Pretreatment Evaluation
Disclosures

- Research supported by Gilead Sciences Inc.:
  - Site investigator for HIV/HCV SWITCH Registry Study
  - Key personnel for FOCUS HCV Screening Program through Vanderbilt University Medical Center Emergency Department
Objective

At the end of this lecture, the learner will be able to:

- Outline the appropriate evaluation of a person infected with HCV in order to assess the benefits and risks of treatment and in anticipation of treatment with direct acting antiviral therapy.
Two Stories

Beth
- Young woman with two children
- Alcohol use
- Intravenous drug use
- Elevated liver function tests
- HCV antibody and RNA positive

Charles
- Older man with comorbidities
- Rare alcohol use
- No drug use
- Elevated liver function tests and low platelets
- HCV antibody and RNA positive
Questions

- How do we determine how HCV has impacted each patient?
- How do we assess liver disease and comorbidities to inform clinical care and HCV treatment?
- How do we reduce harm while moving towards treatment?
Targeted History and Exam

**History**

- Disease History
  - When? How? Why?
  - Prior Staging
  - Prior Treatment
- Symptoms of chronic HCV infection:
  - Fatigue
  - Arthralgias
  - Chronic abdominal pain
  - Insomnia
  - *Many patients are asymptomatic!*
- Symptoms of advanced liver disease:
  - Upper GI bleeding
  - Ascites
  - Hepatic encephalopathy
  - Liver failure
- Medication History
- Alcohol Use History
- Substance Use History

**Physical**

- *May be normal without evidence of disease!*
- Focus on stigmata of chronic liver disease:
  - Palmar erythema
  - Spider nevi
  - Gynecomastia
  - Jaundice
  - Ascites
  - Asterixis
  - Encephalopathy
- Evaluate for stigmata of injection drug use
  - Track marks
  - Thrombophlebitis
  - Skin scarring

Suggested Laboratory Testing

- HCV RNA & Genotype
  - Therapy options
- CBC
  - Evaluate cell lines
- CMP
  - Including LFTs and albumin
- PT/INR
  - Check synthetic function
- HAV and HBV testing
  - Rule out coinfection
  - Evaluate vaccination status
- HIV testing
  - Rule out co-infection
- Vitamin D
  - Often low in patients with HCV
- Urine drug screen
  - Evaluate for ongoing drug use
- Consider:
  - Hemoglobin A1C
    - Evaluate for metabolic disease
  - ANA screen
    - Evaluate for autoimmune disease

Original Research

Hepatitis B Virus Reactivation Associated With Direct-Acting Antiviral Therapy for Chronic Hepatitis C Virus: A Review of Cases Reported to the U.S. Food and Drug Administration Adverse Event Reporting System

Susan J. Bersoff-Matcha, MD; Kelly Cao, PharmD; Mihaela Jason, PharmD; Adebola Ajao, PhD; S. Christopher Jones, PharmD, MS, MPH; Tamra Meyer, PhD, MPH; and Allen Brinker, MD, MS

Published June 6, 2017
Case Series

- 29 cases reported from 11/2013 – 10/2016
  - 13 occurred in patients with positive sAg
  - 4 occurred in patients with negative sAg
  - 12 occurred with unknown baseline sAg status
- 2 deaths and 1 liver transplant
- Resulted in boxed warning with all DAA therapies
Treating HCV In Setting of HBV

- Treat HBV based on guideline recommendations

- Consider closer monitoring of HBV and associated liver disease while on DAA therapy if not on anti-HBV treatment
QUESTION REGARDING STAGING
Hepatitis C Online

Evaluation and Staging of Liver Fibrosis

Lesson Overview  PDF  Share

Last Updated: October 21st, 2015
Authors: Paula P. Cox-North, ARNP, Margaret C. Shuhart, MD, MS

You can always find the most up to date version of this document at https://www.hepatitisc.uw.edu/go/evaluation-staging-monitoring/evaluation-staging/core-concept/all
What Is Liver Fibrosis?

