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Reversible bilateral phrenic nerve paralysis

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ABSTRACT

Bilateral phrenic nerve paralysis is a rare potentially life-threatening condition which is usually due to trauma (including surgery) or neurologic disease. We present a patient with apparent rapid onset bilateral phrenic nerve paralysis whose primary symptom was severe positional (supine) dyspnea with profound supine oxygen desaturation. Nerve conduction study abnormalities of the phrenic nerves and some left brachial plexus nerves suggested a diagnosis of ALS. He was treated with supportive night time ventilatory assistance (BiPAP) and over 4 years his condition recovered essentially completely. In retrospect the most likely diagnosis was a rare brachial plexopathy referred to as neuralgic amyotrophy.

1. Introduction

Bilateral phrenic nerve paralysis is a relatively rare condition characterized by exertional dyspnea, orthopnea which is often marked, and paradoxical (inward) inspiratory abdominal movement [1]. The etiology includes both surgical and non-surgical trauma as well as both focal and generalized neurological conditions. We report a case of bilateral phrenic nerve paralysis initially misdiagnosed as motor neuron disease (amyotrophic lateral sclerosis or ALS) with spontaneous recovery over several years. A diagnosis of neuralgic amyotrophy, a rare brachial plexopathy, seems most likely.

2. Case study

A 62 year old male was referred to our clinic in 2003 with a 6–8 week history of fatigue associated with progressive mild exertional dyspnea and severe dyspnea when lying on his back and, to a lesser extent, when bending forward. He was unable to remain supine for longer than a minute or two. For several weeks he had been sleeping upright in a reclining chair. Past history included remote surgery for peptic ulcer disease, hypertension (hydochorothiazide, enalapril) and gout (allopurinol) as well a 16 year remote 30 pack year smoking history. He did not complain of weakness or other neurologic symptoms. Because of a possibility of pulmonary thromboembolic disease (unexplained dyspnea and bilateral sub-segmental atelectasis) a ventilation perfusion lung scan had been performed and was low probability. Computerized axial tomographic (CAT) scan had been attempted but was technically unsuccessful because of the supine dyspnea.

Physical examination was normal with the exception of increased dyspnea when supine. Oxygen saturation by pulse oximeter was 96% on room air at rest, 93–94% after a well tolerated 200 m walk, and less than 80% after less than 2 min supine (Fig. 1). Additionally, there was concomitant paradoxical abdominal wall motion noted while supine. The detailed neurologic examination, performed later by a neurologist, revealed focal weakness and wasting (generally mild) of the left deltoid and left infraspinatus muscles.

The patient's chest radiograph demonstrated small lung volumes, sub-segmental atelectasis and elevation of both hemi-diaphragms (Fig. 2). Pulmonary function testing revealed a severe non-obstructive restrictive pattern with modest reduction in diffusing capacity which corrected for volume (Table 1). Supine lung function was not performed. Maximum inspiratory pressure (MIPs) and maximum expiratory pressure (MEPs) were reduced to 60 cm H_2O (55%) and 120 (59%) cm H_2O respectively An arterial blood gas showed borderline hypercapnea with a pH of 7.44, PO_2 of 77 mmHg, PCO_2 of 44 mm Hg and HCO_3 of 29 mmol/L. The estimated alveolar arterial gradient (PiO_2 in SK ~ 140 mm. Hg).was normal (<10 mm. Hg.) Chest CAT scan showed no evidence of parenchymal lung disease, adenopathy or pulmonary vascular disease. A preliminary autoimmune work up was normal/negative. Thyroid function was within normal limits. Testing for West Nile Virus was also

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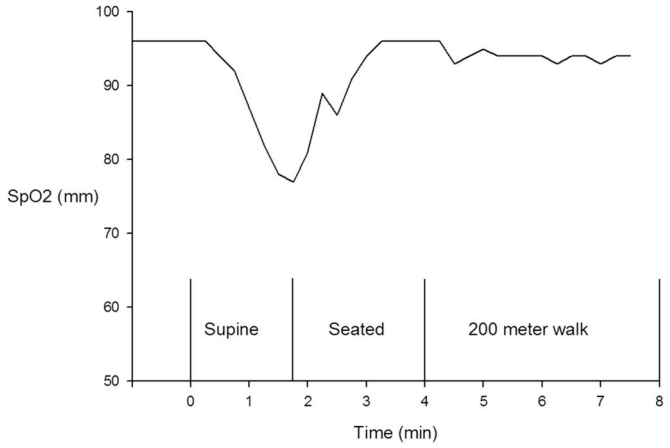

Fig. 1. Pulse oximetry tracing: resting up to time 0, supine time 0–1.8 minutes, seated 1.8–4 minutes, and during a well tolerated 200 m walk 4–8 minutes.

