Isolated Hepatitis B Core Antibody

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Isolated Core Antibody

- Virology & terminology
- Definition & Risk Factors
- Scenarios where we see isolated anti-HBc
- HBV immunization in these patients
- Occult hepatitis B
- Clinical significance
- Practical considerations
Hepatitis B virus
Terminology

www.hivandhepatitis.com
Virologic & Serologic Responses to HBV

http://depts.washington.edu/hepstudy
Anti-HBc does not react to the core of the intact virion since the core is completely surrounded by the envelope. Thus, anti-HBc does not play a direct role in controlling or preventing HBV infection.
Isolated Hepatitis B Core Antibody in HIV-infected Patients

• Definition: anti-HB core(+) but anti-HBs and HBs antigen negative
• Common profile – found in 20-45% in HIV-infected case series
• Factors associated with isolated core Ab:
  - HIV infection
  - Chronic hepatitis C infection
  - Older age
  - CD4 count <100 cells/mm³
  - Antiretroviral therapy: less likely to be isolated core

Sun, J Viral Hepat 2010;17:578-87.
Isolated Hepatitis B Core Antibody in HIV-infected Patients

• Seen in 1 of these 4 scenarios:

1) “Window phase” of acute HBV infection between loss of HB surface antigen and emergence of anti-HB surface Ab;
2) Remote resolved HBV infection with waning of anti-HB surface Ab to level <10 IU;
3) Chronic infection, i.e. occult HBV with HB surface Ag that has escaped detection either due to low production or mutations in envelope protein;
4) False positive → actually never exposed to HBV

Isolated Hepatitis B Core Antibody
HBV Immunization

- Immunization can presumably help distinguish the latter 3 scenarios:

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Vaccine Response</th>
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<tbody>
<tr>
<td>Resolved HBV, waned sAb</td>
<td>Anamnestic response</td>
</tr>
<tr>
<td>Occult (chronic) HBV</td>
<td>No response</td>
</tr>
<tr>
<td>False positive</td>
<td>Primary response</td>
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</tbody>
</table>

- BUT most isolated core Ab patients do NOT mount an anamnestic response
Isolated Hepatitis B Core Antibody
HBV Immunization

- Our experience at Madison Clinic: 46% (13/28) anamnestic after single 20 mcg dose of hep B vaccine.
- Anti-HBe(+) status not predictive of this response but appeared to be associated with higher titer of anti-HBs post-vaccination.
- Presence of anti-HBe infers prior HBV exposure & presence of immunologic memory → less likely isolated core is false(+)

<table>
<thead>
<tr>
<th>Study</th>
<th>n/% Isolated Core</th>
<th>% Anamnestic</th>
<th>Predictors of Anamnestic Vaccine response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gandhi JID 2005</td>
<td>45% (n=44)</td>
<td>24% (7/29)</td>
<td>Anti-HBe(+) 45% vs. 7%</td>
</tr>
<tr>
<td>Jongjirawisan JAMT 2006</td>
<td>20% (28/140)</td>
<td>7% (2/28)</td>
<td></td>
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<tr>
<td>Chakvetadze, CID 2010</td>
<td>N=40</td>
<td>32.5% (13/40)</td>
<td>No baseline factors predictive. Among 7 nonresponders, only 1 had detectable HBV DNA</td>
</tr>
<tr>
<td>Kaech, J Infect 2012</td>
<td>12% (73/605)</td>
<td>22% (8/37)</td>
<td>Anti-HBe(+) OR 9.1, p=0.06</td>
</tr>
</tbody>
</table>
Isolated Hepatitis B Core Antibody
Occult HBV Infection in HIV-infected Patients

• Defined by negative surface Ag, (+)HBV DNA level

• Generally not common – prevalence variable, depending on population & assays
  - More recent US-based case series: prevalence ranges from ~2-10% among isolated core pts
  - True prevalence may be underestimated because case series have been small with single time-point HBV measurement & some on HBV-active antivirals

• HBV viral levels detected typically low <1000 IU/mL range

Shire JAIDS. 2003;36:869-75.
Isolated Hepatitis B Core Antibody
Occult HBV Infection in HIV-infected Patients

http://www.virologyj.com/content/11/1/9

CASE REPORT

Spontaneous reactivation of hepatitis B virus replication in an HIV coinfected patient with isolated anti-Hepatitis B core antibodies

Rongjuan Pei¹², Sebastian Grund³, Jens Verheyen², Stefan Esser⁴, Xinwen Chen¹ and Mengji Lu¹²
Isolated Hepatitis B Core Antibody
Clinical Significance

• Isolated core Ab appears to be a stable pattern over time in most (84%) individuals
  - If retested, still present (i.e. window phase or false positive unlikely)
  - If it changes at all, transitions to/from pattern of natural immunity (anti-HBs and anti-HBc positive)
  - Transition to/from chronic HBV infection (gain or loss of HBsAg) is rare

• Not consistently associated with:
  - ALT/AST elevations (independent of HCV coinfection)
  - Liver stiffness by FibroScan (independent of HCV coinfection)

Practical Considerations
What Do the Guidelines Say?

- **DHHS 2014 OI Guidelines:**
  “Some specialists recommend that HIV-infected individuals with anti-HBc alone be tested for HBV DNA. If positive for HBV DNA they should be treated as chronically infected; if negative they should be considered still susceptible to HBV and vaccinated accordingly.”

- **HIVMA 2014 Primary Care Guidelines:**
  “Patients who are negative for HBsAg and HBsAb but positive for anti-HBc should be screened for chronic HBV infection by determination of HBV DNA; those without evidence of chronic infection should consider vaccination (strong recommendation, low quality evidence).”
Practical Considerations
Expert Opinion

• Screen Isolated anti-HBc for Occult HBV with HBV DNA level:
  • Not on tenofovir, emtricitabine or lamivudine (off ART)
  • ALT or AST elevated
  • Chronic hepatitis C
  • Not responding to vaccination

• Hepatitis B Immunization for isolated anti-HBc:
  • Can do either boost & check or complete series
  • Can consider anti-HBe assessment to differentiate boost/check or simply complete series
  • Vaccinate early (before patient’s CD4 gets <350)
  • Always check anti-HBs 1-2 months after vaccination completed
  • Keep in mind: Magnitude & duration of HBV vaccine response is often lower in HIV-infected patients due to a variety of factors (low CD4, detectable HIV RNA, occult HBV, other health concerns)