Acute Hepatitis C Virus (HCV) Infection in Patients with HIV

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Slide 2 of 30

Financial Relationships With Commercial Entities

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Slide 3 of 30

Learning Objectives

After attending this presentation, participants will be able to:
- Identify patients at risk for acute HCV
- Test for and monitor acute HCV appropriately
- Consider current acute HCV guideline recommendations in management of patients
Introduction

• Acute hepatitis C virus (HCV) infection is defined as the initial 6 months of infection.
• Acute HCV infection is frequently a missed or delayed diagnosis because largely asymptomatic
  – Fewer than 20% of patients have characteristic symptoms
    • I.e., low-grade fever, right upper-quadrant pain, nausea, vomiting, anorexia, dark urine, and jaundice.
  – Unexplained elevations in transaminases may be the only laboratory finding
• Knowing how to recognize and effectively treat HCV in the acute stage of infection is key to preventing liver-related morbidity and mortality in patients with HIV infection and decrease the risk of HCV transmission to susceptible hosts.

Case

• 34 year old male with HIV on TDF/FTC/rilpivirine with CD4 400 cells/mm³ and HIV RNA undetectable, a history of syphilis treated one year ago, and active crystal methamphetamine use (not IV). He often has sex with men while taking this drug and does not always use condoms.
• Labs 4 months ago showed a normal CBC, hepatic function panel.
• Labs 9 months ago showed HAV Ab+, HBV sAg−, HBV sAb+, and HCV Ab−.
• He is without complaints and feels well.

The practitioner decides to test him for syphilis and other sexually transmitted infections (STIs). He has no signs or symptoms that suggest viral hepatitis. Should he also be tested for HCV infection?

81% 1. Yes
19% 2. No
IS HE AT RISK? Acute HCV in Patients with HIV

- Since 2000, epidemics of acute HCV infection in HIV-infected men who have sex with men (MSM) have been reported, predominantly in Western Europe, Australia, and the United States.

- Certain sexual risk behaviors have been hypothesized to be associated with the acquisition of acute HCV infection in this population:
  - unprotected anal intercourse, fisting, enema use, bleeding during intercourse, and non-injection drug use

- Prior to 2000, hepatitis C was thought to have a very low risk of sexual transmission (less than 1% of all documented hepatitis C infections) and was not considered to be a sexually transmitted illness.

- The CDC now estimates that sexual transmission currently accounts for approximately 15% of all HCV infections.

Reported Cases of Acute HCV by Year

- 2013 DATA: Incidence still rising. A total of 2,138 cases of acute hepatitis C were reported from 41 states. After adjusting for under-ascertainment and under-reporting, an estimated 20,718 acute hepatitis C cases occurred in 2013.
Acute HCV Cases Are Increasing in Young Persons

- CDC surveillance study examined trends in incidence of acute hepatitis C among young persons (aged ≤30 years) reported 2006-2012 by state, county, and urbanicity.
- Did not collect information on HIV status or sexual practices.
- Among young persons w/ acute hepatitis C, 31% resided in nonurban and 67% in urban counties.
  - 52% female, 95% white, 77% reported h/o IVDU
- Incidence significantly increased – 13% per year with an overall 170% increase from 2006 to 2012 in nonurban counties (P = .003).
  - 5% per year among urban counties

Sexual transmission of HCV may also be seen in HIV-negative MSM

Retrospective analysis of HIV-negative MSM who sought care at a London STI clinic from 2010-14 (during which estimated 261K attendances)

Findings:
1. Low rate of screening: 15% tested for HCV (estimated # screened ~35K)
2. Identified 44 cases of acute HCV infection
   - 50% reported any recreational drug use
   - 36% reported intranasal use and 21% injection drug use
   - 93% in unprotected anal intercourse and 49% in group sex
   - 30% individuals had a coexisting STI at the time of AHC diagnosis

Larger, prospective cohort data are needed to further clarify the incidence and prevalence of hepatitis C in MSM without HIV infection.
Should we screen HIV+ MSM for acute HCV?

- Screening for acute HCV infection in HIV-infected MSM prolongs life expectancy and is cost-effective (caveat...IFN+PI era modeling study).

- Limitations of HCV Ab for screening:
  - Typically negative during the "window period", which ranges from 2 weeks to 12 weeks after infection.
  - HCV antibody serconversion can be delayed in HIV-infected individuals, with only 2/3 positive at 3 months, and 5% remaining negative up to 1 year after infection.
  - Those who have cleared previous HCV infection remain HCV antibody positive, making it an unhelpful marker for screening for reinfection.

Which is the most appropriate laboratory test to check if considering acute hepatitis due to HCV infection?

1. HCV antibody test (12%)
2. Plasma HCV RNA level test (69%)
3. HCV genotype test (9%)
4. Hepatic function panel (10%)
Acute HCV Laboratory Timeline

- HCV RNA is first detected in the serum 7 days to 21 days after transmission
- Viremia is followed by an increase in serum transaminase levels 2-6 weeks after infection
- HCV antibody seroconversion typically occurs within 2 weeks to 12 weeks

Criteria for Acute HCV Diagnosis

European AIDS Treatment Network (NEAT) consensus guidelines:
- HCV antibody seroconversion or a positive HCV RNA test result, with negative HCV test results in the previous 12 months
  OR
- A positive HCV RNA test result
  - Accompanied by an acute rise in ALT level beyond a threshold of 10 times the upper limit of normal (ULN)
  - \((5 \times \text{ULN if the ALT level was previously normal within the past 12 months or } 3.5 \times \text{ULN if the ALT level was previously abnormal})\)
  - With exclusion of other causes of acute hepatitis.

