HCV/HIV Co-Infection Overview

Presented by: John Guilfoose, MD
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HCV/HIV Co-infection

• **Themes:**
  • Co-infection is common
  • Increased transmission of HCV
    • HCV as an STI when co-infection present
    • Perinatal
  • Accelerated rates of liver damage (fibrosis)
  • Traditional poor response to HCV treatment
    • **Now optimism** w/ new direct acting antivirals
      • Still challenges w/ drug interactions
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• **Epidemiology**
  • Co-infection with HIV and HCV is common
  • share similar routes of transmission
  • In the United States, approximately 25-30 % of patients who are HIV-infected are also co-infected with HCV

• **Rates differ according to risk factor**
  • Example: HCV seroprevalence in HIV-infected in *intravenous drug users* was 73 percent in one large study
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• **Epidemiology**
  • The *sequence* of infections is often different based on *risk factors*:
    • Injection drug users usually acquire HCV before HIV infection
    • Men who have sex with men (MSM) typically are infected with HIV before they acquire HCV infection
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• In Men who have sex with men (MSM)
  • HIV-infection associated with a six-fold increase in HCV incidence
  • Seroprevalence of HCV in HIV-infected MSM is increasing
    • Especially in those whose predominant risk factor is unsafe sex
  • HCV is sexually transmitted more commonly among HIV-infected MSM
    • MSM with HIV infection have higher seminal fluid HCV values than HIV-uninfected MSM
      • More likely to transmit HCV
    • HCV is not as common among HIV-uninfected MSM
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• **Perinatal transmission**
  - Vertical transmission of HCV appears to be facilitated by HIV co-infection
  - Maternal co-infection increases the odds of vertical HCV transmission by approximately 90 percent compared with maternal HCV infection alone
    • 10.8 versus 5.8 percent in large study published in CID 2014
  - HCV has been isolated from cervicovaginal fluid in HIV-seropositive women, but not in women with HCV alone
    • May explain the higher rates of perinatal HCV transmission observed in the setting of coinfection
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• **Virology**
  • Both RNA viruses
    • HIV (a retrovirus)
    • HCV (a flavivirus)
  • Viral production rates
    • HIV $10^{10}$ virions a day
    • HCV $10^{12}$ virions a day

• During the chronic stage of either HIV or HCV infection, a relatively stable viral load or "set point" is maintained
  • Usually in the “thousands” for HIV & in the “millions” for HCV
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**Virology**
- HCV RNA levels increase after HIV seroconversion
  - May be related to immunosuppression
  - The envelope protein of HIV (gp120) also increases HCV replication
- HCV viremia is inversely correlated with lower CD4 counts
- Higher HCV mutational rates
  - Increased sequence variability of the HCV genome has been noted in HIV/HCV-coinfected individuals
  - Harder on the host immune system to mount effective response
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• **Pathogenesis**
  - HIV/HCV co-infected patients have accelerated rates of fibrosis progression compared with patients with HCV alone
    - Decreased immune response to HCV antigens in HIV-infected patients
  - HIV-associated non-directed immune activation
    - Increased pro-inflammatory cytokines
    - Activated hepatic cells increase collagen formation (fibrosis)
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- **Effect of HIV on the Natural History of HCV**
  - Higher rates of morbidity and mortality related to liver disease
    - Mortality rate, 59 versus 39 per 1000 person-years (co-infected vs mono-infected)
  - Less likely to clear HVC viral infection
    - Less than 10% clear (>90% become chronic)
  - More rapid rates of liver fibrosis
    - Paired biopsy studies
      - 2.5 years between biopsies, progression of at least one fibrosis stage was observed in 34 percent, and progression of two or more stages was observed in 9 percent
      - Rapid progression to cirrhosis has also been reported
  - Higher risk of hepatic decompensation compared with HCV mono-infected patients
  - Hepatocellular carcinoma (HCC) occurs faster and is associated with shorter survival in HIV/HCV co-infected patients
    - Co-infected patients (after 26 years)
    - HCV mono-infected patients (after 34 years)
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- **Testing for HCV with HIV co-infection**
  - Sensitivity and specificity of third generation HCV Ab ELISA assays approach 99 percent
  - However, patients with severe immunosuppression (CD4 cell counts <100 cells/mm³) may have a false negative serology
    - Due to impaired antibody formation
    - Occurs in than less than 5 percent of patients
  - In HIV-infected patient w/ low CD4 consider hepatitis C RNA testing
    - Esp. if has significant risk factors for HCV
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• **Effect of cART on HCV progression**
  • Many studies suggest that ART is beneficial
  • Demonstrated benefits:
    • Decline in liver-related mortality
    • Slower rates of fibrosis progression
    • Lower risk of end-stage liver disease
      • Almost percent lower likelihood of hepatic decompensation
      • Lower rates of hepatocellular carcinoma

• BUT cART alone is not enough !!!
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• **HCV and Hepatotoxicity with ART**
  • HCV increases the risk of hepatotoxicity from antiretroviral therapy
  • Some ART regimens are more hepatotoxic than others
    • Ex. nevirapine, ritonavir
  • ART-associated hepatotoxicity may be related to immune reconstitution
    • Hepatotoxicity often correlates with a rise in CD4 count
  • Benefit of antiretroviral therapy outweighs the risk of liver injury
    • Close laboratory follow-up is prudent
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- Treating HCV in setting of HIV co-infection
  - Interferon based regimens (old news)
    - HIV/HCV co-infected patients traditionally had lower response rates to HCV treatment
    - With peginterferon and ribavirin
      - Overall SVR rates 14 - 35 percent compared with 42 - 46 percent in mono-infected patients
  - Direct Acting antivirals (now):
    - HIV/HCV co-infected patients appear to have comparable SVR rates to mono-infected patients w HCV
      - > 90%
      - Curative all-oral treatment is a possibility for most patients w/ HIV-infection!
    - Major issue at this point is potential drug-drug interactions w/ ART and HCV meds
      - Should take into account w/ ART regimen selection
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• **Effect of HCV on the natural hx of HIV**
  - Various studies that suggest:
    - HCV seropositivity is an independent risk factor for progression to *AIDS and death*
    - AIDS-defining events when HCV-seropositive
      - Relative risk 2.6 of
      - Increased mortality
    - Standardized mortality rate HCV co-infection vs HCV-negative 20.8 compared with 4.8
    - *Lower rate of CD4 cell gains* among patients who had chronic HCV infection
    - Greater rates of *non-hepatic complications*
      - Osteoporosis / bone fractures
      - Chronic kidney disease
      - Possibly additional cardiovascular risk
  - The factors responsible are not well understood
    - May result from generalized immune activation
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• QUESTIONS / COMMENTS?