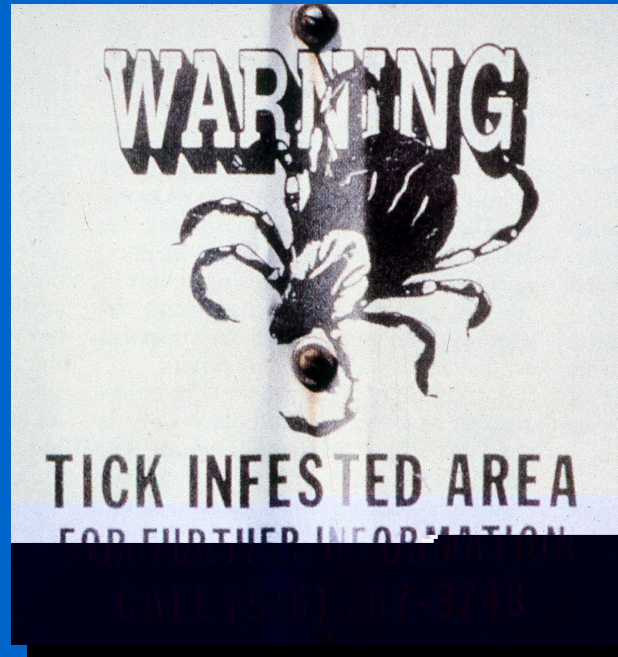


Clinical aspects of Lyme disease



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Case report

- G. 14 y.:
 - since November 2000: recurrent unilateral follicular conjunctivitis
 - July 2001: tick bite, no EM or associated S+
 - April 2002: Lyme serology +
 - doxycycline for 3 months
- Is it a proven manifestation of LD ??
- If yes is it an appropriate treatment (duration, oral administration) ??

Lyme disease

« The beginning of wisdom is to call things by their right names »

- Misuse of language:-LD the great imitator
 - S+ compatible with LD
 - Chronic LD, post Lyme syndrome

Clinical phases

- Early
 - localized: -EM, associated S+
 - disseminated: -EM multiple, as. S+,
heart, neurologic, eyes
- Late disease (>8 w):
 - joint involvement
 - neurologic features
 - acrodermatitis chronica
 - keratitis
- Asymptomatic: > 10 %

North America

Europe

B. burgdorferi

B. afzelii, garinii

<u>Skin</u>	E	-EM inflamed, brief duration	-less inflamed, prolonged
	L	-Acrodermatitis rare	-Acrodermatitis chronica
<u>NS</u>	E	-Meningitis (headache, neck stiffness)	-Radicular pain, pleocytosis
	L	-sensory polyneuropathy	-+ acrodermatitis
		-encephalopathy (cognitive)	-encephalomyelitis (intrathecal Ab)
<u>Cardiac</u>	E	-AV block-subtle myocarditis	- AV block-subtle myocarditis
	L		-dilated cardiomyopathy
<u>Joint</u>	E	-frequent (inflammation)	-less frequent (less inflam)
	L	-treatment-resistant arthritis (autoimmune)	-rare

Steere NEJM 2001

Children // Adults

- Tick bite: -head, neck (C:40%- A:2%)
- Neuroborreliosis: -acute: +++ in Europe (C:28%- A:14%)
(facial palsy, meningitis, optic neuropathy)
-chronic encephalopathy:?
- Arthritis: -knee (rarely temporomandibular)
-no chronic arthritis

Berglund NEJM 1995

Overdiagnosis

<u>Study</u>	<u>N° referred</u>	<u>% LD</u>	<u>% previous LD</u>	<u>% without LD</u>
Mc Reid Ann Inter Med 1998	209	21	19	60
		depression	38	42
		stress	52	45
		adverse ®	53	55
Steere Jama 1993	788 (51% ®)	23	20	57 (CFS, fibromyalgia)

Overdiagnosis

<u>Study</u>	<u>N° referred</u>	<u>% LD</u>	<u>% previous LD</u>	<u>% without LD</u>
Qureshi PIDJ 2002	216	31 arthritis 50% NS 25% EM 22%	18 Ⓡ : 77%	50 79%
Rose Clin Pediatr 1994	227			60
Feder Jama 1995	146	51 (but 25% error Ⓡ)		38

Overdiagnosis

- Ascribing non specific S+ to LD
- Use of protracted courses of antibiotic therapy for persistent S+ in patients with previous LD
- Most patients unresponsive to antibiotic therapy do not have LD but other disease (fibromyalgia)
- Serologic tests should be used only to confirm a well formulated clinical suspicion of LD

Early disease

- EM



- Associated S+ (“Flu-like”) : malaise, fatigue, fever, arthralgias, myalgias, lymphadenopathy but no pulmonary or gastrointestinal S+
- Neuroborreliosis: lymphocytic meningitis, cranial neuropathy (PFP), radiculoneuritis, optic neuropathy, myelitis

