported by patients were (in order of frequency) arthralgia (75%), asthenia (65%), and myalgia (60%).

Overall, 85% of patients (373/440) had already received at least one treatment known to be active against LB (amoxicillin: 39.5% of patients; doxycycline: 32.3%; ceftriaxone: 25.6%).

Several patients also mentioned having received other treatments as part of their LB suspicion management, not limited to and in decreasing order of frequency: hydroxychloroquine, metronidazole, oral amphotericin B, albendazole, flubendazole,

fluconazole, hydroxynaphthoquinone, valacyclovir, dapsone, etc.

Many patients had taken homeopathy, TicTox, vitamin therapies, aromatherapies, etc.

3.1.2. Conclusion and care pathway decided at the end of the first consultation

Data required to classify patients could not be retrieved for 13 of 468 patients.

For the 455 remaining patients:

- seven patients had a positive Lyme serology, but did not present with any symptom indicative of LB. Decision was thus taken to stop any further examination and no treatment was initiated;
- one patient who did not present with symptoms but who consulted because he was worried about having LB as he had been bitten by ticks many times, was reassured by the physician and left without any specific follow-up or treatment scheduled (negative Lyme serology).

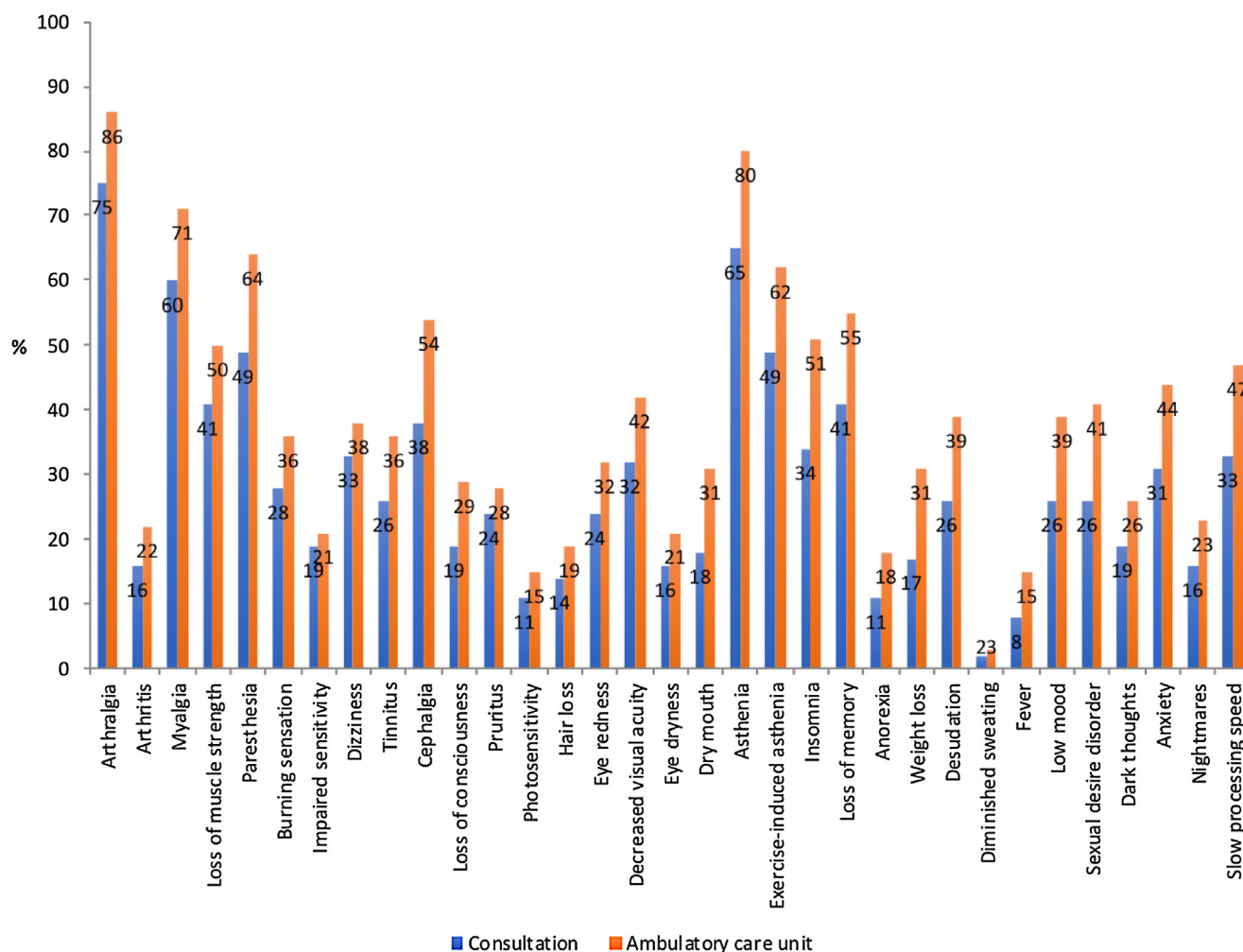


Fig. 1. Proportion of clinical signs presented by patients admitted to consultation as part of the multidisciplinary management of patients presenting with Lyme disease suspicion and of patients referred to the ambulatory care unit (% of patients reporting symptoms).

Proportion des signes cliniques présentés par les patients admis en consultation dans le cadre de l'Approche multidisciplinaire des patients suspects de maladie Lyme et ceux adressés en unité de médecine ambulatoire (% des patients indiquant l'existence de ce symptôme).

LB diagnosis was considered possible or probable by the physician during the first consultation in 71 of the remaining 447 patients (15% of all patients):

- four patients had a negative serology (IgG and IgM by Elisa test) but were treated with antibiotics because, according to the physician, they presented with clinical signs and symptoms consistent with those of the secondary or late phases of LB and had high risk factors for exposure. The physician decided to initiate a first-line treatment – which proved ineffective. Following discussion at the multidisciplinary meeting, the LB diagnosis was finally ruled out;
- LB diagnosis was confirmed in the remaining 67 patients (14% of all patients): 59 had a positive serology for IgG, seven had a positive serology for IgM, and one had a negative serology for IgM and IgG but produced intrathecal antibodies targeted against *B. burgdorferi*:
