

Vocal cord paralysis and respiratory muscle weakness: An unusual presentation of chronic polyneuropathy

LKL Chau BM FRCPC, KA Webb MSc, AC Jackson MD FRCPC, DE O'Donnell MD FRCPI FRCPC
*Division of Respiratory and Critical Care Medicine, and Division of Neurology,
Queen's University, Kingston, Ontario*

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A case of chronic polyneuropathy that manifested with an unusual combination of vocal cord paralysis and respiratory muscle weakness is reported. In addition, results of an exercise test carried out to assess the severity and mechanisms of exertional breathlessness in this unique condition with combined obstructive and restrictive disorders are described.

Key Words: *Charcot-Marie-Tooth disease, Dyspnea, Exercise test, Hereditary motor and sensory neuropathy, Polyneuropathy, Respiratory muscle weakness, Vocal cord paralysis*

Respiratory manifestations of chronic polyneuropathies with vocal cord paralysis and severe respiratory muscle weakness are uncommon. A case of a patient with polyneuropathy who presented with dominant respiratory symptoms and only minimal limb weakness is reported.

CASE PRESENTATION

An 18-year-old woman presented with a two-year history of noisy breathing, dyspnea and poor exercise tolerance, and was referred with a working diagnosis of asthma. Her symp-

Paralysie des cordes vocales et faiblesse des muscles respiratoires - Tableau inhabituel d'une polynévropathie chronique

RÉSUMÉ : Un cas de polynévropathie chronique manifesté par l'association inhabituelle d'une paralysie des cordes vocales et d'une faiblesse des muscles respiratoires est signalé ici. On décrit en outre les résultats d'une épreuve d'effort effectuée pour évaluer la gravité de l'atteinte et examiner les mécanismes de l'essoufflement dû à l'exercice dans le cadre de cette maladie unique où les troubles obstructifs et restrictifs se combinent.

toms occurred gradually towards the end of a full-term pregnancy and persisted postpartum. Her family members were particularly concerned with her noisy breathing, which was described as a wheezing sound that persisted throughout the day as well as nocturnally. The patient's chief complaint was diminished exercise tolerance, having noticed that physical activities such as aerobics and dancing were no longer tolerated. Furthermore, she was unable to keep up with her peers because of exertional breathlessness when walking on a level surface. Her symptoms were not aggravated by cold expo-

Correspondence: Dr Denis O'Donnell, Richardson House, 102 Stuart Street, Kingston General Hospital, Kingston, Ontario K7L 2V7. Telephone 613-545-6328, fax 613-549-1459, e-mail odonnell@post.queensu.ca

sure or smoky environments, and had no seasonal or diurnal fluctuations.

The patient had orthopnea and required four pillows for many years when sleeping. She had no leg discomfort or ankle swelling but had mild bilateral leg weakness and occasional difficulty arising from lying on the floor. She did not notice any other neurological symptoms and denied dysphonia, dysphagia and aspiration. Her past medical history was unremarkable other than for noisy breathing in early childhood, which resolved with maturity and was attributed to asthma. Her developmental milestones were normal, and her athletic abilities were comparable with those of her peers. She was not taking any medication, was a nonsmoker and rarely consumed alcohol. Her family history was noncontributory, although her paternal family history was unavailable because her father was adopted.

Examination revealed a well nourished (157.5 cm, 55.8 kg) young female in no apparent respiratory distress. Resting respiratory rate was 14 breaths/min, and heart rate was regular at 72 beats/min. Occasional quiet stridor was audible, especially with rapid inspiration during speech. Her voice was normal. Nose and throat examinations were unremarkable, and there was no neck swelling or palpable cervical lymphadenopathy. The trachea was central. Lateral chest wall excursions were diminished despite appreciable inspiratory efforts. There was no paradoxical movement of the chest wall or abdomen. Percussion was resonant throughout the chest. Breathing sounds were reduced bilaterally with faint inspiratory and expiratory wheezes audible over the laryngeal area. Results of examination of the cardiovascular system and abdomen were normal. Cranial nerves were normal. Inspection of the limbs revealed modest bilateral wasting of the thenar and hypothenar muscles, mild reduction of shoulder girdle muscle bulk and bilateral pes cavus. Muscle power was mildly diminished in all limbs, especially in the distal muscle groups. Areflexia was noted. Sensory examination revealed reduced vibration sense in the hands and feet, and diminished pin prick and temperature sensations below the knees. There were no signs of cerebellar disease, and her gait appeared normal.

