CASE REPORT

ACUTE VIRAL HEPATITIS A PATIENT WITH EARLY NEGATIVE HAV-IGM ANTIBODY

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Abstract. An acute hepatitis A patient with negative HAV-IgM antibody on presentation is reported. The antibody was measured again 11 days later and became positive. To confirm the diagnosis of hepatitis A with negative HAV-IgM antibody at early stage, the second antibody test approximately 2 weeks apart should be performed.

Acute hepatitis A is usually diagnosed by measuring a single serum HAV-IgM antibody during acute phase of illness. Hepatitis A with negative HAV-IgM antibody at early stage is uncommonly found and should be carefully diagnosed.

A 25-year-old male patient was admitted to the Hospital for Tropical Diseases because of fever, anorexia, nausea, and vomiting for 3 days. Four weeks prior to admission the patient went to Tak Province with two friends. Both of them were also admitted because of fever for 1 week and the investigation showed that they had hepatitis A with positive HAV-IgM antibody.

On admission, physical examination revealed no abnormal findings except fever of 37.7°C. Blood tests showed total bilirubin 0.48 mg/dl, SGOT 320 U/l, SGPT 412 U/l, alkaline phosphatase 25 U/l; viral markers, including HAV-IgM antibody (RIA), HBc-IgM (RIA) antibody, HCV antibody (RIA), HEV-RNA (PCR), HEV-IgM (ELISA), were all negative. Serum levels of aminotransferases and bilirubin reached peaks 5 days and 11 days respectively after the admission. Forteen days after the onset of symptoms, HAV-IgM antibody became positive (Fig 1).

This patient with acute hepatocellular dysfunction showed negative HAV-IgM antibody on presentation but had positive antibody 11 days later. The diagnosis of acute viral hepatitis A is usually established by the detection of HAV-IgM antibody in a single specimen obtained during the acute phase of illness (Koff, 1993). HAV-IgM raises shortly before the onset of symptoms and reach peak values soon after (Gerlich and Thomssen, 1993). HAV-IgM is found in high titers during the first 4-8 weeks after onset of symptoms and generally disappears within 6 months (Hatzakis and Hadziyannis, 1984). Almost all patients with hepatitis A, a single acute-phase serum sample of IgM antibody is present at the time of clinical presentation, however, there are a few patients who have clinical symptoms of hepatitis with negative HAV-IgM tests at the early stages (Hirata *et al*, 1995). Therefore, only a single serum sample of HAV-IgM antibody may not be enough for the confirmative diagnosis of hepatitis A in those patients because the immune reaction to hepatitis A virus at early stages of infection may not be sufficient to produce detectable levels of HAV-IgM antibody. Also, the sensitivity of the method of antibody detection is

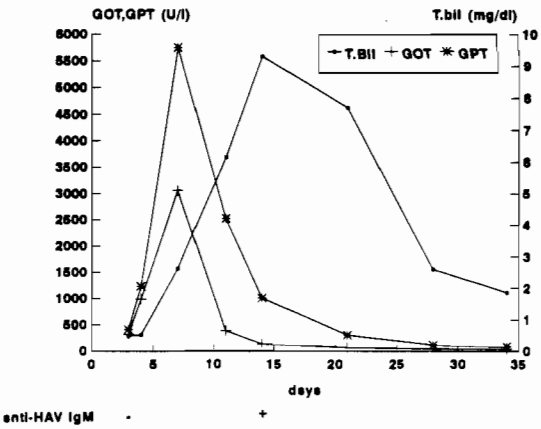

Fig 1–The course of hepatitis A showed the patient had negative HAV-IgM antibody on admission, however, the antibody measured 11 days later became positive.

important. Our study used a sensitive RIA method for HAV-IgM detection.

HAV-IgM antibody may be negative in about 3% of patients tested within 3 days after onset of symptoms, but it becomes positive within the first 2 weeks of illness (Liaw *et al*, 1986). Hirata *et al* (1995) recently reported 2 patients with hepatitis A with negative HAV-IgM antibody at early stages, but became positive a week later. They recommended another antibody assay 2 weeks later to achieve a definite diagnosis. Our patients had also similar presentation with 3 days of symptoms prior to admission and negative HAV-IgM antibody. Antibody measured 11 days apart showed positive HAV-IgM.

Therefore, the diagnosis of hepatitis A should be carefully made because HAV-IgM may be negative in early stage. In suspected case of hepatitis A with negative HAV-IgM antibody on presentation, the antibody should be remeasured 2 weeks later to confirm the diagnosis.

REFERENCES

Hatzakis A, Hadziyannis S. Sex-related differences in immunoglobulin M and total antibody response to hepatitis A observed in two epidemics of hepatitis A. *Am J Epidemiol* 1984; 120 : 936-42.

Hirata R, Hoshino Y, Sakai H, *et al*. Patients with hepatitis A with negative IgM-HA antibody at early stages. *Am J Gastroenterol* 1995; 90 : 1168-9.

Gerlich WH, Thomssen R. Terminology, structure, and laboratory diagnosis of hepatitis viruses. In: McIntyre, Benhamou JP, Bircher J, eds. Oxford textbook of clinical hepatology. Oxford: Oxford Medical Publications, 1993 : 537-65.

Koff RS. Viral hepatitis. In: Schiff L, Schiff ER, eds. Diseases of the liver, 7th ed. Philadelphia: JB Lippincott, 1993 : 492-577.

Liaw YF, Yang CY, Chu CM, *et al*. Appearance and persistence of hepatitis A IgM antibody in acute clinical hepatitis A observed in an outbreak. *Infection* 1986; 14 : 156-8.