 - eight of these patients were treated with ceftriaxone for neuroborreliosis, 41 other patients were also prescribed antibiotics for late stage LB (11 treated with ceftriaxone and 28 with doxycycline [two missing pieces of information]),
 - a total of 18 patients were not prescribed any treatment at the end of the consultation, nor were they offered management in the ambulatory care unit as they had already received one or several treatments known to be effective against LB, but which proved ineffective. A new prescription of that same treatment was therefore deemed irrelevant (three neuroborreliosis cases, seven late stage LB cases, eight unknown stage cases).

For the 376 remaining patients, LB was not ruled out nor was it confirmed at the end of the consultation in 112 patients (24% of all patients). Of these 112 patients, 111 were referred to the ambulatory care unit and one patient was hospitalized (the hospital report later confirmed late stage LB).

For the remaining 264 patients, LB diagnosis was directly ruled out at the end of the consultation:

- a differential diagnosis was suspected at the end of the consultation in 174 patients (37% of all patients); 171 were directly referred to another specialist (in decreasing order of frequency: 51 patients were referred to the rheumatology unit, 48 to the internal medicine unit, 33 to the neurology unit, 8 to the dedicated psychiatrist, and 6 to the dermatology unit). Other specialists were more sporadically solicited. A total of 24 patients were directly referred to the dedicated psychology unit of the AMDPL pathway without being first referred to the ambulatory care unit, and three were referred to the ambulatory care unit to confirm the differential diagnosis;
- LB diagnosis was directly ruled out at the end of the consultation in 90 cases (19% of all patients), without any differential diagnosis mentioned and without any further investigations requested at the day hospital. The clinical examination of these patients was normal; they thus could be reassured and newly referred to their FP;
- Out of the 264 patients who had the LB diagnosis ruled out at the end of the first consultation, 104 had a negative serology,

119 had a positive serology for IgG, 36 had a positive serology for IgM, and six had an unknown serology.

3.2. Management in the ambulatory care unit as part of the AMDPL pathway

A total of 121 patients (26% of all patients) were offered an additional workup as part of their admission to the ambulatory care unit. Seven of these 121 patients were admitted to the ambulatory care unit despite a probable LB diagnosis established at the end of the first consultation; 111 patients because LB diagnosis was neither confirmed nor ruled out; and three patients because the differential diagnosis needed to be confirmed.

