Are Hepatitis C and Lyme Chronic Diseases?

Chronic Disease Symposium
Dr. Galbraith
November 8, 2019
Spotted Lanternfly (Lycorma delicatula)
Hepatitis C
A Chronic Disease?

• Need not be if...
  • Diagnosed
  • Treated

• Why Treat?
  • 8000-13000 deaths/year in USA
  • Major reason for liver transplantation
Hepatitis C Virus

Background

• Identified 1989 as small RNA blood-borne virus

• Worldwide reservoir

• 6 Major Genotypes with subtypes
  • Each genotype has 30% or more difference at nucleotide levels giving viral diversity
# Hepatitis C Virus Genotype Distribution

<table>
<thead>
<tr>
<th>Location</th>
<th>Genotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>North America/Europe</td>
<td>1,2,3</td>
</tr>
<tr>
<td>Asia</td>
<td>1,2,3,6</td>
</tr>
<tr>
<td>Africa/Middle East</td>
<td>4</td>
</tr>
<tr>
<td>South Africa</td>
<td>5</td>
</tr>
</tbody>
</table>
Hepatitis C
Acute Infection

• Symptoms of fever, malaise occur in 6-7 weeks
  • Jaundice is rare
  • 80% are asymptomatic

• Lab Studies
  • ALT elevation may occur 4-12 weeks
  • HCV RNA appears at 1-3 weeks
  • HCV antibody appears at 8-9 weeks
Hepatitis C

- 15% Spontaneous remission
- 85% Chronic liver disease
  - 15-55% cirrhosis @ 20 years
### Hepatitis C Risk Factors

<table>
<thead>
<tr>
<th>Mode of Transmission</th>
<th>Transmission Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transfusion</td>
<td></td>
</tr>
<tr>
<td>• Clotting factors before 1987</td>
<td>85%</td>
</tr>
<tr>
<td>• Blood products before July 1992 after</td>
<td>5%</td>
</tr>
<tr>
<td></td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Organ Transplants</td>
<td></td>
</tr>
<tr>
<td>• Before July 1992</td>
<td>5%</td>
</tr>
<tr>
<td>• Seropositive organs</td>
<td>UNK</td>
</tr>
<tr>
<td>IVDU</td>
<td>80%</td>
</tr>
<tr>
<td>Sexual Contacts</td>
<td></td>
</tr>
<tr>
<td>• Multiple partners</td>
<td>6%</td>
</tr>
<tr>
<td>• Single</td>
<td>3%</td>
</tr>
<tr>
<td>Needle stick</td>
<td>2%</td>
</tr>
<tr>
<td>Infant with Infected mother</td>
<td>&lt;7%</td>
</tr>
</tbody>
</table>
Hepatitis C Virus
Screening Strategies

• Baby Boomers
  • esp. Vietnam Vets - Experimentation without addiction
• Old tattoos/piercings
• Prior incarcerations
• HBV or HIV disease
• Body fluid exposures
• Unexplained ALT/AST elevations
• Standard risk factors
Hepatitis C Screening

Who?
• Anyone with risk factors - even if ALT/AST normal

How?
• Serum HCV antibody - if reactive confirm with quantitative HCV PCR

Remember:
HCV Antibody Positive + HCV PCR Negative =
Prior exposure and resolution
or
False positive antibody test
Chronic Hepatitis C Timeline

• Rapid Progressors
  • Stage 4 Fibrosis (cirrhosis) 10 years

• Intermediate Progressors
  • Stage 4 Fibrosis 30 years

• Slow Progressors
  • Stage 2-3 Fibrosis 50 years
Chronic Hepatitis C
Decompensation with Cirrhosis

• Ascites

• Portal hypertension, Variceal bleeding

• Encephalopathy

• Hepatocellular carcinoma
  • 3% year after dx
Chronic Hepatitis C
Extrahepatic Manifestations

• Hematologic
  • Cryoglobulinemia
  • Aplastic anemia
  • Thrombocytopenia
  • B-cell lymphoma

• Renal
  • Nephrotic syndrome
  • Glomerulonephritis
Chronic Hepatitis C
Extrahepatic Manifestations

• Dermatologic
  • Vasculitis
  • Porphyria cutanea tarda
  • Lichen planus

• Endocrine
  • Insulin resistant diabetes
  • Antithyroid antibodies

• Misc.
  • Sialadenitis
  • Uveitis
  • Corneal ulcer
Chronic Hepatitis C
Risks for Disease Progression

• Male
• Acquisition over age 40
• Co-infection HIV, HBV
• Duration of disease
• Immunosuppression
• Over 2 drinks of alcohol daily
<table>
<thead>
<tr>
<th>Host</th>
<th>Virus</th>
<th>Environment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Genotype</td>
<td>ETOH</td>
</tr>
<tr>
<td>Age</td>
<td>High Viral Load</td>
<td>IVDU</td>
</tr>
<tr>
<td>Genetics</td>
<td></td>
<td>HIV, HBV</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NASH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immunosuppression</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Chronic Hepatitis C
Treatment Targets

• NS 5A Inhibitors
  • Protein required for viral replication

• NS 5B Inhibitors
  • RNA Polymerase

• NS 3/4A Inhibitors
  • Protease required for viral replication
Chronic Hepatitis C
Common Treatment Regimens

Ledipasvir (NS 5A)/ Sofosbuvir (NS 5B)
(Harvoni)

Glecaprevir (NS 3/4A)/Pibrentasvir (NS 5A)
(Mavyret)
Chronic Hepatitis C Barriers to Treatment

- Undiagnosed
- Patient
  - Alcohol and drug use
  - Uncontrolled HIV, HBV
  - Non-compliance
    - Behavioral issues
    - Lack of social support
- Financial
  - Drug Costs 26k-100k
  - No insurance overage
  - High co-pays
  - Formulary benefit plans
Chronic Hepatitis C
Does Treatment Work?

