

Multiphasic presentation of neuralgic amyotrophy associated with hepatitis E virus infection

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Abstract

Background: The aim of this study was to further characterize the clinical phenotype of hepatitis E virus (HEV)-associated neuralgic amyotrophy (NA).

Methods: Three patients with HEV-associated NA underwent clinical, electrodiagnostic, and ultrasound assessment.

Results: In all patients, symptoms developed in several phases within a time span of 4–6 weeks, with three or more nerves involved. Symptoms were bilateral in two. In two patients, nerves of the trunk and the lower limb were affected as well. In one patient, three bouts occurred, each heralded by an increase in pain. In the other two, pain subsided quickly and nerve damage developed in two phases. Segmental enlargement with or without hourglass-like constrictions of the nerves was demonstrated by ultrasound in all.

Conclusions: The multiphasic presentation, together with the extensive multi-nerve involvement, may reflect a severe and protracted inflammation of the nerves in HEV-associated NA.

KEYWORDS

clinical phenotype, hepatitis E virus infection, hourglass-like constriction, multiphasic presentation, neuralgic amyotrophy, Parsonage-Turner syndrome

1 | INTRODUCTION

Neuralgic amyotrophy (NA) is an acute painful dysimmune neuropathy, typically affecting nerves originating from the brachial plexus.^{1,2} Lately, a specific association between hepatitis E virus (HEV) infection and NA has emerged. Since its first report in 2009,³ an increasing number of cases have been published and a distinct clinical phenotype of HEV-associated NA has been described.^{4–7} With the aim of further characterizing HEV-associated NA, we describe here 3 patients with an unusual multiphasic clinical presentation.

2 | METHODS

Approval was obtained from the Institutional Ethics Committee. The following criteria were used for the diagnosis of NA, (1) acute pain in the shoulder or arm, associated with weakness or sensory loss in the distribution of one or more peripheral nerves; (2) electrodiagnostic (EDX) proof of axon loss; (3) absence of other conditions explaining the symptoms. The diagnosis was further

supported by imaging findings. Patients underwent clinical, EDX, and high-resolution ultrasound examination of affected nerves. The diagnosis of HEV infection associated with the acute stage of NA was based on elevated transaminase levels and HEV IgM antibody positivity.

3 | RESULTS

3.1 | Patient 1

The 30-year-old man experienced an acute onset of intense pain in the left forearm, followed by loss of sensation on the lateral aspect of the left forearm (indicative of left lateral antebrachial cutaneous nerve lesion). Two weeks later, fever developed and the pain spread to the whole left arm and shoulder. The fever subsided within days, when he noticed the inability to flex the distal phalanx of his left thumb (presumed left partial anterior interosseous nerve lesion). At this point, he received a single dose of 2 mg of intramuscular betamethasone, leading to pain reduction. One month later (6 weeks after onset), fever lasting for 2–3 days developed again, the pain intensified and became bilateral, associated newly with loss of sensation on

Abbreviations: EDX, electrophysiological assessment; EMG, electromyography; HEV, hepatitis E virus; NA, neuralgic amyotrophy.

the radial aspect of dorsum of the left hand (indicative of left superficial radial nerve lesion).

The patient was first assessed in our department 3 months after onset. Electromyography (EMG) of the left flexor pollicis longus muscle showed fibrillation potentials and absence of motor unit recruitment. The amplitudes of the sensory potentials of left lateral antebrachial cutaneous and superficial radial nerves were reduced by ~70% compared with the contralateral side. Ultrasound showed fascicular abnormality (segmental enlargement or hourglass-like constrictions) within the musculocutaneous, median, and radial nerves proximal to the branching off of the affected nerves from the main nerve trunk, a finding typical of NA.

3.2 | Patient 2

The initial symptom of this 30-year-old man was severe pain in the right shoulder, associated with the inability to raise and rotate the right arm (indicative of right axillary and suprascapular nerve lesions), and numbness on the lateral aspect of the upper arm and on the medial surface of the left lower leg (presumed left saphenous nerve lesion). EMG on day 5 of the right deltoid and infraspinatus muscles showed no fibrillation potentials and absence of motor unit recruitment. MRI scans of the brain, cervical spine and brachial plexus on both sides were normal. Oral methylprednisolone (64 mg/day) was started 5 days after symptom onset, and tapered off over weeks, with pain reduction. Ultrasound examination on day 9 showed hourglass-like constrictions of the right suprascapular and axillary nerves (Figure 1). One month after onset, scapular winging and instability developed on the right, corresponding to right long thoracic nerve and spinal accessory nerve lesions. EMG 8 months after onset showed fibrillation potentials, reduced recruitment, polyphasic and low amplitude motor unit potentials in the right deltoid and infraspinatus muscles, and profuse fibrillation potentials and discrete motor unit recruitment in the right trapezius and serratus anterior muscles. Ultrasound of the right spinal accessory nerve showed marked enlargement and hourglass-like constriction, while the accessible initial segment of the right long thoracic nerve appeared normal.

