

# Transverse Myelitis in Acute Hepatitis A Infection: The Rare Co-Occurrence of Hepatology and Neurology

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## Keywords

Transverse myelitis · Acute hepatitis A · Lower extremity weakness · Jaundice

## Abstract

Transverse myelitis refers to the inflammatory process involving the spinal cord. Clinical features can be either acute or subacute onset that results in neurological deficits such as weakness and/or numbness of extremities as well as autonomic dysfunctions. While there are some etiologies related, a viral infection is common. However, the hepatitis A virus rarely causes myelitis. This report provides details of a hepatitis A infectious patient who developed myelitis as comorbidity. Although, the disability was initially severe, the patient successfully recovered with corticosteroid treatment.

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## Introduction

Hepatitis A virus (HAV) is a nonenveloped positive-strand RNA virus member of the Picornavirus family, Hepatovirus genus. It was first described in 1973 by Steven M. Feinstone [1, 2]. HAV has an icosahedral shape and its size is 27–28 nm. The human is the only reservoir of HAV. It is transmitted by the fecal-oral route. The incubation period is 15–50 days

(mean 28 days). The liver is the major site of replication. Pathogenesis is not well defined. Study in cell culture showed that HAV is not cytopathic. Cell-mediated immune response mediated via CD8+ T lymphocytes is postulated [1]. Hepatitis A is an acute, self-limited infection and never causes chronic infection. Clinical features are classified as (1) asymptomatic, (2) self-limited jaundice, (3) fulminant hepatic failure, (4) cholestasis with prolonged jaundice, and (5) relapsing hepatitis [2]. Hepatitis A triggering autoimmune hepatitis is reported [1, 2]. Extrahepatic manifestations in hepatitis A are less common than in acute hepatitis B. Extrahepatic manifestations of hepatitis A are evanescent rash, urticarial rash, maculopapular rash, toxic epidermal necrolysis, arthralgia, arthritis, leukocytoclastic vasculitis, cryoglobulinemia, myocarditis, pancreatitis, acalculous cholecystitis, glomerulonephritis, hemolysis, aplastic anemia, pure red cell aplasia, thrombocytopenia, autoimmune thrombocytopenic purpura, optic neuritis, encephalitis, meningoencephalitis, meningitis, Guillain-Barre syndrome, chronic inflammatory demyelinating polyradiculoneuropathy, sensory neuropathy, mononeuropathy simplex and multiplex, myasthenia gravis, myopathy, polymyositis, and transverse myelitis (TM) [1–3]. Evanescent rash is the most common extrahepatic manifestation of acute hepatitis A [2]. TM is a rare complication of hepatitis A. Acute hepatitis A with protracted course has a higher frequency of extrahepatic manifestations [2]. Anti-HAVIgM is the test for diagnosis of acute hepatitis A. It is positive from the onset of symptoms and remains positive 4 months after the onset. Treatment of acute hepatitis is supportive and symptomatic. Data about the treatment of extrahepatic manifestations of acute hepatitis A is limited. We report a middle-aged woman with acute hepatitis A and TM who was successfully treated with corticosteroid.

### Case Report

A 49-year-old woman had experienced high-grade fever with chill for 2 weeks. She also noticed a dull aching pain in her right upper abdominal quadrant. Three days later, her fever was spontaneously relieved, but jaundice with passing of clay-colored stool presented. Other symptoms were nausea and vomiting, poor appetite, weight loss of 5 kg (from 43 to 38 kg), and dizziness. One week prior to admission, she developed paresthesia and progressive weakness of both lower limbs. Leg movement was very difficult, while arm and hand functions were intact. The urination and defecation were still preserved. Her past medical illnesses were positive for postcholecystectomy due to gallstones and chronic non-specific dyspepsia. She was allergic to NSAIDs. The family history revealed records of different types of various primary organ involvement of cancer. Physical examinations revealed marked icteric sclera. There was no hepatosplenomegaly. She was conscious and had normal speech. All cranial nerves were intact. The motor strength of the upper extremities was grade 5. The motor power of the lower extremities was bilaterally grade 3 (either proximal or distal parts). The diminished pain sensation was observed just below the C6 dermatome. Proprioception was impaired on both feet. Deep tendon reflexes were generalized hyperreflexia. No ankle clonus was observed. Babinski's sign was the plantar response. The anal sphincter tone was intact. A liver function test showed direct hyperbilirubinemia and elevation of the liver enzyme (total bilirubin 18.8 mg/dl, direct bilirubin 14.7 mg/dl, AST 177 IU/l, and ALT 860 U/l). Prothrombin time was 10.4 s (international normalized ratio 0.88). Complete blood count revealed hemoglobin 9.6 g/dl, WBC 7,500/mm<sup>3</sup> with neutrophil 72%, and platelet 291,000/mm<sup>3</sup>. Blood urea nitrogen was 3 mg/dl and creatinine was 0.4 mg/dl. Serum electrolytes showed sodium 137 mEq/l, potassium 3.7 mEq/l, chloride 102 mEq/l, and bi-

