Chronic Hepatitis and Liver Disease

- HCV
- HBV (and delta)
- Other forms
- HIV coinfection

Case: Hepatitis C and a rash

A 44 year old, anti-HCV and HCV RNA positive man feels bad after a recent alcohol binge. He has a chronic rash on arms that is worse and elevated ALT and AST.

Question: HCV with a rash

The most likely dx is:

A. Cirrhosis due to HCV and alcohol
B. Necrolytic acral erythema
C. Porphyria cutanea tarda
D. Essential mixed cryoglobulinemia
E. Yersinia infection

Porphyria Cutanea Tarda Associated with Hepatitis C

Tysh S. Pulic, M.D., and Eugenio Teteria Mohammed, M.D.

June 10, 2021

©2021 Infectious Disease Board Review, LLC
**39 – Chronic Hepatitis**

*Speaker: David Thomas, MD*

**Porphyria cutanea tarda**

**Cryoglobulin vasculitis**

**Lichen planus**

**Compare**

**Case: HBV and rash**

46 year old woman HBsAg pos, anti-HCV neg

**Question: HBV with a rash**

The most likely dx is:

A. Necrolytic acral erythema
B. Porphyria cutanea tarda
C. Essential mixed cryoglobulinemia
D. Polyarteritis nodosa
E. Secondary syphilis vasculitis

**Question: Who needs an HCV antibody test?**

A. 33 year old woman with normal ALT and negative test during pregnancy at 28
B. 55 year old man with new exposure after HCV treatment
C. 24 year old pregnant woman with no risk factors
D. Former PWID who was HCV negative 1 yr ago
E. HIV positive MSM with negative HCV antibody test 5 years ago and no risk factors

**IDSA/AASLD guidelines**

Recommendations for One-Time Hepatitis C Testing

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>NOT RECOMMENDED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Checking, routine, spot or HCV testing is recommended for all individuals aged 18 years and older.</td>
<td>Checking, routine, spot or HCV testing should be performed for all persons less than 50 years old with diabetes, chronic kidney disease, chronic liver disease, or some risk factors for HCV infection (see below).</td>
</tr>
<tr>
<td>Recommended for all persons who inject drugs, or have risk factors for HCV exposure (see below).</td>
<td>No, O</td>
</tr>
</tbody>
</table>

**USPSTF 2020**

Recommendation: The USPSTF recommends screening for HCV infection in adults aged 18 to 79 years. (B recommendation)

**Case: 54 y/o with HCV antibodies and RNA**

54 year old man was anti-HCV pos after elevated ALT noted by primary. Brief IDU when 20-21; moderate ETOH; otherwise well.

HCV RNA 4 million IU/L; Genotype 1a; ALT 42 IU/ml; AST 65 IU/ml; TB 1.6 mg/dl; Alb 3.9 mg/dl; Hb – 13.4 mg/dl; creatinine 1.2 mg/dl; HBsAg pos; anti-HBc pos. HIV neg

©2021 Infectious Disease Board Review, LLC
Question: 54 y/o with HCV antibodies and RNA
Which of the following is the next appropriate step:
A. Treat with oral regimen for 8-12 weeks
B. Check HCV 1a resistance test
C. Elastography
D. Confirm HCV antibody test

**Chronic Hepatitis**
Speaker: David Thomas, MD

**HCV NS5 RAS testing is uncommonly recommended**

<table>
<thead>
<tr>
<th>Treatment naive</th>
<th>Treatment experienced</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Genotype 1a and elbasvir/grazoprevir</td>
<td>• 1a and ledipasvir/sofosbuvir ‘considered’</td>
</tr>
<tr>
<td>• Genotype 3 AND cirrhosis for sofosbuvir/velpatasvir</td>
<td>• Genotype 3 and sofosbuvir/velpatasvir</td>
</tr>
</tbody>
</table>

NB: no PI resistance testing
Clinically sig is >100-fold in vitro
Wyles, HCVguidelines.org