3.3 | Patient 3

The 41-year-old man experienced acute severe pain in both shoulders lasting for one day, preceded by an episode resembling an upper respiratory tract infection, and followed by a burning sensation and numbness on the lateral aspect of both forearms (presumed bilateral lateral antebrachial cutaneous nerve lesions) and on the mid-abdomen on both sides (presumed bilateral 8-9th thoracic spinal nerve lesions), and weakness of both hands. Initial assessment disclosed weakness of the right flexor pollicis longus and flexor digitorum profundus muscle of the index finger (indicative of right anterior interosseous nerve lesion), and weakness of finger extension on the left (indicative of left posterior interosseous nerve lesion). Starting 1 week after symptom onset, the patient received 64 mg of methylprednisolone, tapered off over

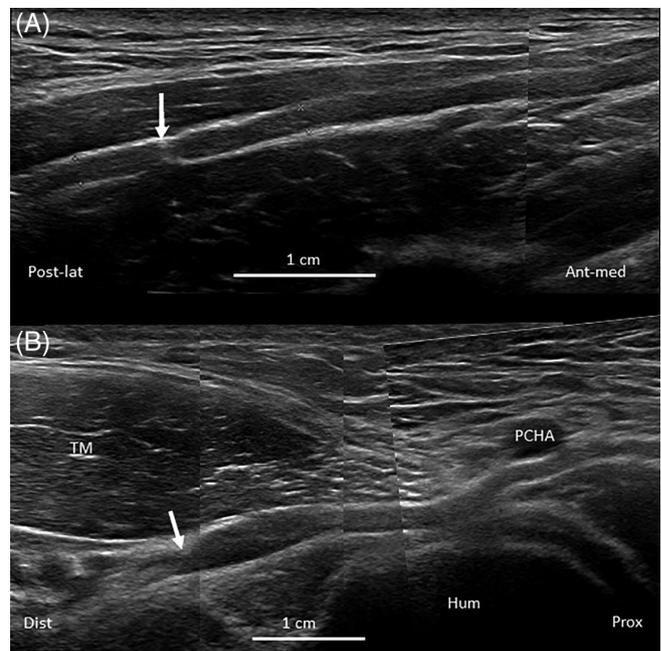


FIGURE 1 A and B are longitudinal images from Patient 2 of the right suprascapular nerve in the supraclavicular fossa and the right axillary nerve immediately proximal to its exit from the axilla, respectively. Note the incomplete hourglass-like constrictions of the nerves (arrows), a specific imaging marker of NA. Post-lat, postero-lateral; Ant-med, antero-medial; TM, teres major muscle; Hum, humerus; PCHA, posterior circumflex humeral artery; Dist, distal; Prox, proximal

weeks. Six weeks after onset, the right flexor pollicis longus muscle power returned to normal, the flexor digitorum profundus muscle of the index finger remained plegic, and right finger extension became weak (indicative of right posterior interosseous nerve lesion). On the left, the flexor pollicis longus muscle became weak (indicative of left partial anterior interosseous nerve lesion). EDX at this point showed reduced amplitude of the motor responses of both radial nerves, with normal sensory potentials. Bilateral median motor and sensory nerve conduction studies were normal. EMG of both extensor digitorum communis and left flexor pollicis longus muscles showed fibrillation potentials and reduced recruitment. Ultrasound showed an hourglass-like constriction of the medial fascicle within the right median nerve just proximal to the elbow. The other affected nerves appeared normal.

4 | DISCUSSION

NA may occur as an extrahepatic manifestation of HEV infection. HEV-associated NA appears to have a particular clinical phenotype in comparison to non-HEV cases. A recent multi-center study demonstrated that HEV-associated NA patients tend to have more extensive and bilateral involvement of nerves, including nerves outside the brachial plexus.⁶ The phenotype of our patients is in line with this conclusion, as all had three or more nerves affected, symptoms were bilateral for two, including involvement of the trunk and lower limb.

Such extensive nerve involvement is unusual in NA. In our cohort of 103 NA patients, the majority of patients (72%) presented with a mononeuropathy, and no other patients had a multiphasic/progressive course such as that described here. Furthermore, involvement of trunk and lower limb nerves is distinctly rare. In a study of lesion distribution in NA, only 2 of 703 lesions were outside the cervical-brachial area.⁸

Typically in NA, nerve palsy develops abruptly within a few days after the onset of pain. A unique finding in our case series is the multiphasic presentation of symptoms within a time span of 4–6 weeks. In one patient, each of the three bouts was heralded by the intensification and spreading of the pain; in the other two, nerve lesions appeared in two phases following the resolution of pain. Multiphasic presentation was not described in the multi-center study on HEV-associated NA of van Eijk et al.,⁶ but it is unclear whether this information was collected. However, in one case report of HEV-associated NA, symptoms were progressive over 3 weeks,⁵ and in another phrenic nerve palsy developed several months after onset.⁷ The multiphasic / progressive presentation of symptoms is probably not an obligatory or specific sign of HEV-associated NA, but, when present may be suggestive of HEV infection as a cause. Moreover, together with the extensive multi-nerve involvement seen in most cases, this mode of presentation may reflect a more severe and protracted nerve inflammation as opposed to non-HEV NA cases. Theoretically, the protracted and severe course in HEV-associated NA may call for a treatment of extended duration. However, prospective evidence on the efficacy of immunomodulatory treatment in both non-HEV and HEV-associated NA is needed.

Limitations of our study include its retrospective nature, the small sample number and the lack of controls, as no information on the HEV status of the rest of our NA cohort was available.

CONFLICT OF INTEREST

None of the authors has any conflict of interest to disclose.

ETHICAL PUBLICATION STATEMENT

Authors confirm that they have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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