

Association of Bell's Palsy with Hepatitis E Virus Infection: A Rare Entity

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Hepatitis E virus (HEV) infection is a common cause of acute hepatitis in India and other developing countries. The data regarding the neurologic manifestation of HEV infection are limited. The neurologic disorders including Guillain-Barré syndrome, polyradiculopathy, neuralgic amyotrophy, encephalitis, bilateral brachial neuritis, ataxia/proximal myopathy, and acute transverse myelitis have been described. Bell's palsy and other cranial nerve involvement in hepatitis A virus (HAV) and HEV infection are rare. We present the second case of Bell's palsy associated with HEV. (J CLIN EXP HEPATOL 2012;2:88-90)

The neurologic manifestations of hepatitis E virus (HEV) infection are rare but are being increasingly recognized. Recently, Bell's palsy and other cranial nerve involvement in hepatitis A virus (HAV) and HEV infection have been reported. We present the second case of Bell's palsy associated with HEV.

CASE REPORT

A 28-year-old man presented to the neurology clinic with anorexia of 2 weeks duration and 4 days history of weakness on the right-side of his face and deviation of the angle of the mouth to the left. There was no history of trauma or recent ear disease. There was no history of loss of taste, visual disturbance, or hearing impairment. Neurologic examination revealed deviation of the angle of the mouth to the left with loss of nasolabial fold on the right-side of the face (Figure 1). Abdominal examination revealed that the liver was just palpable, nontender, and firm with a liver span of 14 cm. The diagnosis of the right-sided facial weakness due to the right-sided lower motor neuron (LMN) facial palsy (Bell's palsy) was made. The hematologic and biochemical investigations revealed serum bilirubin of 2.0 (direct bilirubin 1.2) mg/dL, alanine aminotransferase of 1200 IU/L, aspartate aminotransferase of 1050 IU/L, and alkaline phosphatase of 200 IU/L; rest of the investigations were normal. The immunoglobulin M (IgM) antibody to HEV was positive. Serologic tests for hepatitis A, B, C, herpes simplex virus type 1 (HSV-1), and human immunodeficiency virus were nonreactive. Abdominal ultrasonography

was normal. Diagnosis of acute hepatitis E with Bell's palsy was made. The patient was treated with supportive measures and physical therapies. After 1 week, his liver enzymes started improving and normalized after 4 weeks. His neurologic symptoms recovered almost completely in 3 weeks.

DISCUSSION

Neurologic manifestations resulting from infection with the hepatitis viruses are relatively rare. The peripheral and central nervous systems (CNS) can be involved either in isolation or in combination. The various neurologic syndromes which have been reported in patients with serologically defined viral hepatitis include Guillain-Barré syndrome, mononeuritis multiplex, sensorimotor polyneuropathy, cranial nerve palsy, encephalitis, meningitis, encephalomyelitis, transverse myelopathy, strokes, auditory neuritis, and cognitive impairment.¹⁻⁵

Hepatitis E virus infection is a common cause of acute hepatitis in India and other developing countries. Data regarding the neurologic manifestations of HEV are limited. The initial reports of neurologic disorder in HEV have come mainly from the India.⁶⁻¹² Notably, in all of these



Figure 1 Right-sided lower motor neuron facial palsy.

Keywords: Bell's palsy, facial nerve palsy, hepatitis E virus infection

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Abbreviations: CNS: central nervous systems; CSF: cerebrospinal fluid; HEV: hepatitis E virus; HSV: herpes simplex virus; LMN: lower motor neuron; PEG-IFN: pegylated-interferon

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Table 1 Previously reported neurological manifestations of hepatitis E virus infection.

Total cases	22 (male:female 17:5)
Geographic location	Europe (15 cases), Asia (7 cases)
Patient immune status	Immunocompetent: immunocompromised (17:5 cases)
Neurological manifestations*	Guillain–Barré syndrome (9), polyradiculopathy (3), neuralgic amyotrophy (1), meningoencephalitis (1), encephalitis (1), meningitis (1), Bell’s palsy (1), pseudotumor cerebri (1), acute transverse myelitis (1), ataxia/proximal myopathy (1), bilateral brachial neuritis (1), and peripheral sensory neuropathy (1)
Serum anti-HEV IgM positivity	All 22 cases
Diagnosis based solely on serology	11 cases (anti-HEV IgM positive)
Molecular diagnosis	11 cases
HEV-RNA (serum)	11 cases
HEV-RNA (serum and CSF both)	6 cases
Genotype	11 cases (all genotype 3)
Treatment used	**Intravenous Ig/plasmapheresis, †immunosuppressant modifications/cessation, ‡PEG-IFN/ribavirin
Complete recovery	17 cases
Partial recovery with residual neurological deficit	3 cases
No recovery	2 cases

CSF: cerebrospinal fluid; HEV: hepatitis E virus; Ig: immunoglobulin; PEG-IFN: pegylated-interferon.

