Recurrent Myelitis Associated With Hepatitis C Infection

Vitor H. Pacheco, MD, Jayant Acharya, MD

SAINT LOUIS UNIVERSITY

INTRODUCTION:

Hepatitis C is caused by a single stranded RNA virus of the flaviviridae family and is one of the most common causes of chronic liver disease. A national survey [NHANES III] of the civilian, non-institutionalized U.S. population found that 1.8 percent of Americans (3.9 million) have been infected with HCV, of whom most (2.7 million) are chronically infected with HCV.
Hepatitis C is also known to cause several extra-hepatic complications including vasculitic neuropathy with cryoglobulinemia (2,3) and vasculitic ischemic and hemorrhagic strokes (1-3). Acute disseminated encephalomyelitis was also reported as a complication (4). Myelitis, although rare, has been reported (5-7). In this case report we present a patient with recurrent myelopathy with CSF and serologic evidence of hepatitis C infection.

METHODS

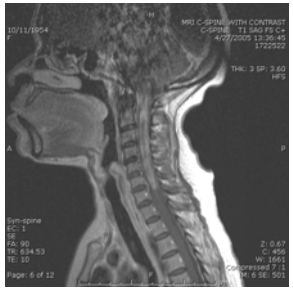
CASE REPORT:

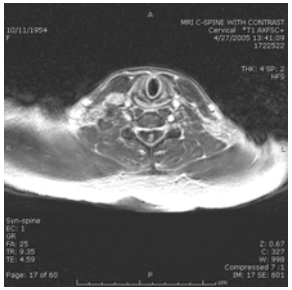
A 50 year-old African American female with previous history of hypertension and IV drug abuse presented with 2 week-history of head and neck pain, bilateral lower extremities paresthesias involving the right limb more than the left and unsteadiness of gait. She denied any abnormalities in bowel or bladder function or fever. Her neurological exam revealed right lower limb weakness 4/5, decreased sensation to vibration and pain distally in bilateral lower extremities but no clear sensory level. She also had unsteady gait. The tone, deep tendon reflexes and plantar reflexes were normal. Brain MRI showed non-specific whiter matter ischemic changes and a right temporal venous angioma. Cervical spine MRI showed enhancing cervical cord lesion extending from the tip of the odontoid body to the C7 vertebral body level (Figs. 1,2). MRI of thoracic and lumbar spines were normal. Her serum tested positive for hepatitis C antibody. Other serological tests were negative (Table 1). Other inflammatory disease markers were also normal (Table 1). Her CSF studies showed glucose 69, protein 52, WBC 3 with 2% of segmented, 45% of lymphocytes. Negative VDRL, CMV, normal ACE level, normal cytology, but increased gamma globulins and myelin basic protein. Culture for acid fast bacilli and fungi were negative. CSF test for HCV was not performed at this time. Liver biopsy revealed mild active hepatitis C. Treatment for HCV was held due to normal liver function. She was treated with 1 gram of methyl-prednisolone a day for 6 days and gabapentin. She had improvement of the paresthesias, but the hypoesthesia persisted.

4 months later she returned with complaints of heaviness of bilateral upper and lower extremities, more severe on the left side. On exam she had weakness 3/5 in the left upper limb, 4/5 in the right upper limb, 4+/5 hip flexion on the left side, increased tone in bilateral upper extremities and hyperreflexia, with positive Hoffman bilaterally. She also had decreased sensation in bilateral lower extremities. Repeated MRI of cervical and thoracic spines showed extension of the intramedullary lesion from C2 to T2 levels (Figs. 3,4). CT of chest, abdomen and pelvis were normal. CSF studies were unremarkable, including ACE levels. Visual evoked potentials were normal. She received IV methyl-predinsolone for 3 days and was discharged with tapering oral prednisone for 3 weeks after showing partial improvement of strength in her limbs.

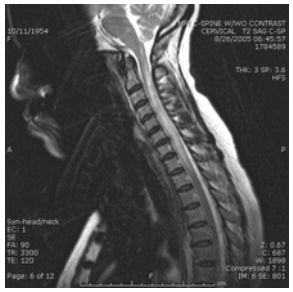
3 months after the second admission she was seen for 4 days of worsening of bilateral upper and lower extremities weakness, now accompanied by chest pain. On exam she showed worsening of spasticity and hyperreflexia compared to previous admission. MRI of cervical and thoracic spines revealed increasing edema of the spinal cord from C4 to T2 (Fig. 5,6). CSF studies showed glucose 54, protein 146, WBC 6 with 11% segmented and 76% lymphocytes. Hepatitis C antibodies in the CSF were positive. She had worsening of the weakness during hospitalization, but after completing 3 days of IV methyl-prednisolone she improved and was transferred to the rehabilitation unit. At that time it was decided to start treatment for hepatitis C.

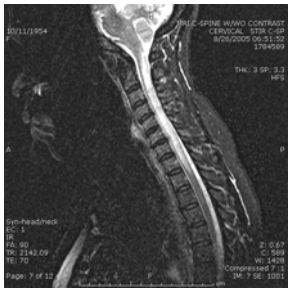
She had no visual symptoms during any of her admissions and clinical neuro-ophthalmologic evaluation and visual evoked potential studies were normal. However, given the extensive spinal lesion on MRI and lack of lesions typical for MS on brain MRI, neuromyelitis optica (NMO) IgG antibodies were checked and found to be positive in September 2006.

