CASE REPORT

Neuralgic amyotrophy complicating acute hepatitis E infection: a rare association

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SUMMARY

Hepatitis E virus infection (HEV) is an emerging pathogen that is under-recognised in developed countries. Preceding infection manifested by acute transaminitis has been associated with neurological manifestations, predominately involving the peripheral nervous system, even in immunocompetent patients. We present a case of a 65-year-old previously fit and well Caucasian man with bilateral neuralgic amyotrophy (NA) and acute transaminitis. Serology testing for immunoglobulin (Ig) M and G established the diagnosis of acute HEV infection. The patient received immunomodulatory treatment with an excellent long-term outcome. The temporal association of the clinical presentation of bilateral NA and acute transaminitis from HEV infection suggested the causal association of HEV to NA. We propose screening for HEV in patients presenting with NA and acute hepatitis.

BACKGROUND

Hepatitis E virus infection (HEV) is an emerging pathogen that is under-recognised in developed countries. Preceding infection manifested by acute transaminitis has been associated with neurological manifestations, predominately involving the peripheral nervous system, even in immunocompetent patients. To our knowledge, this is a rare association with only a handful of cases reported so far in the literature. This association is therefore not well known and further research is required to establish the phenotypic, prognostic and therapeutic implications of HEV infections preceding neurological manifestations.

Our case, where immunomodulatory treatment was offered on presentation, was associated with a long-term favourable outcome. We therefore propose a change in everyday practice by including HEV screening in all patients presenting with acute neurological syndrome and concurrent transaminitis of unknown cause.

CASE PRESENTATION

A 65-year-old previously fit and well Caucasian man presented to the acute medical service with a 3 day history of pain and weakness of the right arm. The symptoms were of acute onset associated with right-sided shoulder pain. The pain progressed to the right arm in its entirety and crossed over to the left shoulder within approximately 2 h, with associated proximal weakness. There were no preceding factors, flu-like or diarrhoeal illness or trauma or strenuous exercise. There was no recent travel or animal contact, although the patient did report manipulating horse manure a month prior

to this presentation. There was no medical history of note, in particular no history of autoimmune diseases or treatment with immunomodulatory medications. Family history was unremarkable. There was no history of alcohol or drug abuse.

Neurological examination showed weakness of deltoid (power 1/5) and infraspinatus (power 2/5) muscles on the right, compared to the respective muscles on the left (power 4/5). Distal muscles were of normal strength. There was no focal wasting and tone was normal. Triceps reflex was reduced on the right side and brachioradialis reflexes were reduced bilaterally. Hypoaesthesia was noted over the right axillary nerve territory and the fingertips, bilaterally.

INVESTIGATIONS

Electrophysiological studies supported the clinical diagnosis of bilateral brachial neuritis with axonal denervation in the muscles clinically affected and in the right teres minor, suggesting high bilateral brachial plexus lesions. MRIs of the spine and the brachial plexus were unremarkable. Serum tests revealed acute transaminitis of unknown origin. Cerebrospinal fluid (CSF) studies showed an inflammatory reaction, with raised protein and lymphocytosis. The cause of the acute transaminitis remained elusive until the follow-up appointment in the neurology outpatient department, where serum was tested for HEV infection. Serum was positive for anti-HEV immunoglobulin (Ig) M and IgG using commercially available ELISAs and the diagnosis of acute HEV infection at the time of presentation was established. As viraemia is brief in immunocompetent patients, HEV serum PCR at that stage was deemed unnecessary. The investigation results are summarised in [table 1](#).

TREATMENT

The patient was treated with a three-day course of intravenous methylprednisolone 1 g, followed by a reducing regime of oral prednisolone.

OUTCOME AND FOLLOW-UP

Prior to discharge, the liver function tests had normalised, adequate pain control was achieved but no other signs of clinical improvement were noted. The symptoms remained unchanged for 6 months; however, after that period the patient started showing signs of rapid recovery with complete resolution of symptoms in 10 months.