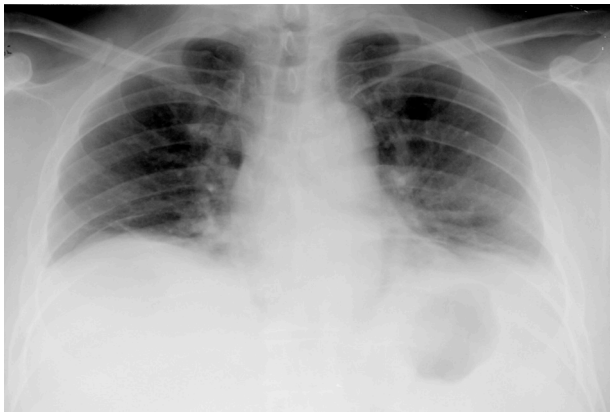

Fig. 2. Inspiratory chest radiograph at the time of initial presentation shows small lung volumes and some areas of sub-segmental atelectasis and bilateral elevation of the hemi-diaphragms to the level of the fourth anterior ribs.

Table 1
Pulmonary function.

	2003	2007	2010
FEV1	1.25	2.51	2.61
	42	93	100
FEV	1.78	3.45	3.65
	42	89	96
FEV1/FVC ratio	0.71	0.71	0.71
RV	1.41	2.34	
	62	106	92
TLC	3.59	6.00	5.92
	58	107	106
DLCO	14.4	20.7	23.0
	45	71	81

Abbreviations: FEV1 Forced Expired Volume in one second.
FVC Forced Vital Capacity.
RV Residual Volume.
TLC Total Lung Capacity.
DLCO Diffusing Capacity for Carbon Monoxide.

negative.

Nerve conduction studies demonstrated abnormal motor responses. There was no response of the left and right phrenic nerve. Electromyography confirmed subacute and chronic neurodegenerative changes of the left infraspinatus muscle and right hemidiaphragm. The right median nerve also demonstrated a mildly prolonged motor latency and slowing of the sensory conduction velocities. An MRI was requested but, since this would have required intubation and general anesthesia to permit the patient to lie supine, the patient declined.

The multifocal nature of our patient's neurologic findings, along with the EMG, were considered by the neurologist to be "essentially diagnostic of ALS". He was started on riluzole, nimodipine, vitamin E 400 and coenzyme Q10 as part of his medical regimen. An urgent sleep laboratory assessment was done 2 weeks after presentation in order to prescribe and titrate bi-level (BiPAP) nocturnal ventilatory support. Nocturnal BiPAP was prescribed at 14/4 (inspiratory positive airway pressure 14 cm H_2O and expiratory positive airway pressure 4 cm H_2O); pressures were later increased to 16/5. He reported immediate improvement in dyspnea when using his BiPAP.

During the next 4 years during his routine follow up assessments, symptoms slowly, but markedly, improved. He reported that he no longer felt dyspnea when lying flat and stopped using his BiPAP. His fatigue and exercise tolerance similarly improved. Pulmonary function had markedly improved to essentially normal in 2007 and was further improved in 2010 (Table 1). His follow-up chest radiograph demonstrated radiographic improvement with increased lung volumes, now normal) compared to his previous (Fig. 3). In 2007, the neurologic examination had normalized and nerve conduction studies had significantly improved. Currently, at the age of age 78, he is doing well and has not required BiPAP for more than 10 years.

3. Discussion

Diaphragmatic dysfunction is more commonly seen unilaterally rather than bilaterally. Common causes include post-surgical traumatic injury of the phrenic nerve, spinal cord tumors, diseases of the anterior horn cell (ALS, spinal muscular atrophies and postpolio syndrome), neuropathies of the phrenic nerve (Guillain-Barre syndrome, neuralgic amyotrophy, etc), disorders of the neuromuscular junction (Myasthenia gravis, Eaton-Lambert syndrome, etc) and disorders of the diaphragm itself (the muscular dystrophies, polymyositis, thyroid dysfunction, etc.) [1].