**Staging is needed for chronic HCV**

**Accepted staging methods**
1. Liver biopsy
2. Blood markers
3. Elastography
4. Combinations of 1-3

**Not for routine staging**
1. Viral load
2. HCV genotype
3. Ultrasound
4. CT scan or MRI

Hcvguidelines.org

**Of imperfect tests elastography is most sensitive for detection of cirrhosis**

<table>
<thead>
<tr>
<th>Test</th>
<th>% Sens</th>
<th>% Spec</th>
<th>AUROC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrotest™ &gt; .56</td>
<td>85</td>
<td>74</td>
<td>.56</td>
</tr>
<tr>
<td>Fibrotest &gt; .73</td>
<td>56</td>
<td>81</td>
<td>-</td>
</tr>
<tr>
<td>FIB4® &gt; 1.45</td>
<td>87</td>
<td>61</td>
<td>.87</td>
</tr>
<tr>
<td>APRI® &gt; 1.5</td>
<td>51</td>
<td>91</td>
<td>0.73</td>
</tr>
<tr>
<td>Elastography 12.5 kPa</td>
<td>89</td>
<td>91</td>
<td>0.93</td>
</tr>
</tbody>
</table>


**Case con’t: 54 year old with HCV**

Elastography (17.3 kPa) and Fib-4 (5.5) consistent with cirrhosis. Ultrasound and UGI are ok and you recommend treatment. He wants to know why. Which can you NOT say is true of successful treatment?
A. reduces risk of reinfection
B. reduces risk of death
C. reduces risk of HCC
D. reduces risk of liver failure

©2021 Infectious Disease Board Review, LLC
SVR reduces clinical outcomes


SVR reduces clinical outcomes


SVR reduces clinical outcomes


SVR reduces clinical outcomes


54 y/o with HCV antibodies, RNA, and cirrhosis

Treatment is given with glecaprevir and pibrentasvir

Treatment week 8: HCV RNA undet; ALT 1279 IU/L; AST 987 IU/L; TB 3.2 mg/dl.

Which test is likely to be most helpful?

A. Glecaprevir level
B. HCV resistance test
C. HCV IRIS T cell marker
D. HBV DNA
E. Liver biopsy with EM

©2021 Infectious Disease Board Review, LLC
Which is NOT a pangenotypic regimen?

A. Glecaprevir and pibrentasvir
B. Sofosbuvir and velpatasvir
C. Sofosbuvir and ledipasvir

Which regimen is approved for ESRD?

A. Glecaprevir and pibrentasvir
B. Sofosbuvir and velpatasvir
C. Sofosbuvir and ledipasvir
D. Elbasvir and grazoprevir
E. All of the above

Which regimen is worst with darunavir?

A. Glecaprevir and pibrentasvir
B. Sofosbuvir and velpatasvir
C. Sofosbuvir and ledipasvir

HCV treatment summary 2021

- Test, stage, and treat
- Two pangenotypic regimens: SOF/VEL and GP
- Watch for HBV relapse at week 8
- No change for HIV (avoid drug interactions), renal insufficiency, acute infection, cirrhosis

Case of chronic hepatitis B

31 yr old Asian woman is referred to see you because she had a positive HBsAg test. She is otherwise feeling fine.

HBsAg pos, HBeAg neg, anti-HBe pos, ALT 78 IU/ml, AST 86 IU/ml, TB 0.8, albumin 4.2 g/dl, INR 1.
Which of the following tests is NOT recommended?

A. HIV test
B. HBV resistance
C. HBV genotype
D. Hepatitis Delta testing
E. Quantitative HBV DNA level

The essential evaluation of persons with CHB

- HBeAg, HIV, HBV DNA, delta, genotype
- Stage (liver enzymes and/or elastography or biopsy)
- Renal status
- US to r/o HCC
  - Asian: male 40; female 50
  - African: 25-30

Use testing to define disease phase

Phase 2
- HBeAg positive: chronic HBV infection
- HBeAg negative: chronic hepatitis B

Phase 1
- HBeAg positive: chronic HBV infection
- HBeAg negative: chronic hepatitis B

Phase 4
- HBeAg positive: chronic HBV infection
- HBeAg negative: chronic hepatitis B

Use disease phase to determine whom to treat

- Treat with both high DNA and ALT

Test pregnant women for HBsAg and, if pos, for HBV DNA* and treat if > 200,000 IU/ml

- Rec for all pregnant women to have quantitative HBV DNA TEST

*test in 3rd trimester

Terrault Hepatology 2015; Pan NEJM 2016
Four preferred treatments for chronic hepatitis B

<table>
<thead>
<tr>
<th>HBV Status</th>
<th>Peg-IFN</th>
<th>Entecavir</th>
<th>TAF 25 mg</th>
<th>TDF 300 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBeAg Positive</td>
<td>20-42 (20-83 ng/mL)</td>
<td>36-63 (36-111 ng/mL)</td>
<td>64 (64-100 ng/mL)</td>
<td>64 (64-100 ng/mL)</td>
</tr>
<tr>
<td>HBeAg Negative</td>
<td>4 (4-8 ng/mL)</td>
<td>0.06-1.92 (0.06-1.92 ng/mL)</td>
<td>0.06-1.92 (0.06-1.92 ng/mL)</td>
<td>0.06-1.92 (0.06-1.92 ng/mL)</td>
</tr>
</tbody>
</table>

