

Chronic Hepatitis C Infection Associated with Neuromyelitis Optica and Antinuclear Antibodies

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Abstract

The neurological manifestations of chronic hepatitis C is most often a peripheral sensory neuropathy characterised by numbness, burning and sensation of "pins and needles". Peripheral motor neuropathy, mononeuropathy, mononeuropathy multiplex and transverse myelitis also occur. Ischemic stroke and transient cerebral ischemia have also been reported. Anterior ischemic optic neuropathy is seen, often following interferon therapy. We report an exceptional case of neuromyelitis optica in chronic hepatitis C infection in the absence of interferon therapy.

Introduction

The extrahepatic manifestations of hepatitis C include cryoglobulinemia, glomerulonephritis, lichen planus, porphyria cutanea tarda, Sjögren's syndrome (SS) and lymphoma.^{1,2} Neurologic manifestations include neuropathy and transverse myelitis.^{1,3,4} Ocular manifestations are usually due to Sjögren's syndrome (xerophthalmia) or interferon (IFN) therapy –nonarteritic anterior ischemic optic neuropathy (NAION), central retinal vein occlusion, central retinal artery occlusion, uveitis or scleritis.⁵

Case report

A 49-year-old post menopausal woman, a known case of chronic hepatitis C, was admitted with complaints of weakness and loss of sensation below the level of the waist of 36 hours' duration (in May 2008). The weakness was more on the left than on the right. She also had loss of bowel and bladder continence. Patient did not have complaints of dryness of the mouth, itching or gritty feeling of the eyes, orbital pain aggravated by eye movements or pressure on the globe, painful jaw muscle spasms, unintentional weight loss, fatigue, myalgias or loss of appetite.

The patient had a similar episode 1 year ago (May 2007) when she had weakness and loss of sensation involving the body below the neck with bowel and bladder incontinence. She was bed bound but had been able to move her limbs. MRI of the spine was done at the time and showed mild edema of the spinal cord at C5-7 level. She was diagnosed to have transverse myelitis –from which she recovered completely with steroids over a period of about 12 weeks. However, 3 weeks from the onset of quadriplegia, she had sudden loss of vision in the right eye which was evaluated and diagnosed as optic neuritis (papillitis) in the right eye. The left eye was normal. Multiple sclerosis was considered, but an MRI of the brain performed at the time was normal. Patient did not recover from this initial episode but progressed to develop optic atrophy in the right eye over the next five weeks. She was also found to have anti-hepatitis C antibodies during this first episode. Interferon therapy had never

been initiated throughout the episode or following this. Patient was not a diabetic or hypertensive and did not give history of hospitalisation or medications for any other medical problems.

On examination she was conscious, oriented and was in no apparent respiratory distress. She was not pale or icteric. The tongue and oral mucosa appeared moist. There was no enlargement of the parotids. The cornea and conjunctiva were normal. Schirmer's test was negative. Examination of the central nervous system showed loss of all modalities of sensation below the level of the epigastrium. The power in the left lower limb was 0/5 and in the right lower limb was 1/5. There was hypotonia, deep tendon reflexes were diminished and the plantar reflex was bilaterally extensor. Visual acuity was only perception of light in the right eye and 6/12 in the left eye. Field of vision and colour vision were normal in the left eye. There was no pain on eye movements, tenderness on pressure over the globe or scalp tenderness. Ophthalmoscopy showed optic atrophy in the right eye and the left eye showed edema of the optic disc giving an appearance of pseudo-Foster-Kennedy syndrome. Other cranial nerves were intact and there were no tremors or other involuntary movements. Examination of the cardiovascular and respiratory system did not reveal any abnormalities.

Investigations revealed Hb 11.8 g/dL, total WBC count 14400/cumm, differential count showed neutrophils 64.5%, lymphocytes 29.4%, monocytes 5.3%, eosinophils 0.3% and basophils 0.4%, ESR was 36 mm/hr. RBS 5.7 mmol/L, blood urea 5.4 mmol/L, creatinine 52 mmol/L, electrolytes Na: 139 mEq/L, K: 3 mEq/L and Cl: 106 mEq/L. Urinalysis, ECG and chest x-ray were normal. MRI of the spine and brain (done after 3 weeks of steroids) showed no abnormalities. ANA was positive. RA factor and cryoglobulins were negative but they were done after initiation of high dose steroids. Antibodies to extractable nuclear antigen were also negative. LFT showed mildly elevated transaminases (AST 56 U/L [Normal 2-34 U/L], ALT 85 U/L [Normal 0-55 U/L]) but was otherwise normal. HCV antibodies were positive. HIV and HBsAg were negative. HCV RNA was 1.6×10^6 IU/ml. CSF analysis showed an acellular tap with protein 18 mg/dL and glucose 64 mg/dL. Labial mucosal salivary gland biopsy was considered but was not done as the patient did not consent.

Patient was treated with methyl prednisolone 500 mg once daily for 3 days followed by oral prednisolone 1 mg/kg/day for 6 weeks. Physiotherapy was initiated. Treatment for HCV was not initiated as neurological lesions are known to worsen with interferon therapy.⁵ Following this patient's power improved to 2/5 in the left knee (flexion and extension) and 3/5 in the

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left ankle (plantar flexion and dorsiflexion) and 4/5 in the right lower limb. However, visual acuity in the left eye worsened after six weeks of presentation with the visual acuity deteriorating to 6/24 and optic atrophy developed in the left eye as well.

Discussion

The neurologic manifestation of chronic hepatitis C is most commonly a peripheral polyneuropathy⁶ associated with pathological changes of vasculitis of the epineurial vessels and demyelination. These were initially thought to be related to cryoglobulinemia but were later found to be not significantly associated with neuropathy in a larger study.⁷

Mononeuropathy (peripheral and cranial) and mononeuropathy multiplex were less common than polyneuropathy in hepatitis C. Pathological changes in these patients (in sural nerve biopsy specimens) were similar to polyneuropathy. Reports of cranial nerve and spinal cord biopsy specimens are lacking for obvious reasons. However, it may be reasonable to extrapolate the findings on sural nerve biopsy to other nervous tissue. These pathological changes are similar to those in multiple sclerosis which also shows perivascular inflammation in addition to demyelination. Spinal cord involvement in hepatitis C has often been reported as transverse myelitis.^{3,4,8,9} It has also been described as a vasculitis of the spinal arteries.¹⁰ It may not be unreasonable to conclude that vasculitis and demyelination similar to those seen in peripheral nerves of patients with hepatitis C could explain these clinical findings.

The presence of antinuclear antibodies in this patient supports an immunological mechanism, probably, activation and proliferation of B-lymphocytes, leading to production of humoral immune response against myelin resulting in an immune mediated demyelination.² Hence, an etiological association is possible. It is interesting to note that chronic hepatitis C has been known to cause clonal expansion of B lymphocytes and extranodal B cell lymphomas in exocrine glands, liver and stomach.¹¹ This phenotype of neuromyelitis optica may be classified under the third type described by Cross SA.¹²

Even though an infectious etiology for multiple sclerosis has been suspected for many decades,¹³ it remains unproved. Similarly, a causative relationship of hepatitis C to neuromyelitis optica has so far not been established and a coincidence of the two cannot be ruled out.

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