At the end of the study period, 13 patients were still waiting for their admission to the ambulatory care unit, four patients directly refused to be admitted to the unit, and five did not come to the scheduled appointment in the ambulatory care unit. Overall, on October 31, 2017, 99 patients had completed the whole pathway. Mean time between the first consultation and admission to the ambulatory care unit was 2.7 months (± 1.4). Sociodemographic characteristics and risk factors for tick exposure are detailed in Table 1. All patients consulted for symptoms indicative of late stage LB. Sixty-eight per cent (82/121) of them remembered having had one tick bite and 41% (50/121) reported ECM (Table 1).

Among these patients, 85% (103/121) had already received at least one LB treatment: 41% received amoxicillin, 41% doxycycline, and 30% ceftriaxone (several patients had received several treatments).

A total of 39 patients had a negative serology (32%), 61 a positive serology for IgG (50%), and 21 a positive serology for IgM (17%).

Patients presented with various symptoms. The three most frequent symptoms (in decreasing order) were arthralgia (86%), asthenia (80%), and myalgia (71%) (Fig. 1).

Further investigations performed as part of the patients' management in the ambulatory care unit are detailed in Fig. 2. The other specialists of the AMDPL pathway were solicited for 51% (50/99) of patients managed in the ambulatory care unit: 26 patients consulted a rheumatologist, 17 an internist, 14 a neurologist, 3 a dermatologist, and 3 a psychiatrist. Fifty-five per cent (54/99) of patients benefited from a dedicated psychological management as part of the AMDPL pathway.

3.2.1. Conclusion reached at the end of the management in the ambulatory care unit

Of the 99 patients who completed the whole management pathway, eight received a LB diagnosis (8%) including seven diagnoses of neuroborreliosis confirmed by lumbar puncture and one late joint presentation. These patients were always offered treatment with ceftriaxone and an infectious disease follow-up was implemented.

Of the 91 patients whose LB diagnosis was ruled out: 59 received a differential diagnosis (Table 2); LB diagnosis was ruled out in the remaining 32 patients but no other diagnosis was established, despite the investigations performed (7% of all patients).