DISCUSSION

We present a rare association of NA secondary to acute HEV infection. This association is likely to be

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Table 1 CSF and serological test results on admission, prior to discharge and at 3-month follow-up

Test	On admission	Prior to discharge (19 days hospital stay)	3/12 follow-up
ALT	1368 U/L	158 U/L	18 U/L
ALP	167 U/L	117 U/L	82 U/L
CSF protein	0.85 g/L	0.75 g/L	–
CSF WCC	58 (100% lymphocytes)	13 (100% lymphocytes)	–
CSF RBC	<1	<1	–
CSF glucose	3.3 mmol/L	3.2 mmol/L	–
CSF microbiology (EBV, HSV, VZV, enterococci)	Negative	Negative	–
CSF AAFB culture and auramine	Negative	–	–
CSF oligoclonal bands	Negative	Negative	–
Serum glucose	5 mmol/L	5 mmol/L	–
ANA, ANCA	Negative	–	–
HEV IgM	–	–	Positive
HEV IgG	–	–	Positive
HAV, HBV, HCV screen, CMV, EBV	Negative	–	–

AAFB, alcohol and acid-fast bacilli; ALP, alkaline phosphatase; ALT, alanine transaminase; ANA, antinuclear antibodies; ANCA, antineutrophil cytoplasmic antibodies; CMV, cytomegalovirus; EBV, Epstein-Barr virus; HAV, hepatitis A; HBV, hepatitis B; HCV, hepatitis C; HEV, hepatitis E; HSV, herpes simplex virus; RBC, red blood cells; VZV, varicella zoster virus; WCC, white cell count.

causal, as suggested by the temporal relationship between the development of the neurological syndrome and the concurrent transaminitis due to acute autochthonous HEV infection.

HEV is an emerging porcine zoonosis causing a self-limiting or commonly subclinical infection, as viraemia is often brief in immunocompetent patients. Autochthonous infections outside the traditionally hyperendemic developing countries remain under-diagnosed. Neurological extrahepatic manifestations of acute and chronic HEV infection have been described.¹ The peripheral nerve system has been reported as predominately affected, most commonly manifesting as Guillain-Barré syndrome (GBS) followed by NA.^{2–3} Other manifestations include transverse myelitis, cranial nerve palsies, intracranial hypertension, seizures, Bell's palsy, inflammatory polyradiculopathy and ataxia/proximal myopathy.^{4–6} NA is an acute monophasic disorder, of unknown cause, of the brachial plexus, although preceding infections have commonly been reported. In 25–30% of NA cases there is bilateral asymmetric involvement of the brachial plexus.² All the cases reported so far in the literature associated with HEV infection show bilateral involvement of the brachial plexus, as in our case.³ It is unclear whether the type of the preceding infection is associated with different clinical presentation and outcome as in other acute peripheral nerve inflammatory disorders such as GBS.³ The pathophysiological mechanism remains unclear. It is possible that an autoimmune mechanism is implicated rather than direct infection of the nervous system.^{4–6} It is unclear whether antiviral treatment aiming to reduce the viral load and antigenic challenge that drives the autoimmune response could be of therapeutic benefit. Our case, where immunomodulatory treatment was offered on presentation, was associated with a favourable long-term outcome. Further research is required to establish the phenotypic, prognostic and therapeutic implications of HEV infection preceding neurological manifestations. We propose HEV screening in all patients presenting with acute neurological syndrome and concurrent transaminitis.

Learning points

- ▶ The peripheral nerve system has been reported as predominately affected, most commonly manifesting as Guillain-Barré syndrome (GBS) followed by neuralgic amyotrophy.
- ▶ The pathophysiological mechanism remains unclear; it is possible that an autoimmune mechanism is implicated rather than direct infection of the nervous system.
- ▶ Our case, where immunomodulatory treatment was offered on presentation, was associated with a favourable long-term outcome.
- ▶ We propose hepatitis E virus screening in all patients presenting with acute neurological syndrome and concurrent transaminitis.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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