carbonate 25 mEq/l. AntiHAVIgM was positive. AntiHIV, HBsAg, antiHBcIgM, antinuclear antibody, and anti-smooth muscle antibody were all negative. Ceruloplasmin was 25.2 mg/dl (normal 20–60 mg/dl). Magnetic resonance imaging (MRI) of the cervical spine demonstrated increased signal intensity of the cervical spinal cord C4–C6 level in T2-weighted images with fat saturation. The faint enhancement of affected areas was observed on T1-weighted images after intravenous gadolinium contrast injection (fig. 1, fig. 2). Brain MRI was normal. Lumbar puncture was performed with normal open and closed pressure (12 and 4 cm H<sub>2</sub>O, respectively). Cerebrospinal fluid (CSF) analysis showed WBC 10/mm<sup>3</sup>. CSF protein was 54.6 mg/dl and CSF sugar was 48 mg/dl (blood sugar 122 mg/dl). CSF polymerase chain reaction for cytomegalovirus, varicella zoster, herpes zoster, and Epstein-Barr virus were all negative. Due to an isolated spinal involvement without optic nerve or subcortical lesions, multiple sclerosis was less likely. The patient was diagnosed with TM and acute hepatitis A infection. An intravenous pulse methylprednisolone 1 g/day was given for 5 days' duration and then continued with oral prednisolone 60 mg/day. Oral prednisolone was tapered to 5 mg/day within 1 week before discontinuation. Rehabilitation and physiotherapy were non-pharmacological treatments both during admission and when the patient was discharged. After 1 month of treatment, she impressively recovered to perform normal gait and maintain all daily activities. Liver function tests returned to normal within 2 months after therapy. AntiHAV IgG was positive 6 months later.

## Discussion

TM is a heterogeneous group of inflammatory disorders characterized by acute or sub-acute motor, sensory, and autonomic (bladder, bowel, and sexual) spinal cord dysfunction [4, 5]. It may arise from various etiologies. An immune response to an infection or vaccination that then causes spinal cord lesions has been reported. A direct infection of the spinal cord is common. A systemic autoimmune disease initiates an inflammatory process in the spinal cord and results in neuronal death or tract lesions. An acquired demyelinating disease or the spectrum of disorders related to neuromyelitis optica was also found [5]. About 15–30% of TM cases are categorized as idiopathic [5]. Many viral infections are associated with TM. In the literature, the following have been reported: varicella zoster, rubella, mumps, measles, dengue, Japanese encephalitis virus, HIV, herpes simplex, Epstein-Barr virus, cytomegalovirus, influenza A, coxsackie virus A and B, echoviruses, smallpox, rabies, paramyxovirus, enterovirus-70 and -71, human herpes virus 6 and 7, poliovirus type 1, 2, and 3, tick-borne encephalitis, West Nile virus, St. Louis encephalitis virus, and hepatitis virus type A, B, and C [6–9]. Approximately 25–40% of TM cases are caused by herpes viruses and poliovirus [8]. Hepatitis A is a rare cause of TM.

Hepatitis A is a RNA virus in the *Picornaviridae* family. The usual route of transmission is feco-oral. Liver cell damage is mediated by HLA-restricted T lymphocytes. Mechanisms to clear hepatitis A are postulated as follows: (1) recruitment of cytotoxic T cells/NK cells from the periphery to the liver, (2) HLA-restricted killing of virus-specific CD8+ T lymphocytes, and (3) secretion of interferon gamma by CD8+ T lymphocytes, which may facilitate chemotaxis and have direct antiviral properties [10]. Neurological complications from hepatitis A are very rare, including encephalitis, meningoencephalitis, meningitis, Guillain-Barre syndrome, chronic inflammatory demyelinating polyradiculoneuropathy, sensory neuropathy, mononeuropathy simplex and multiplex, myasthenia gravis, myopathy, and TM [10].

The pathogenesis of TM from hepatitis A is still unclear. In one case report, hepatitis A was not isolated from the CSF of TM patients [4]. Therefore, an autoimmune process was proposed. Our patient met the Transverse Myelitis Consortium Working Group's criteria for TM due to compatible neurological symptoms, evidence of inflammation in the spinal cord obtained from the MRI, and exclusion of other etiologies. Although corticosteroids are the standard first-line treatment in idiopathic TM [3], there are no established treatment regimens for TM caused by hepatitis A. We treated the patient with pulse methylprednisolone and continued with oral prednisolone for suppression of the inflammation. The good recovery of our patient confirms our hypothesis that spinal dysfunction was due to an immune-mediated process. Thus, it results in functional deficits without changes of the neuroanatomy of the spinal cord.

### Statement of Ethics

The authors have no ethical conflicts to disclose.

### Disclosure Statement

The authors have no conflicts of interest to disclose.

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**Fig. 1.** Mild-increase signal in the spinal cord from C4–C6 level on sagittal T2-weighted image (arrows).



**Fig. 2.** After intravenous Gd-DTPA contrast administration, there was a faint enhancement of the involved area (arrows) on sagittal T1-weighted image with fat saturation, suggestive of myelopathy.