

Meningoencephalitis of Hepatitis A in Adult Man: A Case Report

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Acute hepatitis A virus is almost always a mild illness with a benign outcome in babies and children but the disease is often symptomatic in adults and the fulminant form may occur in them. Also infrequent atypical clinical forms of infection, such as relapsing hepatitis, prolonged hepatitis, and cholestatic hepatitis may be seen in adults. We did not found any cases of hepatitis A meningoencephalitis in the review of literature, so we decided to introduce this case. We report a case of meningoencephalitis of hepatitis A virus infection. He had cerebrospinal fluid abnormality due to meningoencephalitis. Meningoencephalitis is an atypical presentation of hepatitis A virus infection. Atypical manifestations of hepatitis A should be considered in adult patients.

Keywords: Hepatitis A, Adult, Atypical Form, Meningoencephalitis

Introduction

The prevalence of anti-hepatitis A virus antibodies in the general population varies from 15 to 100% in different parts of the world. An estimated 1.5 million clinical cases of hepatitis A virus infection occur in the world each year ⁽¹⁾. Hepatitis A viral infection can be superinfected or coinfecting with other viral infections and it is one of the most widespread liver infections in the world, particularly in developing countries. In Iran, the most common cause of acute hepatitis is hepatitis A which is endemic and more than 97% of adults are immune to it, but sporadic cases may be seen. However, in areas with low endemicity, this infection mainly occurs in adults in high-risk groups such as homosexual men, injecting drug users, and those traveling to countries with high endemicity ⁽²⁾.

Acute hepatitis A virus is almost always a mild illness with a benign outcome in infants and children ⁽³⁾ but the disease is often symptomatic in adults and fulminant form may occur in them. Also infrequent atypical clinical forms of infection, such as relapsing hepatitis, prolonged hepatitis, and cholestatic hepatitis may be seen in adults ⁽⁴⁾. The disease severity and manifestations have been correlated with host factors, such as the presence of

an underlying chronic liver disease or older age of the patients ⁽⁵⁾.

Neurological complications of hepatitis A virus infection is very rare. Meningoencephalitis of hepatitis A is an atypical presentation and other neurological diseases such as Guillain-Barré syndrome are also very rare ⁽⁶⁾. Neurological diseases may be related to the immunopathogenetic mechanism of hepatitis A virus infection. Therefore, hepatitis A virus should also be considered as one of the etiological agents in meningoencephalitis as suggested by Matsushima and *et al.* ⁽⁷⁾. The aim of this study is to introduce the first case report of hepatitis A meningoencephalitis in Iran which is a rare case of hepatitis A virus infection with atypical presentation.

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Case Report

Presentation, examination and imaging

The patient, a 21-year-old university student of business from Golstan province in north of Iran, was admitted to Baqiyatallah hospital affiliated to Baqiyatallah University of Medical Sciences in Tehran, Iran, in July 2008. He had a fever, headache, myalgia, vomiting, vertigo, abdominal pain without tenderness and was confused. A persistent fever had begun 10 days before his admission. He had meningismus, exudative pharyngitis, mouth candidiasis and mild conjunctivitis.

Vital signs at the time of admission were as follows: Body temperature (T)=39-40 °C, blood pressure (BP)=100/80 mmHg, respiratory rate (RR)=24/min, pulse rate (PR)=100/min.

Past history of any disease and drug was negative including preexisting liver disease, addiction, alcohol abuse, sexual contact, surgery and tattooing. He had received 3 doses of hepatitis B virus (HBV) vaccine four years ago.

Abdominal sonography showed splenomegaly of about 131×50 cm, but brain computer tomography (CT) scan and brain magnetic resonance imaging (MRI) were normal. Transthoracic echocardiography was also normal. Electroencephalogram revealed slow delta waves compatible with encephalitis.

Laboratory tests

Complete blood count (CBC) was normal, white blood cell (WBC)=7500/ml, hemoglobin (HB)=14.3 mg/dl, mean corpuscular volume (MCV)=80fL, creatine phosphokinase (CPK)= 87 U/L normal, erythrocyte sedimentation rate (ESR)=4mm/h and C-reactive protein (CRP)= 1+. Hepatitis B surface antigen (HBsAg), Hepatitis B core antibody (HBcAb) and Hepatitis C Virus antibody (HCV Ab) were negative. Hepatitis B surface antibody (HBsAb) was more than 1000MIU/ml. Prothrombin time (PT), partial thromboplastin time (PTT) and international normalized ratio (INR) were normal. Urine analysis was also unremarkable. Widal, Wright, 2-mercaptoethanol (2ME) and Coombs Wright and blood culture, urine culture and pharyngeal culture were negative. Other laboratory tests are shown in table 1. Cerebrospinal fluid (CSF) abnormal parameters were Protein = 85mg/dl, WBC = 860/ml, mononuclear leukocytes (MN) = 70% and red blood cell (RBC) = 806/ml (Table 2). Herpes virus (HSV) polymerase chain reaction (PCR) in

Table 1. Abnormal laboratory findings.

Findings	Measures of lab
Aspartate amino transferase (AST)	2282U/L
Alanine amino transferase (ALT)	1188U/L
Lactate dehydrogenase (LDH)	4032U/L
Alkaline phosphatase (ALP)	502U/L
Total Bilirubin	3.5mg/dl
HAV IgM Antibody	Positive

Table 2. Cerebrospinal fluid (CSF) analysis.