*Number of total cases is shown in brackets; **in Guillain–Barré syndrome and demyelinating polyradiculoneuropathy; †in immunocompromised patients; ‡in peripheral sensory neuropathy.

initially reported cases, HEV diagnosis was based only on the detection of anti-HEV IgM in serum. Recently, HEV-ribonucleic acid (RNA) has been detected in the serum and cerebrospinal fluid (CSF).^{1,13–15} Kamar et al¹ have reported neurologic complications in 7/126 (5.5%) patients with locally acquired acute and chronic HEV genotype 3 infections. Four of the 7 patients were immunocompromised. The HEV-RNA was detected in serum of all 7 patients with HEV infection. Among the seven reported cases, HEV-RNA was detected in the CSF of 4 patients.¹

Neurologic involvement in HEV is distinctly rare and approximately 24 cases have been described so far.^{1,6–21} Reports of 22 cases are summarized in Table 1.^{1,6–11,13–20} Guillain–Barré syndrome,^{1,6,8,9,13,14,16–18} polyradiculopathy,^{1,15} neuralgic amyotrophy,¹⁹ meningoencephalitis,⁷ encephalitis,¹ meningitis,¹⁵ Bell’s palsy,¹⁰ pseudotumor cerebri,²⁰ acute transverse myelitis,¹¹ ataxia/proximal myopathy,¹ brachial neuritis,¹ and peripheral sensory neuropathy¹ have been reported in patients with HEV (Table 1). Anti-HEV IgM was positive in the serum of all the 22 reported cases. Molecular diagnosis was made in 11 cases, based on the detection of serum HEV-RNA.^{1,13–15} Hepatitis E virus-RNA was detected in CSF of 6 cases.^{1,14,15} The HEV-RNA sequences in serum and CSF have showed differences, suggesting that neurologic symptoms may have been related to the emergence of neurotropic variants. Genotyping was done in 11 European patients, all were genotype 3.^{1,13–15} Notably, genotype 3 is the predominant genotype in these communities. However, a case of genotype 3 HEV infection associated with neuralgic amyotrophy

has been described from Asia (Thailand) too.²¹ Therefore, the relationship between the neurologic involvement and genotype appears to be debatable.

The Guillain–Barré syndrome and demyelinating polyradiculoneuropathy were treated with intravenous (i.v.) immunoglobulins/plasmapheresis.^{1,6,8,9,13,14,16–18} In immunocompromised organ-transplant patients, dose modification or cessation of immunosuppressant drugs was done.¹ In a patient of retroviral infection, pegylated interferon/ribavirin was given for painful sensory peripheral neuropathy.¹ The rest of the patients were managed with supportive measures. Patients generally have good prognosis. Complete recovery was seen in 17 of 22 patients, three cases had partial recovery with residual neurologic deficit while two cases showed no sign of recovery (Table 1).

Bell’s palsy is an acute, unilateral, peripheral, LMN facial-nerve paralysis that usually resolves spontaneously. Bell’s palsy has been defined as idiopathic, and the cause of the inflammatory process in the facial-nerve remains uncertain. Recently, HSV-1 has been identified as a possible etiologic agent.²²

A case of Bell’s palsy associated with HEV has been described in 2006 by Dixit et al¹⁰ To the best of our knowledge, our case is the second reported case of Bell’s palsy associated with HEV. This case of Bell’s palsy is possibly caused by HEV infection because of the following reasons. Firstly, we had clinical, biochemical, and serologic evidence of HEV. Moreover, the clinical courses of HEV and Bell’s palsy were parallel. Secondly, HEV as a cause of neurologic manifestations has been previously confirmed by the

detection of HEV-RNA in CSF of patients of HEV with neurologic manifestations. Thirdly, associations between Bell's palsy/other cranial nerve palsies and HEV/HAV infection have been previously described.^{5,10,12,23} Many viruses (including hepatotropic viruses) may trigger neurologic manifestations, as in Guillain-Barré syndrome. The mechanism of such nerve damage is possibly caused by cross-reacting immune response. As the HEV-RNA has been detected in the CSF, local viral replication in the CNS and direct neuronal damage is the other possible mechanism.¹ These mechanisms may be responsible for Bell's palsy in HEV infection. Unfortunately, we did not perform the test for serum HEV-RNA.

Treatment of Bell's palsy includes the use of steroids and antivirals, ideally within 72 hours but up to 7 days from the onset of symptoms.²² In view of the possible exacerbation of viral hepatitis, steroid was not given to our patient.

In conclusion, Bell's palsy may be one of the neurologic manifestations of HEV infection; however, whether it is a coincidence or a causal relationship remains a question.

CONFLICTS OF INTEREST

All authors have none to declare.

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