Hepatitis C and HIV

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Issues

- Similarities between HIV and HCV
- Incidence/prevalence of co-infection
- Overlapping risk groups
- HIV effects on HCV
- HCV effects on HIV
- The impact of HAART
- The role of liver biopsy
- Treatment

Similarities between HIV and HCV

- Antibody testing is useful in screening
- Quantitative PCR is the backbone of diagnosis
- Astronomical amounts of virus produced each day [au: OK to add “produced”? (or do you mean “turnover)?]
- Viral kinetics: biphasic ?triphasic
- Response to treatment is related to kinetics

Similarities between HIV and HCV (Cont'd)

- Mutation rate faster in HIV
- Evolution of quasispecies faster in HIV
- Naturally resistant virus to treatment
- Genotyping may be useful
- Imbalance of Th1 (low) to Th2 (high) immunity
- Virus (different quasispecies) isolated from many sites in the body

Prevalence of HCV in HIV

- Asia: 26% (28% HGV+) [au: HGV, really?]
- Europe: 28% to 46% (76% in long-term non-progressors)
- US: NY 40%; Buffalo 42%; Boston 56%
- Hepatitis C prevalence is declining in methadone programs
- Hepatitis C risk increases with age (> 90% at 45 years) in IDUs [au: IDU instead of IDUs OK?]

How Does HIV Affect Hepatitis C?

- HIV viral load correlates with HCV viral load (inversely with CD4+ count)
- HCV viral load correlates loosely with prognosis and biopsy findings
- Fibrosis from HCV was more severe in HIV (3 studies)

How Does HIV Affect Hepatitis C? (Cont'd)

- Cirrhosis was more frequent (33%) in co-infected patients than in HCV alone (11%)
- Mortality in 2 studies increased. Latest data reveal death rate 11% in coinfected (40% from liver disease) and 6.8% in HIV alone
- Maternal-fetal transmission of HCV increased from 7% to 11-25%

How Does Hepatitis C Affect HIV?

[au: delete “c” in “Hemophiliac” OK?]

- Royal Free Hemophilia study showed more rapid progression to AIDS or death for genotype 1a/1b than for other genotypes
- US/Greece Hemophilia study: RR of AIDS or death: 2.8 for genotype 1a/1b confirmed
- Pennsylvania study in nonhemophiliacs showed co-infected patients were more likely to have both increasing HIV viral load and decreasing CD4+ count

Why Does HIV Worsen HCV?

- Expansion of Th1 clones and Th cell recognition of multiple core epitopes are important in the elimination of HCV by interferon or naturally
- HIV infection alters T cell immune response to hepatitis C virus antigens
- Coinfected CD3/CD30 cells produced mostly Th2 response while HCV infected cells produced the expected Th1

The Effect of HAART on HCV

- HIV protease inhibitors have no activity against HCV itself
- Control of HIV to <400 HIV RNA c/mL has no effect on HCV RNA
- However, initiation of HAART may increase ALT/AST and HCV viral load for the first 3 to 4 months. By month 12, both are back to baseline (conflicting data)

Is HAART Liver Toxicity Related to Hepatitis C?

- Several studies related indinavir-associated hyperbilirubinemia to chronic hepatitis (8 of 10, 2 of 3, 7 of 46, 56 of 138)
- In one larger (JHU) study, ritonavir was the major cause of liver toxicity (10% gr 3-4) and was not related to hepatitis C
- However in 2 European studies, ritonavir toxicity was related to chronic hepatitis C and hepatitis C was an independent predictor of hepatotoxicity

Is HAART Liver Toxicity Related to Hepatitis (Cont'd)

- Richmond study: 56% of patients with liver toxicity HCVAb+
- Buffalo study: 42% HCVAb+ patients with HCV had higher ALT on nelfinavir than on indinavir (ritonavir and saquinavir excluded)
- Wurzberg study: ritonavir trough levels and ALT 2x higher in patients with HCV

Alfa Interferon for HCV in HIV-Infected Patients

- 6 previous studies with ALT endpoints and no PCR all showed 8% to 44% sustained response
- Hannover: sustained response 10% with 6MU TIW at 1yr (IFN alfa 2a)
- Madrid: SR (ALT) 22% HIV+ and 26% HIV- with 3MU TIW at 1 yr: 107 patients 3-year follow-up (IFN alfa 2b)
- Puerto Rico: SR (PCR) 17% ALT 56% with 3MU TIW 6 months (alfa 2b)

Alfa Interferon for HCV in HIV-Infected Patients (Cont'd)

- Madrid: SR (PCR) 11% vs 36% in HIV- with 3MU TIW at 1 yr
- Palermo: SR (PCR) 6% 3MU increased to 6MU all had decreases in HCV; no change in HIV or CD4+ count
- Response appears to correlate loosely with CD4+ count

Alfa Interferon and Ribavirn for HCV in HIV-Infected Patients

- Paris: 5 patients <400 HIV RNA c/mL had no change in HIV on IFN/RBV. 2 of 5 patients >40 c/mL had increases by 1 log in HIV RNA. No change in CD4+ count
- SR: 40% PCR in non-responders
- New York: (PC) 6/12 PCR- at 3 months, dropout rate was high (8 of 20). Anemia and neutropenia was common, but treatable. 1 patient with <400 HIV RNA c/mL increased to 52,000 c/mL on IFN/RBV
- Studies are ongoing

Conclusions

- Hepatitis C is a very large problem in HIV-infected patients
- HIV increases HCV viral load, cirrhosis, hepatoma, and mortality in coinfected patients
- HCV worsens HIV in hemophilia and others dependent on genotype
- HAART may increase HCV and ALT temporarily, but has no effect in the long term

Conclusions (Cont'd)

- HAART liver toxicity worse with ritonavir
- Indinavir and ?RTV worse in HCV patients
- Treatment with alfa interferon appears to be a viable option with SR close to that in a HIV-seronegative patient
- Treatment with IFN/RBV is possible, but complicated: does not appear to be contraindicated

The Role of Liver Biopsy in HIV/HCV

- Liver biopsy is the only reliable staging method for hepatitis C. Viral load and ALT are not
- Liver biopsy is expensive and may have more complications in HIV (3/501 bled, 1 death)
- There may be a role for using PCR first for treatment and then if no response, biopsy
- Liver biopsy remains a valuable prognostic tool

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Adapted from: