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Scientific letter

Bilateral Diaphragmatic Paralysis Requiring Non-Invasive Ventilatory Support as a Consequence of Hepatitis E Virus-Associated Neuralgic Amyotrophy

Parálisis bilateral diafragmática con requerimiento de soporte ventilatorio no invasivo como consecuencia de amiotrofia neurálgica asociada al virus de la hepatitis E

Dear Editor,

Neuralgic amyotrophy (NA), also known as Parsonage-Turner Syndrome, is a multifocal inflammatory neuropathy primarily affecting the brachial and lumbosacral plexuses.[1] This condition manifests in various phenotypic forms, with the classic type observed in 75% of patients, typically presenting as an acute onset of asymmetric upper extremity symptoms, including intense pain, paresis, and winged scapula.[1] Another recognized variant is hereditary NA, and recurrence occurs in approximately 25% of cases.[1,2] Diaphragmatic paralysis is reported in 10% of cases.[3] A recent prospective study estimated a one-year incidence rate of 1/1000 for classic NA, mainly affecting middle-aged men.[4]

Pathophysiology is believed to be autoimmune, with immune-related factors serving as potential triggers. These include infections, vaccinations, immunotherapy, surgery, trauma, pregnancy or psychological stress.[2] In this report, we present a case of hepatitis E virus (HEV) associated NA with bilateral diaphragmatic paralysis, highlighting its clinical course, diagnostic challenges, and treatment outcomes.

A 43-year-old-man presented with acute dyspnea, orthopnoea, myalgia and right upper limb weakness over 48 h. His medical history included high-risk alcohol consumption, a body mass index of 30.4 kg/m^2, type 2 diabetes, dyslipidaemia, schizophrenia, and psoriasis, with no smoking history.

On examination, the patient exhibited intolerance to supine position, abdominal paradoxical breathing, a right winged scapula (Fig. 1A), and diminished motor strength (4/5) in the right deltoid. Respiratory rate increased from 18 to 32 breaths per minute (bpm) from seated to supine position. Biochemical tests showed elevated acute-phase reactants and transaminases. HEV IgM and IgG were positive, with a viral load of 83,000 IU/mL. Arterial blood gas analysis indicated mild hypoxemia without hypercapnia. Lung ultrasound (Fig. 1B) and chest X-ray (Fig. 1C, D) confirmed bilateral diaphragmatic paralysis.

Electromyography (EMG) revealed severe bilateral phrenic demyelinating neuropathy and peripheral proximal involvement of the right upper extremity (long thoracic nerve). Head CT scan was normal and cerebrospinal fluid (CSF) analysis revealed albumin-cytologic dissociation. Autoimmune screening showed antinuclear antibodies (ANA) positivity at 1/80 with a fine speckled pattern (AC-4) and low-titer anti-SSA (Ro60). Pulmonary function tests (PFT) indicated moderate restrictive impairment: vital capacity was 2.66 L (53.6% predicted), with a decline of 49.8% in the supine position to 1.34 L (26.9% predicted). A diagnosis of bilateral diaphragmatic paralysis secondary to HEV-associated NA was established. There was no family history of NA. Treatment was initiated with intravenous immunoglobulins (0.4 mg/kg/day for 5 days) and acute non-invasive ventilation (NIV) for severe orthopnoea.

Within a week, HEV viral load became undetectable, and the patient showed clinical improvement, including reduced pain and increased right deltoid strength. Despite these gains, orthopnoea persisted, necessitating ongoing home NIV support. The patient used bilevel positive airway pressure for nocturnal ventilation with inspiratory pressure of 14 cmH_2O, expiratory pressure of 4 cmH_2O and backup respiratory rate of 14 bpm. At the 3-month follow-up, no significant changes were observed in EMG or PFT results, with a mean daily use of NIV of 11 h. However, the patient reported a notable symptomatic improvement and returned to work.

Hepatitis E virus is a global cause of acute hepatitis and is increasingly recognized for its extrahepatic manifestations, including neurological symptoms such as NA. HEV has been implicated in over 10% of NA cases, likely through immune-mediated mechanisms rather than direct viral invasion.[2,5] In this case, the presence of ANA antibodies and the absence of HEV in the CSF further support an immune-mediated pathogenesis. This is consistent with prior studies reporting ANA positivity in up to 50% of HEV-associated NA patients and the higher prevalence of NA among immunocompetent patients, reinforcing the role of an immune response triggered by HEV.[5,6]

When NA is associated with HEV, it often presents more severely and bilaterally (80%), frequently extending beyond the brachial plexus, such as the phrenic nerves (25%).[7] Phrenic nerve involvement usually results in incomplete recovery, leading to persistent symptoms and limited treatment options.[2,3] An observational study showed that among patients with bilateral diaphragmatic paralysis secondary to NA, 78% initiated NIV, which was beneficial in most cases. However, at five years, only 16% achieved full recovery, 48% experienced some improvement and 36% showed no significant improvement.[3]

Therapeutic options for NA include prednisone, ribavirin and immunoglobulins, with variable outcomes.[5,7] NIV is indicated for orthopnoea or nocturnal hypoventilation, with proven positive effects.[2,3,8] In our case, prednisone was avoided due to the risk of worsening viral replication/hepatitis, while ribavirin was excluded because of limited evidence supporting its efficacy.[5,7] Due to the condition's severity and according to the current model of immune-mediated pathogenesis, immunoglobulins were started within 24 h of admission, supported by evidence from multiple case series and reports indicating that early treatment improves the likelihood of a