Case continued...

- On labs sent the patient was noted to have elevated transaminase levels.
- He was brought in for further testing which revealed: HCV RNA level 420,000 IU/mL and HCV antibody negative.
- Based on these results, the practitioner makes the diagnosis of acute HCV infection.
What is the minimum recommended time the practitioner should wait to begin treatment to allow for spontaneous resolution of HCV infection?

<table>
<thead>
<tr>
<th>Option</th>
<th>Time from Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. 12 weeks from time of presumed exposure to HCV</td>
<td>28%</td>
</tr>
<tr>
<td>B. 12 weeks from time of first laboratory evidence of HCV</td>
<td>45%</td>
</tr>
<tr>
<td>C. 6 weeks from time of presumed exposure to HCV</td>
<td>27%</td>
</tr>
<tr>
<td>D. 6 weeks from time of first laboratory evidence of HCV</td>
<td>20%</td>
</tr>
</tbody>
</table>

Timing of Acute HCV Treatment

- In up to 40% of patients with HIV infection who contract HCV infection, the HCV infection will spontaneously resolve.
- Treatment guidelines uniformly recommend waiting a minimum of 12 weeks from first detection of HCV infection to allow for spontaneous resolution without compromising treatment outcomes (IFN era).
- Predictors of spontaneous resolution include: jaundice, elevated ALT level, HBV SAg seropositivity, female sex, favorable IL28B genotype (CC), and HCV genotype 1.

Timing of Acute HCV Treatment

- As the response rates for treatment of chronic HCV infection begin to approach 100%, treatment may be delayed more than 12 weeks to allow for the occasional late spontaneous resolution.
- Because of limited treatment data with DAAs for acute HCV, newer guidelines (hcvguidelines.org) endorse waiting 6 months when a delay in treatment is acceptable.
Which regimen is the most well studied for treatment of acute HCV infection in the context of HIV coinfection?

- A. Peginterferon alone
- B. Peginterferon alfa plus ribavirin for up to 24 weeks
- C. Peginterferon + telaprevir + ribavirin
- D. Ledipasvir/sofosbuvir

Acute HCV Treatment

- No medications are approved by the US Food and Drug Administration (FDA) to treat acute HCV infection, so the use is off-label.
- While the most experience exists with peginterferon and ribavirin to date, it no longer represents the best treatment option.
- Little data about usage of DAAs in acute HCV. Studies ongoing.
- Current guidelines recommend using the same regimens used for the initial treatment of chronic HCV if the decision is made to treat HCV during the acute period.

Current FDA-Approved Therapies for Treatment

<table>
<thead>
<tr>
<th>GT1 (Genotype 1)</th>
<th>Peg</th>
<th>RBV</th>
<th>SOF</th>
<th>OMV</th>
<th>LDV</th>
<th>DAC</th>
<th>X12w</th>
<th>X12w*</th>
<th>X12w</th>
<th>X12w*</th>
</tr>
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<tbody>
<tr>
<td>GTT efficiency</td>
<td>86%</td>
<td>60%</td>
<td>&gt;95%</td>
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In patients with HIV, it is important to investigate for potential drug interactions between ARVs and the HCV regimen!
Case continued...
The patient chose to defer treatment to see if his acute HCV infection would spontaneously resolve. During the observation period, he committed to safe sex practices and abstinence from drugs.

However, after 6 months, his HCV RNA remained detectable, so he was treated with ledipasvir/sofosbuvir for 12 weeks for chronic HCV infection. His HCV RNA remained undetectable 24 weeks after completing this therapy, reflective of a cure.

On a subsequent follow-up visit, it was learned that he had resumed his prior sexual practices and crystal methamphetamine use.

Which statement is true about this patient’s risk of future HCV infection?

A. The patient is not at risk for future HCV infection because his infection has been adequately treated.

B. The patient is at risk for HCV reinfection because he has an IL28B CC genotype.

C. The patient is at risk for HCV reinfection because of his ongoing high-risk sexual practices.

D. None of these statements is true.

Acute HCV Reinfection

- Patients with ongoing sexual risk factors or IVDU are at risk for HCV reinfection and must continue to be monitored.

- The MOSAIC (MSM Observational Study of Acute Infection with hepatitis C) trial in Amsterdam showed a high incidence of HCV reinfection in HIV-infected MSM who were previously diagnosed with a sexually transmitted acute HCV infection and who were HCV RNA-seronegative following HCV treatment of the acute primary infection.
MOSAIC Study

- Reinfection was defined as a new detectable HCV RNA after successful treatment, accompanied by a switch in HCV genotype or clade.
- The incidence of HCV reinfection in this group was 15.2 per 100 person-years. The cumulative incidence was 33% within 2 years.

Conclusions

• Acute HCV is increasingly recognized among HIV-infected men who have sex with men (MSM) and is linked to recreational drug use and high-risk sexual behaviors.
• Annual testing for HCV is recommended in HIV-infected MSM.
• Guidelines recommend waiting up to 6 months before commencing HCV treatment to allow time for spontaneous clearance.
• If treating during acute period, recommended to use same therapies as for chronic HCV infection (direct-acting antiviral agents).
• Patients that remain at risk for HCV acquisition after treatment should undergo routine testing with at least serial ALT tests and possibly HCV RNA tests.

THANK YOU

Questions?

New York, NY: September 21, 2015