Given our patients' improvement, the initial diagnosis of ALS was a misdiagnosis. Retrospectively, the most likely diagnosis is neuralgic amyotrophy (NA). The marked improvement in symptoms and diaphragmatic function essentially exclude the original diagnosis of ALS. Originally described as Parsonage-Turner syndrome, this peripheral neuropathy (NA) typically involves the brachial plexus, but can involve

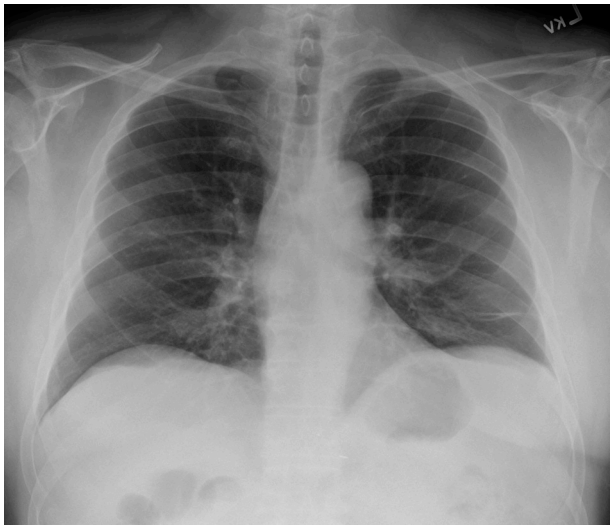

Fig. 3. Inspiratory chest radiograph 4 years later demonstrates normal lung volumes compared with previous: the hemi-diaphragms are now at the level of the sixth anterior ribs.

other nerves and nerve roots such as those of the lumbosacral plexus, recurrent laryngeal and phrenic nerves [2]. It is often preceded by an infectious, surgical or traumatic event. It can however occur in a sporadic or autosomal dominant form [3]. There is often shoulder or upper limb pain, which typically lasts from 1 to 2 weeks to several months. This eventually leads to weakness and muscle atrophy of the affected muscle groups. While our patient did not give a history of a preceding infection, traumatic event or pain, he did have clinical findings that suggested brachial plexus involvement.

Diagnosis of diaphragmatic dysfunction characteristically involves demonstration of a FVC of less than 50% predicted as well as MIPs less than 30 cm H_2O [1]. Ultrasonography of the diaphragm demonstrating diminished thickening and transdiaphragmatic pressure attenuation is also helpful in solidifying the diagnosis. Our patient did not meet the MIPs criteria but, clinically, his clinical assessment and electromyographic features were diagnostic of bilateral phrenic nerve palsy.

Despite no specific treatment of NA, management of this patient population is largely supportive and centers around providing ventilatory support in the form of noninvasive positive-pressure ventilation (NIPPV). Given that the diaphragm is the sole muscle of ventilation during rapid eye movement (REM) sleep, patients with NA, like other forms of diaphragmatic dysfunction, hypoventilate when in REM and are prone to hypercapnea. More invasive therapies can be considered if NIPPV fails to correct any underlying hypoventilation. It is generally recommended that, after a long period of observation to ensure no long-term recovery, other invasive therapies such as diaphragmatic pacing, plication of the diaphragm or tracheostomy be considered.

The long-term prognosis for NA with diaphragmatic involvement is variable. The majority of patients do experience some recovery of the diaphragm. In one case series, partial or full recovery occurred in 71% of patients and was noted as early as 2 years after diagnosis. The majority of patients, however, demonstrated some recovery after a latent period of at least 3 years, however recovery is often incomplete [4,5].

The differential diagnosis of NA, particularly painless NA includes other neurologic conditions such as ALS which this patient was initially thought to have. Key features differentiating NA from ALS are summarized in Table 2 [6,7]. As well as generally being painful, NA is usually more abrupt in onset, more focal in distribution, and non-progressive, eventually resolving over a periods of a few years in most [6].

In our patient, the most likely diagnosis only became evident several years after his initial presentation. Initially, his clinical features were consistent with ALS. However, his lack of disease progression and long term resolution lead us to consider alternate diagnoses. Given the additional involvement of the left brachial plexus, NA was deemed most likely. When evaluating patients with diaphragmatic dysfunction, a thorough history and clinical assessment is paramount in establishing a diagnosis. Despite this however, a period of prolonged observation with concurrent management may be additionally required to confirm or refute that diagnosis.

Table 2
Clinical features of neualgic amyotrophy and amyotrophic lateral sclerosis [6,7].

	Neuralgic Amyotrophy	Amyotrophic Lateral Sclerosis
Prevalence	2:100,000 Likely more common	1.89:100,000
Male:Female ratio	2:1	1.5:1
Onset	Abrupt	Insidious
Pain	Usual (90%) Often severe and refractory to analgesia	Painless
Distribution	Focal Arm, shoulder & diaphragm. Occasionally other nerves	Usually diffuse Can be focal initially
Prognosis	Generally good Resolution in 75–80% over 2–3 years Improvement usual in the rest	Relentlessly progressive Median survival 2–5 years depending on presentation Worse for bulbar or respiratory presentations
Etiology	Unknown Query auto-immune	Unknown

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Disclosure

None.

Declaration of competing interest

The authors listed above, Dr Neil Maharaj and Dr Don Cockcroft declare that they have no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmcr.2019.100953.

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