Hepatitis E virus-associated brachial neuritis presenting with orthopnoea as a result of bilateral diaphragmatic weakness

Samuel Mackrill[1]
Prithwiraj Chakrabarti[2]
Richard Butterworth[3]
Veeresh Patil[4]
Author details can be found at the end of this article
Correspondence to:
Samuel Mackrill;
s.mackrill@nhs.net

Introduction

The spectrum of neurological complications of acute infection with hepatitis E virus are well described, including the characteristic syndrome of bilateral brachial neuritis which presents with a combination of bilateral shoulder pain and upper limb neurological deficits. In this case, a 69-year-old man developed persistent and disabling orthopnoea following an acute presentation consistent with acute brachial neuritis. Later outpatient follow up identified bilateral diaphragmatic weakness thought to be secondary to phrenic neuropathy, and serological testing confirmed acute hepatitis E virus infection. While brachial neuritis with phrenic nerve involvement is described in this context, cases with such prominent respiratory symptoms are uncommon.

Discussion

In the absence of fluid overload, patients with orthopnoea should be assessed for diaphragmatic weakness. A high index of suspicion is required as bilateral elevation of the hemidiaphragms is easily dismissed as an inadequate inspiratory effort. At the bedside,

Case report

A 69-year-old man presented to the emergency department when an episode of acute-onset dyspnoea and bilateral shoulder pain woke him from sleep. He described the pain as a tight band and noted that the dyspnoea was far worse when lying supine (orthopnoea). Blood results on admission were notable for moderately elevated levels of alanine aminotransferase at 226 iU/litre (Table 1). He underwent a computed tomography pulmonary angiogram which showed no evidence of pulmonary embolism, although some subtle bibasal collapse was noted. He also had an echocardiogram which showed mild aortic regurgitation, but cardiac causes of his presentation were thought to be unlikely in the absence of pulmonary oedema. The pain settled during a short admission and he was discharged home.

In the respiratory clinic 4 months later he had persistent orthopnoea and was unable to sleep lying flat, although he had no other respiratory symptoms. On systems review he reported a 2-month history of reduced appetite and weight loss of 1 stone; for the last 2 years he had noticed that food stuck in his throat which had been diagnosed as cricopharyngeal spasm. He had a background of atrial fibrillation (managed with apixaban), hypertension and gout. He was an ex-smoker, having stopped 35 years ago, drank heavily but was in the process of cutting down, and worked part-time as an accountant. Review of his imaging identified elevation of both hemidiaphragms which was new compared with historic films (Figure 1), so he was referred for diagnostic testing and a neurology opinion.

Subsequent fluoroscopy was consistent with bilateral diaphragmatic weakness which was then confirmed on spirometry with >50% reduction in forced vital capacity when supine (Table 2). He also underwent a sleep study which was normal. The neurology team thought that his presentation was consistent with bilateral brachial neuritis, although the only abnormality on neurological examination was right-sided scapular winging. A magnetic resonance imaging scan of the brachial plexus and a repeat computed tomography scan of the thorax were both unremarkable. Neurophysiological testing was not performed. Finally, in view of his systemic symptoms and abnormal liver function tests he was tested for hepatitis E infection for which he was found to be IgG and IgM positive. One year after onset there was interval improvement in his forced vital capacity (Table 2). At 18 months he reported feeling almost 100% back to normal and was able to sleep lying flat again.

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Table 1. Blood test results

Test	On admission with bilateral shoulder pain	In respiratory clinic 4 months after initial presentation	Normal range
Haemoglobin	151	150	130–170 g/litre
White blood cell count	3.0	5.2	3.7–11.1x10^9/litre
Neutrophil count	1.4	2.5	1.7–7.5x10^9/litre
Lymphocyte count	1.2	1.9	0.9–3.2x10^9/litre
Platelet count	172	193	150–450x10^9/litre
Sodium	136	137	133–146 mmol/litre
Potassium	4.0	4.2	3.5–5.3 mmol/litre
Urea	5.5	5.4	2.5–7.8 mmol/litre
Creatinine	53	60	64–104 umol/litre
Bilirubin	8	11	3–21 umol/litre
Alanine aminotransferase	226	30	1–49 iU/litre
Gamma-glutamyl transferase	226	105	0–55 iU/litre
Alkaline phosphatase	71	89	30–130 iU/litre
C-reactive protein	12.5	13.2	<6 mg/litre
Troponin	3.6	–	2.3–19.9ng/litre