WBC	860/ml
Mononuclear	70%
RBC	806/ml
Protein	85mg/dl
Glucose	75mg/dl
Bacterial smear	Negative
Bacterial culture	Negative
HSV PCR	Negative

cerebrospinal fluid (CSF) was negative. Viral capsid antigen (VCA) immunoglobulin M (IgM) and immunoglobulin G (IgG) of Epstein Barr virus were negative. Hetrophil antibody, anti IgM and IgG antibody of cytomegalovirus and anti human immunodeficiency virus (HIV) enzyme-linked immunosorbent assay (ELISA) antibody were negative. Serology for leptospirosis and anti Hepatitis E virus IgM and IgG antibody were also negative but anti Hepatitis A virus IgM antibody was positive.

Treatment

The patient had photophobia and terminal neck rigidity; therefore, he was treated empirically with acyclovir for herpes simplex encephalitis and due to his persistent fever, he took empiric treatment for typhoid fever but after both diseases were ruled out, his treatment ended.

Because the patient had meningoencephalitis and protracted headache and symptoms of increase intracranial pressure, he was treated with dexamethason 4mg/TDS for two consecutive days.

Outcome

Ultimately, his diagnosis was confirmed as meningoencephalitis of hepatitis A virus infection and treatment continues as supportive and after twenty days he healed and all abnormal laboratories was normal and he discharged from hospital with a good condition.

Discussion

Hereby, we report a rare case of hepatitis A virus infection who presented with acute meningoencephalitis. Differential diagnosis is very important, because many other diseases are similar to it. Hepatic encephalopathy can cause confusion, delirium, bleeding, severe coagulopathy and metabolic acidosis that are accompanied by liver failure. Cerebrospinal fluid analysis is normal in encephalopathy but abnormal in meningencepalitis, similar to this study (8).

Meningitis and encephalitis have overlapping manifestations; therefore, meningoencephalitis is the best term for this disease. Symptoms and signs of meningeal irritation (photophobia and nuchal rigidity) are usually absent with a pure encephalitis but often accompany a meningoencephalitis. Herpes encephalitis is the most common cause of fatal sporadic encephalitis, but polymerase chain reaction (PCR) of herpes simplex virus DNA as gold standard diagnosis was negative in our patient and meningoencephalitis of hepatitis A virus was confirmed as a very rare manifestation of hepatitis A virus infection (9).

Hepatitis A characteristically has an acute, sudden influenza-like onset with a predominance of myalgia, headache, fever and malaise which are nonspecific symptoms that may sometimes cause problems in differential diagnosis (1).

Epstein-Barr virus (EBV) infection has a broad spectrum of clinical manifestations. Leukocytosis, exudative pharyngitis, high fever, mild elevation of transaminases and lymphadenopathy are seen in infection mononucleosis. Diagnosis of EBV is confirmed by serology to VCA IgM and heterophile antibody. In our patient, serology against EBV infection was negative. Hepatitis A infection and EBV have similar manifestations and their differentiation is important, although sometime both diseases may be seen together (10, 11).

On the other hand, heterophile antibody negative infectious mononucleosis is seen in cytomegalovirus (CMV) infection. CMV disease can cause mild hepatitis but our patient had high levels of transaminases while CMV serology also was negative (12, 13).

Fecal-oral route is the most common mode of transmission for enteric fever, hepatitis A and E, and thus infection by these agents may occur concurrently especially in tropical endemic areas. These diseases are endemic in developing countries such as Iran. Differentiation between these diseases is important because typhoid fever should be treated with antibiotics but the two other need

symptomatic treatments. Typhoid fever causes a mild hepatitis and persistent fever that is similar to hepatitis A infection except for its atypical presentations as in this case (14, 15).

Viral infection can cause hepatitis alone but coinfection or superinfection can occur. Hepatitis B and C are prevalent in Iran, but hepatitis B virus infection has decreased in recent years due to the introduction of Hepatitis B vaccination to children and high risk groups such as military forces. Acute manifestations are similar in different types of viral hepatitis such as hepatitis A, B, C and E. Our patient was vaccinated against HBV and had HBsAb level of more than 1000 MIU/ML. Hepatitis C virus (HCV) and hepatitis E virus (HEV) infections were also negative and he only had hepatitis A infection (16, 17).

Although most adults in Iran are immune to hepatitis A and hepatitis E infection is also endemic, HAV was positive in our patient; therefore, atypical infection of hepatitis A virus was considered (18).

Leptospirosis or rice-field fever is a zoonosis disease that infects humans through contaminated water with urine or feces of rodents. Leptospirosis presents with an abrupt onset of fever, rigors, myalgias, headache, nausea, vomiting, sore throat, and abdominal pain. Aseptic meningitis can be documented. Because in north of Iran there are abundant rice fields, it is prevalent and in patients with these manifestations, leptospirosis should be considered as differential diagnosis of hepatitis A infection (19).

Conclusions

The results showed that atypical hepatitis A virus infection in adults can present as meningoencephalitis; therefore, atypical manifestations of hepatitis A should be considered in adults.

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