95% sustained viral response

- Halt disease progression? Yes
- Reverse disease damage? Maybe
- Provide immunity? Probably not
Emerald Ash Borer
Lyme Disease
History

• 1909 Afzelius (Europe)
  • Correlates tick bite with erythema migrans

• 1921 Lipshitz (Europe)
  • Identifies Ixodes ricinus as vector

• 1940’s in Europe
  • EM associated with neurologic and dermatologic conditions

• 1948 Lenhoff (Europe)
  • Spirochete-like structures in skin bx of EM
Lyme Disease
History

• 1970 Scrimenti (Wisconsin)
  • First documented EM case in USA

• 1970’s Steere (Connecticut)
  • EM associated with arthritis
  • Children and adults in Old Lyme, CT

• 1982 Burgdorfer
  • Isolated new borrelia species
## Lyme Disease Agents

<table>
<thead>
<tr>
<th>Agent</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Borrelia burgdorferi</td>
<td>USA, Europe</td>
</tr>
<tr>
<td>Borrelia afzelli</td>
<td>Asia, Europe</td>
</tr>
<tr>
<td>Borrelia garinii</td>
<td>Asia, Europe</td>
</tr>
</tbody>
</table>

## Relapsing Fever Agents

<table>
<thead>
<tr>
<th>Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Borrelia miyamotii</td>
</tr>
<tr>
<td>Borrelia hermsii</td>
</tr>
<tr>
<td>Borrelia recurrentis</td>
</tr>
</tbody>
</table>
Tick Borne Diseases

The Asian longhorned tick has been reported in nine states.
Lyme Disease
Vectors (Tick)

<table>
<thead>
<tr>
<th>Species</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ixodes scapularis</td>
<td>USA East Coast</td>
</tr>
<tr>
<td>“deer tick” “black-legged tick”</td>
<td></td>
</tr>
<tr>
<td>Ixodes dammini</td>
<td>USA East Coast, Midwest</td>
</tr>
<tr>
<td>Ixodes pacificus</td>
<td>USA West Coast</td>
</tr>
<tr>
<td>Ixodes ricinus</td>
<td>Europe</td>
</tr>
<tr>
<td>Ixodes persulcatus</td>
<td>Asia</td>
</tr>
</tbody>
</table>
Lyme Disease

Reservoirs
• Rodents
• Fowl

Disseminators
• White-footed mice
• White-tailed deer
Lyme Disease
Blood Tests

• Screening for any antibody

• Western blot specific molecular weight antibodies

• Specific $C_6$ peptide antibody (IgG)

• Blood smears for borrelia on RBC’s
  • Not standardized
Lyme Disease Tests

• CSF-RNA PCR

• Synovial Fluid-RNA PCR

• Skin biopsy- borrelia difficult to visualize
Lyme Disease
Antibodies

• May stay reactive for life
  • Sequential testing not useful

• Indicate exposure not immunity

• May not help with re-infection

• Some people don’t develop good antibody response

• Take time to develop
Lyme Disease

Common Symptoms

- Constitutional
  - Fatigue, headache, anorexia, fever
- Neurologic
  - Dysesthesias, weakness
- CNS
  - Bell’s Palsy, ataxia, cognitive impairment
- Cardiac
  - Bradycardia, heart block, palpitations
- Orthopedic
  - Arthritis, arthralgia, myalgia
- Dermatologic
  - Rashes
Lyme Disease
Stages

• Early
  • EM within one month

• Early disseminated
  • Cardiac, Neurological

• Late
  • Arthritis, CNS involvement
Lyme Disease
Standard Antibiotic Therapies

• Oral for 14-28 days
  • Doxycycline 100mg B.I.D.
  • Ampicillin 1000mg B.I.D.
  • Cefuroxime 500mg B.I.D.

• IV for 21 days
  • Penicillin 20,000,000 units daily
  • Ceftriaxone 2gm daily
Lyme Disease
Causes for Chronic Disease

• Undiagnosed
  • Alternative diagnosis
  • Seronegative *

• Treatment failure
  • Borrelia related
    • Dormant phase *
    • Resistant *

* Controversial
Lyme Disease
Causes for Chronic Disease

• Antibiotic related
  • Poor tissue penetration *
  • Poor GI absorption

• Patient related
  • Allergic to antibiotics
  • Poor compliance
  • Co-morbid conditions
  • Co-infections

* Controversial
Lyme Disease
Recurrent Symptoms Post Treatment

• Relapse due to inadequate initial Rx

• Reinfection

• Post Lyme Syndrome

• Co-morbid conditions
Lyme Disease
Post-Lyme Syndrome

• Persisting symptoms after treatment
• Damage from initial infection
Lyme Disease
Chronic Symptoms 6 months After Treatment

Post-Lyme Syndrome
vs
Unremitting Infection
plus
Co-morbid conditions
Lyme Disease
Treatment Controversies

• Multiple antibiotics

• Duration of antibiotics

• Complimentary therapies

• Symptomatic therapies