HIV and Hepatitis B CoInfection
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History

- 44 yo male with AIDS who had fallen out of care and returned in October 2013
  - Last seen in November 2012
  - CD4 at that time 340 cells/cmm
  - HIV RNA 307 copies/mL
  - HAART was tenofovir/emtricitabine (Truvada) and raltegravir (Isentress)
- HIV diagnosed in 1995
- Only has K103N mutation from 5 prior resistance tests, dating to 2002
Present Illness

- In ED with severe weakness, nausea and vomiting – bed bound
- Also had abdominal pain
- No documented fever
- Unbathed for a week

Other PMH

- HIV CDC classification B3
- Bipolar disorder
- Herpes zoster
- Recurrent nausea/vomiting
- Seborrheic dermatitis
- Heavy smoker – no other substances
Physical Exam

- Temp 36.4 C, Pulse 140, BP 125/95, R 18, & Pulse oximetry 95% on room air.
- Cachectic and disheveled
- Skin caked with seborrhea to face, arms and feet
- Chest clear
- Heart showed tachycardia
- Abdomen mildly distended, and tender in upper quadrants
- Affect blunted; spoke few words

Labs

- WBC 6000 cells/cmm
- Hgb 13 g/dL
- Platelets 380,000
- Albumin 2.4 g/dL
- Na+ 134, K+ 3.3, & CO2 31
- BUN/Cr 16/1.0 mg/dL
- Bilirubin 1.0 mg/dL
- ALT 12 IU/L
- Lipase 92
- LDH 400 IU/L
Imaging

- CXR with atelectasis, and suspicious for bronchopneumonia in both lower lobes
- CT scan – nodular, cirrhotic-appearing liver with hypodense lesions, and large omental masses, with caking of the omentum and a large amount of ascites

Hepatitis Serologies

- 1995 and 1997 – Hepatitis B surface Ag negative, and core and surface antibodies positive - Immune
  - Immune to hepatitis A
  - Hepatitis C Ab negative

- 2013 Hepatitis C Ab negative

- 2013 Hepatitis B surface Ag and core Ab both positive, with negative HB surface Ab
• Current antiviral agents can control, but not eliminate, hepatitis B virus (HBV).

• HBV establishes a stable, nuclear covalently closed circular DNA (cccDNA, or episomal DNA).
  ◦ A double-stranded DNA that originates in a linear form that gets ligated by means of DNA ligase to a covalently closed ring

• Transcription of viral DNA can occur from this cccDNA form.


cccDNA

• HBV persists in the liver even after serologic conversion to surface Ab positive.
• Can occur with severe immune suppression seen with HIV, including:
  ◦ Following immune reconstitution with antiretroviral therapy
  ◦ Discontinuation of antiretroviral drugs that have anti-HBV activity
  ◦ Drug-induced liver injury
  ◦ Superinfection with other hepatitis viruses.
• Rituximab, used to treat NHL, CLL, RA, and some forms of vasculitis, and Ofatumumab, used to treat CLL, also associated with reactivation of HBV


Reactivation Hepatitis B
Among 47 patients who did experience HBeAg seroconversion, reactivation (loss of anti-HBe with reappearance of HBeAg) occurred in eight subjects within two years of follow-up:

- This was significantly associated with HIV infection (5 of 14 HIV-seropositive patients compared with 3 of 33 HIV-seronegative patients).


**HBV Reactivation due to HIV**

- 32 cases judged to be HBV reactivation
- 22/32 had sero-reversion to B surface Ag positivity
- 5 also had HBS antibody positivity
- “Time of reactivation in relation to exposure to the anti-CD20 monoclonal antibody ranged from 63 days after the first dose to a year after the last dose.”
- Screening with HBSAg and HBcore Ab recommended before using these drugs

FDA Alert September 25, 2013

**AntiCD20 Monoclonal Ab**
Additional Labs

- Current CD4 was 50 cells/cmm, down from 340 one year prior
- HIV RNA 755,000 c/mL
- HBV DNA PCR 7,000 IU/mL
- Hepatitis C Ab negative

What about those hypodense lesions and omental masses?

- CT scan – nodular, cirrhotic-appearing liver with hypodense lesions, and large omental masses, with caking of the omentum and a large amount of ascites
Follow-up

- Abdominal node biopsy by VIR – diffuse, large, B-cell lymphoma
- Bone marrow and CSF negative for lymphoma
- Started HAART of tenofovir/emtricitabine (Truvada), raltegravir (Isentress) and etravirine (Intelence)
  - Current CD4 48 cells/cmm and VL < 40 c/mL
- Hepatitis B DNA undetectable
- Received R-CHOP and is in full remission
  - Rituxan held during first 2/6 cycles, until HBV fully suppressed with the tenofovir + emtricitabine (Truvada)

Take-Home Points

- Latent HBV virus remains in the liver if previously infected, even though tests may show immunity
  - Virus is never really “gone”
- Reactivation of HBV can occur from immune suppression
- Reactivation of HBV can occur after some monoclonal Ab therapies