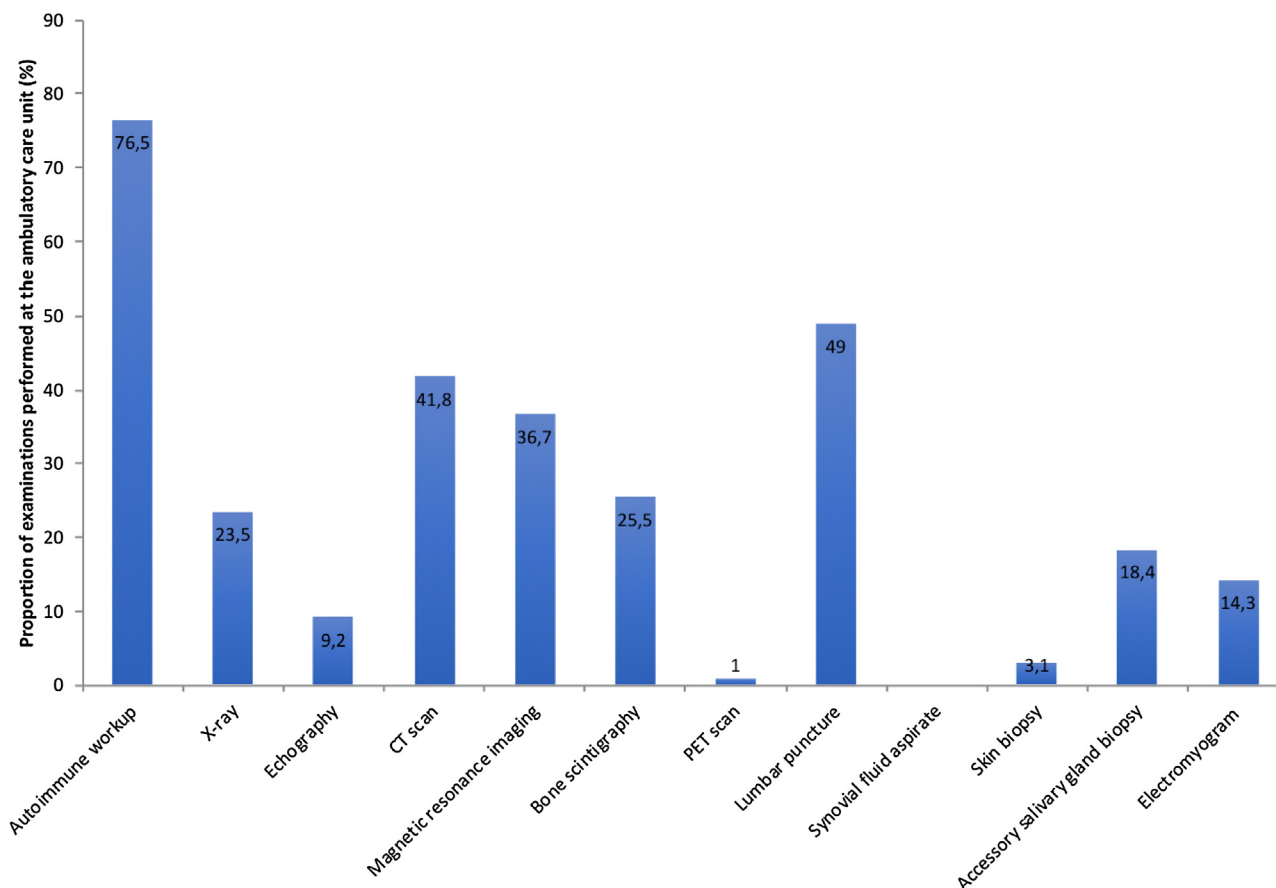


Fig. 2. Further investigations performed at the ambulatory care unit as part of the multidisciplinary management of patients presenting with Lyme disease suspicion. *Examens complémentaires réalisés au cours de l'unité de médecine ambulatoire dans le cadre de l'approche multidisciplinaire des patients suspects de maladie Lyme.*

Table 2

Differential diagnoses established at the end of the day hospitalization as part of the multidisciplinary management of patients presenting with Lyme disease suspicion. *Diagnostics différentiels portés à l'issue de l'hospitalisation de jour de l'approche multidisciplinaire de patients suspects de maladie de Lyme.*

Rheumatologic diseases	Auto-immune/systemic diseases	Neurological diseases	Endocrine/metabolic diseases	Functional psychiatric disorders	Other
Psoriatic arthritis (3)	Vasculitis (2)	Cervicobrachial neuralgia (1)	Vitamin B12 deficiency (1)	Fibromyalgia (6)	Huntington disease (1)
Spondylarthritis (3)	Myositis (1)	Occipital neuralgia (1)	Iron deficiency (1)	Chronic fatigue syndrome (2)	Hemochromatosis (1)
Rheumatoid arthritis (1)	Gougerot-Houwer-Sjögren syndrome (2)	Sensory polyneuropathy (1)	Hyperammonemia (1)	Postural deficiency syndrome (3)	Pulmonary arterial hypertension (1)
Plantar fascia (1)	Mixed connective tissue disease (1)	Multiple sclerosis (1)	Hypocortisolemia (1)	Mixed anxiety–depressive disorder (2)	
Coxarthrosis (2)	Polyarteritis nodosa (1)	Entrapment neuropathy (2)	Hyperparathyroidism (1)		
Rhizarthrosis (1)	Sarcoidosis (1)				
Cervical spondylotic myelopathy (1)	Ongoing workup (2)				
Generalized arthrosis (6)					
Cervical stenosis (1)					
Lumbar stenosis (1)					
Gout (1)					
Ongoing inflammatory rheumatism workup (2)					

Irrespective of the conclusion reached at this stage, all patients were once again seen at a postambulatory care unit consultation by an infectious disease specialist or another specialist.

3.3. Diagnosis at the end of the AMDPL pathway

Of the 468 patients managed as part of the AMDPL pathway:

- data was missing for 13 patients (3%);
- seven patients (1.5%) had a positive Lyme serology but did not present with any symptom and were thus reassured;
- one patient (0.2%) consulted because he was worried about having LB as he had been bitten by ticks many times, although he did not present with any symptom. His Lyme serology was negative, and he was thus reassured and asked to be vigilant about potential symptom onset that would require a new consultation with his FP;
- four patients (0.8%) presenting with symptoms consistent with late stage LB were considered “possible LB” cases, although their serology was negative. They received a first-line treatment which proved ineffective. LB diagnosis was in the end ruled out;
- LB diagnosis was established in 69 patients (15%) (67 at the end of the first consultation, with confirmation at the end of the ambulatory care unit management stay for seven of them and one following hospitalization);
- a differential diagnosis was established in 230 patients (49%) (171 at the first consultation and 59 at the ambulatory care unit);
- LB diagnosis was ruled out in 122 patients (26%) who did not receive any other diagnosis (90 LB diagnoses ruled out at the first consultation in patients whose clinical examination was normal – they were reassured and newly referred to their FP; 32 at the ambulatory care unit);
- a total of 13 patients (3%) were waiting to be managed at the ambulatory care unit or were waiting for the final results of the management at the ambulatory care unit at the end of the study period;
- a total of nine patients (2%) refused to be managed at the ambulatory care unit or did not come to the ambulatory care unit consultation.

4. Discussion

Various centers for Lyme disease have been created in Europe [8–10], in the United States [11,12], and in Canada [13], but this is to our knowledge the first facility of this kind created in France. The first step of the pathway is the consultation with an infectious disease specialist. This is a fundamental step as it can guide diagnosis in 75% of cases and as only 25% of patients require additional management at the end of this first consultation to try and find the right diagnosis considering the symptoms reported by patients. This first step also falls under the responsibility of infectious disease specialists in some of the centers abroad [8], but is also jointly taken care of by neurologists and internists in others [10], with similar results.

Patients were referred by their FP in 85% of cases and the main reason for consultation was the presence of clinical signs that could be consistent with late stage LB. However, only 52% of these patients had a positive Lyme serology for IgG and 85% had already been treated for LB (with a treatment known to be effective but which proved ineffective). The AMDPL pathway is targeted at patients who are doctor-shopping and who have already been informed about the possibility of LB diagnosis by their FP, their relatives or who themselves thought about this diagnosis. Patients usually report subjective symptoms that fluctuate, persist, and worsen but the final diagnosis cannot usually be established. A negative serology or an ineffective first-line treatment does not seem to convince patients that they do not have LB. Taking the time to listen to patients and explaining things are in the end enough to convince them that they do not have LB. This type of management also seems to answer the FPs’ expectations as 98% of respondents who took part in our 2016 survey declared having difficulties in managing LB suspicions at later stages and 87% declared being uncomfortable with suggesting a treatment strategy in case of symptom persistence [7].

At the end of this management pathway, only 15% of LB diagnoses were established. This figure is similar to that reported by LB centers in other countries [8,11,12,14]. The high number of patients asking for a consultation compared with the small number of patients receiving LB diagnosis may be explained by the media coverage of this disease with contradictory information on diagnostic modalities and treatment. The small number of LB diagnoses confirmed in our patients may also be explained by the inclusion in our pathway of patients who had already been seen by other physicians who had already recognized and treated true LB cases and who had been able to document an alternative diagnosis in most of the remaining patients. Consequently, few patients included in the AMDPL pathway had LB and in most cases alternative diagnoses had already been established. However, the number of established differential diagnoses remains quite high (49% of cases). This figure is higher than those observed in other studies such as Coumou et al.’s study (36%). These studies indicate that these differential diagnoses are lately established, which is often detrimental to patients [8,9,12,13].

Thus, at the end of the AMDPL pathway, 20% of patients were newly referred to their FP after ruling out LB diagnosis. They all had normal clinical examination and were reassured as they were told they did not have LB. We thus observed that such pathway did not upset patients and/or FPs, but rather reassure them and met their expectations as to what strategies should be implemented to address the reported symptoms [7]. Patients thus often stopped asking for antibiotics or other prescriptions, which are not recommended considering the associated risk of adverse events [6,15].

For exhaustivity purposes, we must mention that symptoms and complaints of 6% of patients could not be explained despite their management in the ambulatory care unit.

We also observed that practices varied from one physician to another. According to their years of experience, some physicians more often tend to ask for additional

investigations before establishing diagnosis. Others tend to prescribe first-line treatments when such prescription is debated. Further study must be performed to try and understand the latter two points.

Our study helped collect many data in the first French center for Lyme disease, created a year ago. This new approach could be extended to other regions. These centers could offer a comprehensive and standardized management and data could be collected in an objective way as part of a prospective cohort study. The final aim is to improve knowledge on persisting symptoms and long-term treatments, to determine the profile of patients, and to better comprehend the diagnostic criteria of LB.

5. Conclusion

This is the first assessment of the first center for the multidisciplinary management of Lyme disease suspicions in France. Only 15% of patients managed as part of our pathway had progressive LB; 49% of patients received a differential diagnosis and were referred to a specialist.

We thus believe that this center allows for a multidisciplinary and routine assessment by experienced specialists of patients presenting with various symptoms who have often received several lines of treatment and are doctor-shopping.

Creating more centers of this type and sharing data and experience could help improve our knowledge through clinical research on LB and its alternative diagnoses.

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Disclosure of interest

The author declares that he has no competing interest.

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