TAF 25 mg with or without FTC

AASLD guidelines, Terrault Hepatology 2018

TAF is as effective and safer than tenofovir DF for chronic hepatitis B

Chan Lancet Gastro 2016

Treatment of HBV changes with renal insufficiency

- GFR 30-60 mL/min/1.73 m²: TAF 25 mg preferred
- GFR <30-10: TAF 25 mg or entecavir 0.5 mg q 3d
- GFR <10 no dialysis: entecavir 0.5 mg
- Dialysis: TDF 300 mg/wk PD or entecavir 0.5 mg/wk or TAF 25 mg PD

It is hard to stop HBV treatment

- If HBeAg conversion noted and no cirrhosis consider stopping after 6 months
- HBeAg neg when treatment started and all with cirrhosis stay on indefinitely

HIV/HBV coinfectected need treatment for both

- All are treated and tested for both
- HBV-active ART
- Entecavir less effective if LAM exposure
- Watch switch from TAF- or TDF-containing regimen

What if HBV levels stay detectable?

- Continue monotherapy, ideally with TAF or TDF
- Rising levels (breakthrough)
  - Add second drug or switch esp if initial Rx with ETV

©2021 Infectious Disease Board Review, LLC
You are called about 62 year old Vietnamese scientist who is in oncology suite where he is about to get R-CHOP for Non Hodgkins lymphoma. Baseline labs: normal AST, ALT, and TBili. Total HAV detectable; anti-HBc pos; HBsAg neg; anti-HCV neg.

What do you recommend?
A. Hold rituximab
B. Hold prednisone
C. Entecavir 0.5 mg
D. HCV PCR
E. HBV DNA

Rituximab, high-dose prednisone, and BM transplant high risk for HBV reactivation
- If HBsAg pos, prophylaxis always recommended
- If anti-HBc pos but HBsAg neg, prophylaxis still recommended with high risk exposures
- Use TAF or ETV

Isolated anti-core antibodies usually reflect occult hepatitis B in high risk groups
- Primary responses to vaccination
- 29 anti-HBc and 40 negative for anti-HBc
  - anamnestic response in anti-HBc pos (24%) vs anti-HBc neg (10%)
  - 50% anti-HBc pos also tested positive for anti-HBe
  - Anti-HBs seroconversion in ~60% both groups

HBV vaccination recommended in persons with isolated anti-HBc

Pre-exposure:
- vaccinate and get post vaccination titers (<2 months) if exposure likely

Post Exposure:
- vaccinate if not already done or not known to respond
- add HBIG when infection likely
- infants of HBsAg pos mothers get immediate vaccination and HBIG

HBV Prevention is with vaccine and sometimes HBIG

©2021 Infectious Disease Board Review, LLC
Chronic Hepatitis for the Boards Summary

- HCV-associated conditions: PCT or cryoglobulinemia
- HBV-associated: PAN
- HCV: staging or treatment outcome
- HBV: relapse post rituximab
- Guess b and good luck

Thanks and good luck on the test!

Questions:
Dave Thomas
–dthomas@jhmi.edu

BONUS CASE

A final case of chronic hepatitis in transplant recipient

51 y/o HTN, and ankylosing spondylitis s/p renal transplant presents with elevated liver enzymes. Pred 20/d; MMF 1g bid; etanercept 25mg twice/wk; tacrol 4mg bid. Hunts wild boar in Texas. HBsAg neg, anti-HBs pos, anti-HBc neg; anti-HCV neg; HCV RNA neg; CMV IgG neg; EBV neg; VZV neg. ALT 132 IU/ml, AST 65 IU/ml; INR 1. ALT and AST remained elevated; HBV, HCV, HAV, CMV, EBV serologies remain neg.

Which test is most likely abnormal

1. HEV PCR
2. HCV IgM
3. Tacrolimus level
4. Adenovirus PCR
5. Delta RNA PCR

Chronic HEV in transplant recipient

- Europe (boar)
- Can cause cirrhosis
- Tacrolimus associated
- Ribavirin may be effective

©2021 Infectious Disease Board Review, LLC