- Chronic inflammation stimulates production of collagen and additional proteins
- Hepatic stellate cells recruited to produce extracellular matrix proteins
- As collagen and protein is deposited, fibrosis develops
- May remodel and regress depending on additional enzymes
## METAVIR Scoring

<table>
<thead>
<tr>
<th>Score</th>
<th>Pathologic Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No fibrosis</td>
</tr>
<tr>
<td>1</td>
<td>Periportal fibrosis</td>
</tr>
<tr>
<td>2</td>
<td>Periportal septae</td>
</tr>
<tr>
<td>3</td>
<td>Bridging fibrosis (portal-central septae)</td>
</tr>
<tr>
<td>4</td>
<td>Cirrhosis</td>
</tr>
</tbody>
</table>
Staging Liver Disease

- Importance of Staging
  - Identify patients with greatest need for therapy
  - Identify patients for cirrhosis-specific care
  - Triage resources

- Types of Staging
  - Liver biopsy
  - Biomarkers
  - Elastography
Liver Biopsy To Stage Liver Fibrosis

- Gold standard
- May be helpful in evaluating other causes of liver disease
- Results may be impacted by quality of specimen (i.e. length of biopsy)
- Limited by invasive nature of test, cost, and access to proceduralist
Indirect Markers of Liver Fibrosis

- Ideally would allow staging of liver disease without invasive procedures or specialized imaging
- Multiple scoring systems and proprietary tests available but vary in utility
- All perform better on the “extremes” (i.e. no fibrosis vs. cirrhosis rather than intermediate stages)

APRI
- AST-To-Platelet Ratio Index
- \([(\text{AST}/ \text{ULN})/\text{PLT}] \times 100\)
- Sens 76% and Spec 72% at cutoff of 1.0 for predicting cirrhosis
- Sens 46% and Spec 91% at cutoff of 2.0 for predicting cirrhosis

FIB-4 Index
- Age x AST / [PLT x (ALT)\(^{1/2}\)]
- Negative predictive value 90% for advanced fibrosis if <1.45
- Positive predictive value 65% and specificity 97% for advanced fibrosis if >3.25

Fibrosure®
- Multiple known inputs and proprietary equation
- Recognized by many payers
Elastography

- Measures mechanical shear wave velocity, which is proportional to liver stiffness
- Multiple methods (transient, magnetic resonance, acoustic radiation force impulse)
- May be a reasonable alternative to biopsy
Notes About Anatomic Imaging

- Anatomic imaging (i.e. ultrasound, CT, MRI) are NOT adequate for staging
  - However, if advanced fibrotic changes are present, they likely correlate with tissue pathology
- Appropriate for hepatocellular carcinoma monitoring
- Reasonable to consider in any patient undergoing HCV evaluation with unknown or suspected advanced fibrosis
EXAMPLE OF A CHALLENGING CASES WITH LIMITED DATA...
Example Case: Beth

- 22 y/o woman with PMH of injection drug use, likely infected within past three years, presents for HCV evaluation.
- ALT 80, AST 55, Plt 200
- Additional elastography/imaging not available
- APRI 0.688
  - Not high enough to reliably rule in advanced fibrosis; however, APRI is not effective for ruling out advanced fibrosis
- FIB-4 0.68
  - As score <1.45, very unlikely to have advanced fibrosis (90% negative predictive value)
Different Numbers…

- 22 y/o woman with PMH of injection drug use, likely infected within past three years, presents for HCV evaluation.
- ALT 360, AST 180, Plt 150
- Additional elastography/imaging not available
- APRI 3.0
  - Specificity of 91% in studies but may not apply to this patient
- FIB-4 1.39
  - As score <1.45, very unlikely to have advanced fibrosis (90% negative predictive value)
  - Age drives prediction
Different Age…

- 55 y/o woman with PMH of injection drug use, likely infected within past three years, presents for HCV evaluation.
- ALT 80, AST 55, Plt 200
- Additional elastography/imaging not available
- APRI 0.688
  - Not high enough to reliably rule in advanced fibrosis; however, APRI is not effective for ruling out advanced fibrosis
- FIB-4 1.69
  - Indeterminate
55 y/o woman with PMH of injection drug use, likely infected within past three years, presents for HCV evaluation.

ALT 360, AST 180, Plt 150

Additional elastography/imaging not available

APRI 3.0
  - Specificity of 91% in studies but may not apply to this patient

FIB-4 3.48
  - 97% specificity and 67% positive predictive value for advanced fibrosis
Interventions to Reduce Progression of Liver Disease

- Immunization for Hepatitis A and B
- Alcohol abstinence
- Appropriate acetaminophen use
- Avoiding NSAIDs
Counseling to Reduce Transmission of HCV

- Avoid blood borne exposure
  - Shared personal devices such as razors or nail clippers
  - Barrier protection for intimate contact
  - Safer approaches to injection drug use
QUESTIONS?