State of Alaska Epidemiology Bulletin

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Bulletin No. 3 February 11, 2005

Reactive Hepatitis A Virus IgM Antibody Tests Do Not Always Indicate Acute Disease: A Review of 10 Case Reports

Background

From 2002 to date, 10 patients with reactive hepatitis A virus (HAV) IgM tests were reported to the Section of Epidemiology who upon routine investigation, did not demonstrate clinical or epidemiological profiles consistent with a diagnosis of HAV.

HAV symptoms and laboratory tests

Hepatitis A is an acute viral infection characterized by jaundice, fever, abdominal pain, malaise or anorexia. Most adults and older children exhibit symptoms, which usually resolve after 1-2 months. A confirmed case must meet both clinical and laboratory criteria: acute illness with discrete onset of symptoms and jaundice or elevated serum aminotransferase levels, plus detectable HAV IgM.[1] Clinical cases may also be counted if they are epidemiologically-linked to a laboratory-confirmed case.

Serum HAV IgM is present for several days before symptom onset and can persist for 6 months after illness.[2] HAV IgM also may be detectable for at least several weeks after receipt of HAV vaccine. Serologic testing for HAV following vaccination is not recommended as persons may test negative for HAV antibodies and yet still have protective levels.[2] HAV IgG rises at the same time as IgM, but unlike IgM, IgG remains elevated for life. The Alaska State Virology Laboratory (ASVL) evaluates sera for total HAV antibody (IgM and IgG); reactive sera are reflexively tested for HAV IgM only.

Suspected cases of HAV must be reported to Epidemiology staff who investigate to determine if a common or ongoing source of infection exists, and if persons exposed to a case are candidates for post-exposure prophylaxis with immune globulin.

Results

The median age of the patients was 60 years, range 9-77 years (Table 1). Six patients were male. Only one patient was jaundiced, although four patients had symptoms compatible with HAV infection. One patient had a discrete onset of acute symptoms; the remaining three reported ongoing symptoms for weeks to months. Seven patients were tested because of elevated transaminases. One patient each was tested at a health fair, for a refugee health assessment, and to determine if a second dose of HAV vaccine was needed. ASVL performed three of the tests; three other laboratories performed the remaining seven tests.

Discussion

None of the 10 patients met the case definition for acute HAV, nor did they report exposure to known risk factors for HAV. Reports of reactive HAV IgM that are inconsistent with acute infection are not uncommon and may occur for several reasons.[3] For example, an HAV test kit might be overly sensitive, detect clinically irrelevant levels of circulating IgM in persons with past HAV infections, or cross-react with other serum circulating factors that increase with age.

Reactive results for Patients D and H, who received vaccine within a month of testing, were not unexpected. Most of the remaining eight patients were >60 years old and some may have had HAV in the past. Whether their reactive results were related to previous HAV infection or related to their current medical condition remains unknown. Results did not appear to be related to the use of a particular test kit or a particular laboratory.

Recommendations

1. Testing for HAV IgM is indicated for persons with illnesses clinically compatible with acute HAV; **NOT** to assess response to vaccination or to screen asymptomatic persons with no known recent exposure to an HAV-infected person. ASVL will only test specifically for HAV IgM antibody when the HAV total antibody test is positive, and the patient is symptomatic.
2. All reactive HAV IgM tests should be immediately reported to Epidemiology to determine HAV case status and to initiate immediate public health action if warranted. Each report of a reactive HAV IgM will be reviewed in light of relevant clinical information, potential exposures to, and risk factors for, HAV. Retesting a patient using a different serum sample or preferably using a different testing format may yield a negative HAV IgM.[3]

References

[1]CDC. Case Definitions for Infectious Conditions Under Public Health Surveillance. *MMWR* 46(RR-10), May 2, 1997.
[2]CDC. Prevention of Hepatitis A Through Active or Passive Immunization. *MMWR* 48(RR-12), October 1, 1999.
[3]Personal communication with Dr. Anthony Fiore, Division of Viral Hepatitis, Centers for Disease Control and Prevention.

Table 1. Ten Patients, with Reactive HAV IgM Tests, who were Reported to the Section of Epidemiology, 2002-2005.

Patient	Sex, Age (years)	ALT[a] AST[b]	Current Diagnosis and/or Past Medical History	Reason for Testing
A	Male; 77	~1500 ~1500	Multiple chronic medical problems; echogenic changes to liver consistent with hepatitis or cancer	Elevated AST/ALT
B	Male; 60	nd[c]	Asymptomatic	Blood draw at a health fair
C	Female; 75	581 / 99[d] 352 / 17[d]	Acetaminophen toxicity	Elevated AST/ALT
D	Male; 11	nd[c]	Asymptomatic	Determine need for 2nd dose of HAV vaccine; 1st dose given a month before
E	Female; 63	106 / 245[d] 45 / 202[d]	History of splenic abscess rupture and chronic elevation of serum alkaline phosphatase	Pre-operative work-up for cardiac procedure revealed elevated AST/ALT
F	Male; 55	~150 ~150	Vague illness consistent with hepatitis C virus infection	Elevated AST/ALT
G	Male; 74	"severely" high[e] "severely" high[e]	Liver failure related to cryptogenic cirrhosis, chronic hepatitis, and probable hepatic cancer	Elevated AST/ALT
H	Male; 9	nd[c]	Asymptomatic	Part of a refugee health screen; patient given HAV vaccine 10 days before
I	Female; 60	87 nr[f]	Psoriasis	Elevated ALT
J	Female; 44	111 69	Current salmonellosis; patient reported having HAV infection as a child	Elevated AST/ALT

[a]Alanine aminotransferase, reference range 1-21 µ/L. [b]Aspartate aminotransferase, reference range 7-27 µ/L. [c]Not done.
[d]Repeat testing performed 4 days after initial blood draw. [e]As reported in the patient's medical record. [f]Not reported.