Lyme meningitis // Aseptic meningitis

	<u>NB (n=14)</u>		<u>AM (n=14)</u>
	PFP (n=7)	LM(n=7)	
Age	9.7	7.7	6.3
Duration	1.3 (1-3)	15 (3-30)	1.8 (1-4) *
Fever	(+)	(+)	++
Neck stiffness	(+)	(+)	+(+)
EM	1	3	0
CSF findings			
WBC	265 (36-638)	396 (100-960)	557 (16-2680)
Neutrophils (%)	5.3 (0-10)	2.4 (0-10)	54.6 (11-90) *
Protein (g/l)	0.55	1.12	0.42 *

* p < 0.005

Late disease

- Distinction between Lyme arthritis, encephalopathy or polyneuropathy from CFS or fibromyalgia which may develop with or soon after LD or rheumatoid arthritis .
- “Chronic LD”:- patients with non specific musculoskeletal and/or neurological S+(fatigue, malaise, memory disorder, arthralgia) in association with positive Lyme serology
 - patients with non specific S+ after treatment of documented LD: “post Lyme syndrome”

Post-Lyme syndrome

- Seltzer :
 - community-based longitudinal cohort study
(678 P, 64% met CDC criteria, 86% treated)
 - matched cohort study (212)
 - median 51 months (15-135) after diagnosis
 - self-reports S+, daily activities, functional status measure
- ⇒ 69% of patients had S+ (fatigue, pain) or difficulties with daily activities with the greater frequency in the group that did not meet the case definition
- ⇒ frequencies of S+ similar between the groups

Post-Lyme syndrome

- Shadick:
 - population-based retrospective cohort study
 - 186 previous (6y) treated LD - 167 controls
 - medical history, physical examination, neurocognitive tests, functional status

⇒ Patients with previous LD had more S+ (joint pain, memory impairment) and poorer functional status due to pain than controls BUT on physical examination there were no differences in musculoskeletal or neurologic abnormalities or cognitive performance

Ann Intern Med 1999

Late disease

- Steere (1987) :55 patients EM →20% no manifestation LD
others: arthritis - chronic synovitis (60%), musculoskeletal pain, neurologic abnormalities (11%)
- Szer (1991) : 46 children (EM,arthralgia) →
arthritis (median 3,4 m) (knee 98%)
2 keratitis, 2 encephalopathy (>10 y)

Joint involvement

Adults

- 60% untreated patients with previous (mean 6 months) LD (Steere,1987)
- asymmetric mono or oligoarticular arthritis (large joint, sometime temporomandibular): joint are swollen -warm but mildly painfull
- higher borrelia-specific antibody titers
- treatment resistant-arthritis (10%): arthritis persits (knee) despite antibiotic therapy and negative PCR in synovium or joint fluid (HLA DRB1-0401, auto-immune)

Joint involvement

Children

- Untreated LD:
(Szer NEJM 1991)
 - attacks of arthritis (knee 98%) (1-3w)
 - 2 w to 2 y (median 3,4 months)
after the onset of disease
 - ↓recurrence each year
 - >10y follow-up no chronic arthritis but 30%
had arthralgia and 2 patients encephalopathy
- Treated LA:
Gerber Pediatrics 1998
 - follow-up 2-12y: no evidence of active
arthritis

Neurologic involvement

Adults

-Chronic axonal polyneuropathy (radicular pain, distal paresthesias)

-NA: encephalopathy (memory impairment, intrathecal antibodies,
response to IV ceftriaxone) *(Logigian NEJM 1990)*

-Europe: encephalomyelitis (spastic paraparesis, cranial neuropathy,
cognitive impairment, marked intrathecal antibodies)
(Oschmann J Neurol 1998)

Neurologic involvement

Children

- Cognitive effects: patients appropriately treated for LD have no long-term (4 y follow up) deterioration in cognitive function
(Prospective blinded control study; Adams Pediatrics 1994, Appl Neuropsychol 1999)
- A few cases of encephalopathy occurred in children with previous LD (memory impairment, ↓school performance, fatigue, intrathecal antibodies, improvement after ceftriaxone) *(Szer NEJM 1991, Bloom PIDJ 1998)*

Summary

- LD is a clinical diagnosis based on explicit evidence of the disease and should never been a diagnosis of exclusion specially when late disease is suspected
- Misuse of language and physician reliance on serologic rather than clinical evidence of the disease induce major pitfalls in the diagnosis

Summary

- Long-term outcomes of patients with LD treated with appropriate antibiotic therapy is excellent but many patients had persisting S+ (fatigue, pain) misinterpreted by patients or physicians as recurrent LD or post Lyme syndrome: these patients are unresponsive to antibiotic therapy

Case report

- Has G. Lyme disease ?
- No:
 - tick bite after 1^o symptoms
 - not a proven manifestation of LD
 - serology: Ig G: 56; Ig: M - (Elisa)
 - control (Mont-Godinne): Ig G and Ig M -
- If yes: would it be the appropriate treatment ?
 - ⇒See after coffee break