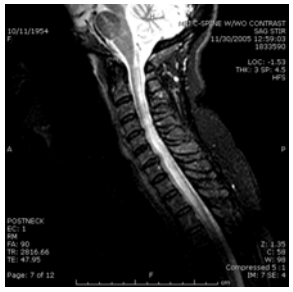


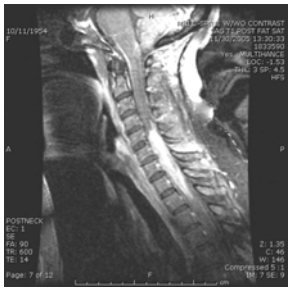


Serum		CSF	
B12	549	Culture	No organisms
Methylmalonic ac.	0.14	Culture AFB	No growth
Hep. A Ab. IGM	Negative	Cryptococcal ag.	Negative
Hep. B surface Ag.	Negative	Fungus culture	No growth
Hep. B. core IgM	Negative	Oligoclonal bands	Negative
Hep. C Ab.	Positive	Total protein	52 / 146 mg/dL
HIV Ab.	Negative	Albumin	50 / 66.9 mg/dL
RPR	Nonreactive	Alpha 1 globulin	4.4/ 3.0 mg/dL
Total protein	7.5 g/dL	Alpha 2 globulin	6.3/ 4.1 mg/dL
Alpha 1 globulin	0.2 g/dL	Beta globulin	18.1/ 13.5 mg/dL
Alpha 2 globulin	0.6 g/dL	Gamma globulin	19.6/ 11.2 mg/dL
Beta globulin	0.8 g/dL	Myelin basic protein	55.66 ng/mL
Gamma globulin	1.3 g/dL	Immmunofixsation	No OCB
CRP	< 0.3 Mg/dL	ACE	1.2 U/l
Rheumatoid factor	< 20 IU/mL	VDRL	Nonreactive
Immunofixsation	No OCB	FTA	Nonreactive
Cryoglobulins	Negative	VZV IgG	0.23 IV
ACE	27 IU/L	VZV IgM	0.0 ISR
ANA Ab.	None detected	EBV capsid IgG	0.61 IV
SS-A Ab.	6 U	EBV capsid IgM	0.04 IV
SS-B Ab.	13 U	West Nile virus	Negative
ANCA Ab.	< 1:16	CMV PCR	Negative
DNASE B Ab.	< 1:60	JC Virus DNA PCR	None detected
CMV IgG Ab.	> 250 IU/mL	Hep. C AB.	Positive
CMV antigenemia	Negative		
CMV IgM Ab.	0.65 IV (neg)		
Toxo Ab. IgM	0.76 IV		
Toxo Ab. IgG	< 5 IU/mL		
HTLV I/II Abs.	Negative		
NMO IgG Ab.	Positive		
LA profile	Negative		
Anticardiolipin Abs.	Normal		
B2 glycoprotein	Normal		
TSH	1.130		









DISCUSSION:

We report a patient with recurrent myelitis in association with recently diagnosed hepatitis C infection. Serum and CSF antibodies against hepatitis C virus were detected. Initial evaluation for other causes for myelitis failed to show another etiology. Sarcoidosis is unlikely given the normal levels of serum and CSF ACE and normal chest CT. Multiple sclerosis was also potentially excluded with negative visual evoked potentials, negative oligoclonal bands in the CSF and absence of typical lesions in the brain MRI scan. Vasculitis and other infectious etiologies were also excluded. Later on, NMO antibodies were found to be positive, suggesting neuromyelitis optica as another potential etiology. HCV infection is related to several extra-hepatic manifestations. There are very few reports of spinal cord involvement. Zandman-Goddard et al. (6) have reported one case of transverse myelitis associated with chronic hepatitis C infection in a 34 year-old patient with positive CSF antibodies against HCV. Grewal et al. (5) described a 46 year-old patient with recurrent myelitis and HCV infection. Although liver biopsy showed evidence of the infection, the spinal cord biopsy failed to reveal HCV RNA. CSF antibodies for HCV were positive, but HCV RNA was not detected in the cerebrospinal fluid. Nolte et al. (7) described a 61 year-old man with sensory ataxia and myelopathy with HCV RNA positive in the CSF. The spinal cord MRI was normal, but there was electrophysiological evidence of spinal cord damage. There are also reports of encephalomyelitis associated with HCV infection. Bolay et al. (9) described a patient with encephalomyelitis and rigidity. Sacconi et al. (4) described a patient with acute disseminated encephalomyelitis developed 50 days after acquiring HCV infection from blood transfusion.
The pathophysiology of the spinal cord involvement by HCV infection is still not certain. Both direct viral invasion and immune-mediated mechanisms have been reported. (9) As seen in the patient described by Nolte et al., HCV RNA has been detected in the CSF. However, some other reports only showed evidence of positive antibodies against HCV.
Our patient had positive HCV antibodies in the CSF which is consistent with the idea of a possible immune mediated mechanism. The impact of HCV specific treatment with interferon in myelopathy is not established. Our patient is being currently treated, but no conclusions can be made at this point. Positive NMO antibodies identified later are suggestive of NMO. However, she did not have any visual complaints and the visual evoked potentials were normal. Her CSF also showed normal or minimally elevated WBC count, unlike the usual pleocytosis seen in NMO. Based on published criteria for NMO it is possible that our patient could have an incomplete presentation of the disease, since visual problems were not detected. (10) The patient will be followed for the potential development of visual changes. The presence of antibodies for both hepatitis C and NMO also raises the question of a possible relationship between positive serology for hepatitis C and the development of neuromyelitis otpica or its variants.

CONCLUSIONS:

1- Hepatitis C should be in the differential diagnosis for recurrent myelopathy.
2- Steroids help with improvement of symptoms, but did not prevent recurrence.
3- There are no reports of the role for interferon alpha in the treatment of myelitis related to hepatitis C virus.

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