Acute Bilateral Phrenic Neuropathy: from Diabetes Mellitus to Focal Guillain-Barré Syndrome

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ABSTRACT

Bilateral phrenic neuropathy is a rare cause of acute ventilatory failure posing both diagnostic and therapeutic difficulties. We report the case of a 55-years-old diabetic male presenting with acute onset orthopnea. Clinical and radioscopic evaluations suggested bilateral diaphragmatic paralysis, electroneuromyographic studies revealed bilateral acute phrenic neuropathy, and cerebrospinal fluid examination found albuminocytologic dissociation. The administration of high-dose intravenous immunoglobulin was followed by prompt improvement. During the next months the symptoms continued to regress. There were no recurrences. We consider the patient had a spatially limited form of acute inflammatory demyelinating polyradiculoneuropathy. The case underlies the importance of considering an immune mediated etiology in patients with acute bilateral phrenic neuropathy. To the best of our knowledge no similar case has been reported.

Keywords: acute polyradiculoneuropathy, diaphragmatic paresis, phrenic neuropathy, diabetic neuropathy, Guillain-Barré syndrome, intravenous immunoglobulin, ventilatory failure

INTRODUCTION

Complete diaphragmatic paralysis produces life threatening ventilatory failure demanding immediate treatment. The causative lesion may be located anywhere from brainstem to the neuromuscular plate or the muscle itself. Bilateral phrenic neuropathy unaccompanied by other notable findings is a rare but well documented occurrence. Typically its presentation is not acute (1).
CASE REPORT

A 55-years-old Caucasian man presented to the emergency room with sudden onset orthopnea exacerbated over the following hours to the point of minimal activity orthostatic dyspnea. Two weeks earlier, he had self-limited watery diarrhea and an accidental fall from his own height causing minor nasal trauma. Neither of these events required medical assistance. For the past six years he had type 2 diabetes mellitus (treated with metformin). He associated asymptomatic chronic sensorimotor axonal polyneuropathy considered to be diabetes-related. He had no other known conditions, no recent change in his daily routine, no exposure to vaccines or toxins.

The physical examination revealed mild polynea, increased accessory respiratory muscle utilization, thoraco-abdominal paradox, bilateral basal dullness and absent vesicular murmur. Oxygen saturation depended upon position: 95% while standing, 82% on right lateral decubitus, 88% on left decubitus, 78% while supine. Stretch reflexes and plantar responses were absent. No other signs or symptoms were found. Noninvasive ventilation with bilevel positive airway pressure was required for maintaining adequate oxygenation in recumbent position.

The radioscopic examination revealed bilateral diaphragmatic elevation and absence of deep breathing orthograde excursions. Pulmonary function testing confirmed a pattern of ventilatory restriction: first second forced expiratory volume (FEV1) 34% of predicted, forced vital capacity (FVC) 36%, reference range FEV1/FVC ratio, decreased maximal inspiratory and expiratory pressures. The thoracic computed tomography showed bilateral basal atelectasia (secondary to the ventilation impairment). Imagistic investigations excluded intraabdominal masses, diaphragmatic lesions, cervical spinal cord or bilateral phrenic compression. Routine blood tests found only a mild inflammatory syndrome. Fasting blood glucose was 83 mg/dl. Glycated hemoglobin was within physiological limits (5.8%). Additional serologic investigations (including Campylobacter jejuni antibodies) were unrevealing.

The electroneuromyographic study diagnosed bilateral phrenic neuropathy (prolonged distal motor latencies and decreased amplitudes, more severe on the left). Limb findings were compatible with chronic sensorimotor length-dependent axonal polyneuropathy (the examination was performed in the third day since symptom onset, therefore not ruling out acute superimposed involvement). The cerebrospinal fluid (CSF) analysis revealed one nucleic cell/mm³, increased immunoglobulin G (Ig G) fraction, and mildly increased total protein and albumin levels (59.9 mg/dl, 40 mg/dl respectively). The CSF to plasma albumin coefficient was within limits (suggesting blood-brain barrier alteration) while the Ig G coefficient was slightly increased (suggesting intratechal synthesis).

Administration of high-dose intravenous immunoglobulin (IVIG) was followed by prompt improvement - Octagam® (Octapharm, Pyrmont, Australia) 0.4 g/kg/day, from the 7th day of disease, total dose 1.2 g/kg, not continued up to 2 g/kg due to non-medical reasons. Long term respiratory kinesytherapy was also prescribed.

Serum antiganglioside antibodies were absent however the test was performed after obtaining remission. Abolition of upper limbs stretch reflexes proved to be transitory. Over the next three months the evolution was favorable with almost complete recovery. Six months later the patient was well, with no recurrences.

DISCUSSION

Guillain-Barré syndrome (GBS) designates a heterogenous etiopathogenic spectrum of self-limited (but potentially deadly) autoimmune acute inflammatory polyradiculoneuropathies that may have spatially restricted patterns of presentation. Campylobacter jejuni and other infections are putative triggers. Nadir is reached in less than four weeks. The benefit of plasmapheresis and IVIG is widely acknowledged. Rapidly progressive diaphragmatic paralysis is not uncommon in typical cases (2). Bilateral phrenic neuropathies with less acute presentations have been reported in late stage chronic demyelinating polyradiculoneuropathy and Charcot-Marie-Tooth disease (3). It may also occur in the setting of diabetes mellitus, autoimmune brachial plexopathy / neuralgic amyotrophy / Parsonage-Turner syndrome, multifocal motor neuropathy with conduction block, trauma (usually iatrogenic), infections (e.g., certain viruses, Borrelia burgdorferi), toxin ex-
posure (e.g. chronic uremia, tetanus, arsenic poisoning), radiation therapy, critical illness, systemic lupus erythematosus, amyloidosis, porphyria and sarcoidosis (1,3-6). Acute bilateral phrenic neuropathy was reported during adalimumab treatment for psoriasis (7). Truly isolated involvement is very rare, certain authors proposing it as a distinct entity (3).

Our patient had severe acute bilateral demyelinating phrenic neuropathy accompanied by transitory abolition of upper limbs stretch reflexes and probable radicular involvement (suggested by the albuminocytologic dissociation). IVIG administration was followed by prompt improvement, thus supporting the hypothesis of an immune mediated pathogenesis. It has been reported that patients with prolonged diabetes may have increased CSF protein levels (8). Diabetic neuropathy remains our main differential diagnosis but is very unlikely (optimal glycemic control, acute presentation, antecedent diarrhea, response to IVIG). The clinical evolution and paraclinical findings excluded other potential causes. We consider that all the available evidence supports the diagnosis of spatially limited acute inflammatory demyelinating polyradiculoneuropathy (reminiscent of the pharyngeal-cervical-brachial motor variant of GBS (2)). This case emphasizes the importance of considering IVIG administration whenever autoimmunity is a plausible pathogenic mechanism. To the best of our knowledge no similar case has been reported.

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