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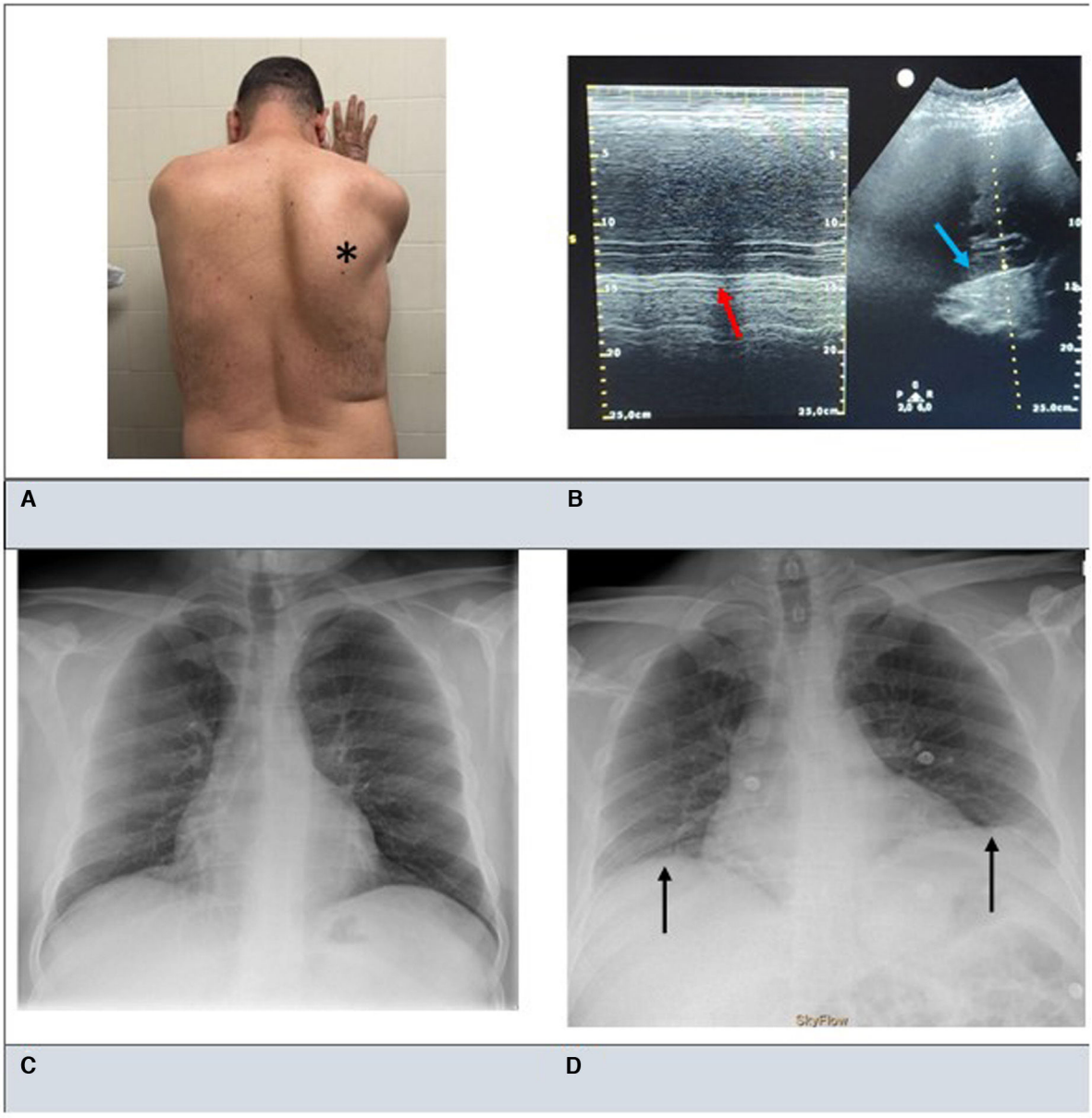

Fig. 1. Bilateral diaphragmatic paralysis due to HEV-associated neuralgic amyotrophy. (A) Right winged scapula on physical examination (black asterisk). (B) Lung ultrasound of the right diaphragm showing a quiet breathing excursion of approximately 0.5 cm (normal values for right diaphragmatic excursion in men range from 0.9 to 2.8 cm during quiet breathing). The red and blue arrows indicate the right hemidiaphragmatic excursion in M-mode and B-mode ultrasonography, respectively. (C) Chest X-ray taken 5 years before symptom onset. (D) Chest X-ray taken on the same day of hospital admission, revealing elevation of both diaphragms (black arrows).

positive outcome, while treatment beyond two weeks offers minima benefit.[2,5]

In conclusion, this case report describes a patient with NA of known etiology leading to acute respiratory failure and underscores the potential benefit of prompt treatment with immunoglobulins and NIV. However, the impact of early diagnosis and treatment on patient outcomes remains uncertain due to the prolonged recovery period of the phrenic nerve, which can extend up to 3 years.[9] Long-term follow-up is warranted to evaluate treatment effectiveness.

Informed consent

I confirm that I have obtained all consents required by applicable law for the ublication of any personal details or images of patients, research subjects or other individuals that are used in the materials submitted to Elsevier. I have retained a written copy of all such consents and I agree to provide Elsevier with copies of the consents or evidence that such consents have been obtained if requested by Elsevier.

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Authors' contributions

All substantially contributed to the final version of the manuscript.

Conflicts of interest

The authors declare not to have any conflicts of interest that may be considered to influence directly or indirectly the content of the manuscript.

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