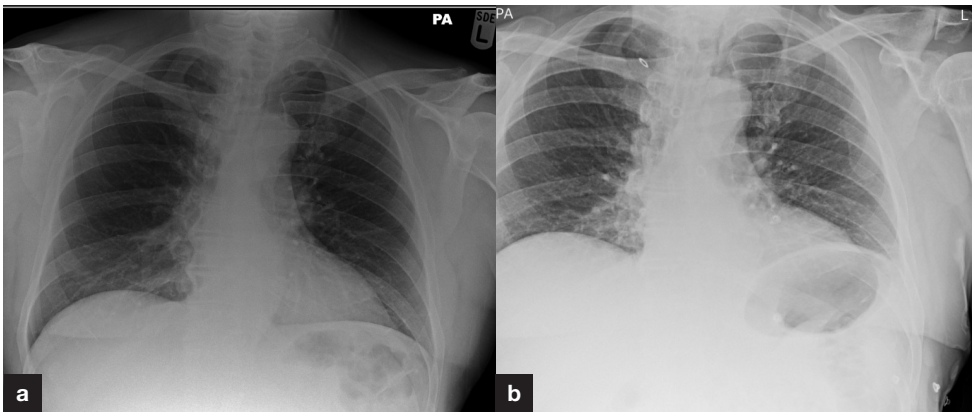

Figure 1. Chest X-ray appearance (a) historic film for comparison and (b) on admission.

short 'sniffs' may reveal paradoxical retraction of the abdominal wall with inspiration, although the diagnostic test is erect and supine spirometry demonstrating a decrease in forced vital capacity when supine (up to 10% is allowed in unaffected patients).

Brachial neuritis may be unilateral or bilateral and presents with acute shoulder pain that may radiate down the arms. Patients may also report weakness, and lower motor neurone signs may be found. Involvement of the phrenic nerve is well recognised (Shinder et al,

Table 2. Forced vital capacity results

Time	Sitting	Supine	Percentage change	Predicted
4 months after symptoms onset	2.60 litres	0.66 litres	–75.6%	4.09 litres
11 months after symptoms onset	2.78 litres	1.04 litres	–62.6%	4.12 litres

Learning points

- Diaphragmatic weakness should be considered in the differential diagnosis of orthopnoea, especially when evidence of fluid overload is insufficient to explain the clinical picture.
- The bedside 'sniff test' supported by diagnostic spirometry can be used to confirm diaphragmatic weakness.
- Brachial neuritis presenting with acute shoulder pain and lower motor neurone upper limb weakness may extend to involve the phrenic nerve and it roots, resulting in symptomatic diaphragmatic weakness.
- The combination of bilateral shoulder pain, dyspnoea and abnormal liver function is highly suggestive of acute infection with hepatitis E virus, and patients should be tested so that other complications can be recognised early.

1998). The diagnosis is primarily clinical, with nerve conduction studies often normal. In this case, the respiratory symptoms were disproportionate to the motor features, suggesting limited involvement of the wider brachial plexus (although scapular winging suggested long thoracic nerve involvement).

When seen in men aged 35–60 years, acute shoulder pain associated with abnormal liver function tests is almost pathognomonic of bilateral brachial neuritis resulting from acute hepatitis E virus infection, although abnormal liver function tests are not required to make this diagnosis (McLean et al, 2017; van Eijk et al, 2017). In addition to bilateral disease, symptomatic involvement of the phrenic nerve suggests associated infection with hepatitis E virus, seen in 24.5% of the hepatitis E virus-positive group compared with only 3.5% of hepatitis E virus-negative controls in one case series (van Eijk et al, 2017). In rare cases respiratory organ support has been required (Noushad et al, 2021), likely part of a spectrum of neurological complications of hepatitis E virus that include classical Guillain–Barré syndrome, although such a restricted respiratory presentation as seen in this case is rare in the reported literature.

Author details

[1]Department of Medicine, Milton Keynes University Hospital, Milton Keynes, UK

[2]Department of Microbiology, Milton Keynes University Hospital, Milton Keynes, UK

[3]Department of Neurology, Milton Keynes University Hospital, Milton Keynes, UK

[4]Department of Respiratory Medicine, Milton Keynes University Hospital, Milton Keynes, UK

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