Blood tests, comprising a full blood count; measurement of serum electrolytes, glucose, ionized calcium, vitamin B₁₂, folate and electrophoresis; and renal, liver and thyroid function tests, were normal. Measurement of arterial blood gases at room air demonstrated a PaO₂ of 92 mmHg and a PaCO₂ of 41.7 mmHg. Forced vital capacity (FVC), forced expiratory volume in 1 s, maximal midexpiratory flow (FEF₅₀), peak expiratory flow rate, total lung capacity and residual volume were all diminished at 2.79 L (73% predicted), 1.76 L (57% predicted), 1.43 L/s (33% predicted), 2.21 L/s (33% predicted), 3.69 L (77% predicted) and 1.12 L (85% predicted), respectively. Reduction in FVC from a sitting to supine position was exaggerated at 0.49 L. Maximal inspiratory flow rates were diminished at any given volume (with a maximal midinspiratory flow [FIF₅₀] of 0.98 L/s, 25% predicted and a FEF₅₀:FIF₅₀ ratio of 1.46). Specific airway resistance was elevated (252% predicted), and carbon

monoxide diffusing capacity was normal. Maximal inspiratory and expiratory pressures were markedly diminished at 30 cm H₂O (37% predicted) and 25 cm H₂O (26% predicted), respectively.

Chest radiograph was normal. Fluoroscopic sniff test showed normal diaphragmatic motion. Polysomnography showed a respiratory disturbance index of less than 1/min, with no oxygen desaturation or hypercapnia. Laryngoscopy identified a narrowed glottis, minimal cord abduction on inspiration and normal cord adduction during phonation. Magnetic resonance imaging of the brain was normal. Electrophysiological testing showed normal compound muscle action potentials, prolonged distal latencies of the posterior tibial and common peroneal nerves, and absent sural nerve action potentials. Motor and sensory nerve conduction velocities were within normal limits. Electromyography showed large motor units. Calf muscle biopsy demonstrated fibre-type grouping, which is evidence of denervation with subsequent reinnervation. Sural nerve biopsy revealed a loss of large myelinated fibres with fibrosis. Myelin sheaths were disproportionately small for the size of axons, and there were prominent onion bulbs. Occasional macrophages containing myelin debris were present, but no other inflammatory changes were found. These studies provided evidence of a chronic pathological process involving both the myelin sheaths and axons of peripheral nerves.

An incremental symptom-limited cycle exercise test with esophageal pressure (P_{es}) monitoring was carried out to assess the severity and mechanisms of exertional breathlessness. Exercise was terminated at 60 W (39% of the predicted maximal work rate) with a maximal oxygen consumption of 1.29 L/min (61% of the predicted maximum) because of 'very, very severe' dyspnea (Borg scale rating of 9) (Figure 1). Intensity of the perceived leg effort at peak exercise was also 'very severe' (Borg scale rating of 7) but was not the primary factor limiting exercise in this instance. Maximum heart rate was 173 beats/min (87% of the predicted maximum), and blood pressure responses to exercise were within normal limits. There was no oxygen desaturation. Rapid, shallow breathing was noted, and there was a modest increase in the ventilatory slope (Figure 1) increasing oxygen consumption. Given the inspiratory and expiratory flow constraints at the operating volumes during exercise (Figure 2), the maximum ventilation achieved was very close to the ventilatory capacity. Exaggerated tidal P_{es} swings during respiration and an increased area within the pressure-volume loops at rest and during exercise suggested increased work of breathing related to increased resistive load from the narrowed glottis (Figure 2). Dynamic compliance, calculated as the change in inspired volume divided by the corresponding change in pressure between points of zero flow, was only modestly reduced with values of 90 mL/cm H₂O at rest and 75 mL/cm H₂O at peak exercise (Figure 2). The ratio of the tidal P_{es} swing:concurrent maximal static inspiratory pressure (P_{I,max}) at peak exercise was abnormally high relative to the low maximal oxygen consumption (P_{es}:P_{I,max} 58%) (Figure 1). Further examination of tidal P_{es} relative to the corre-

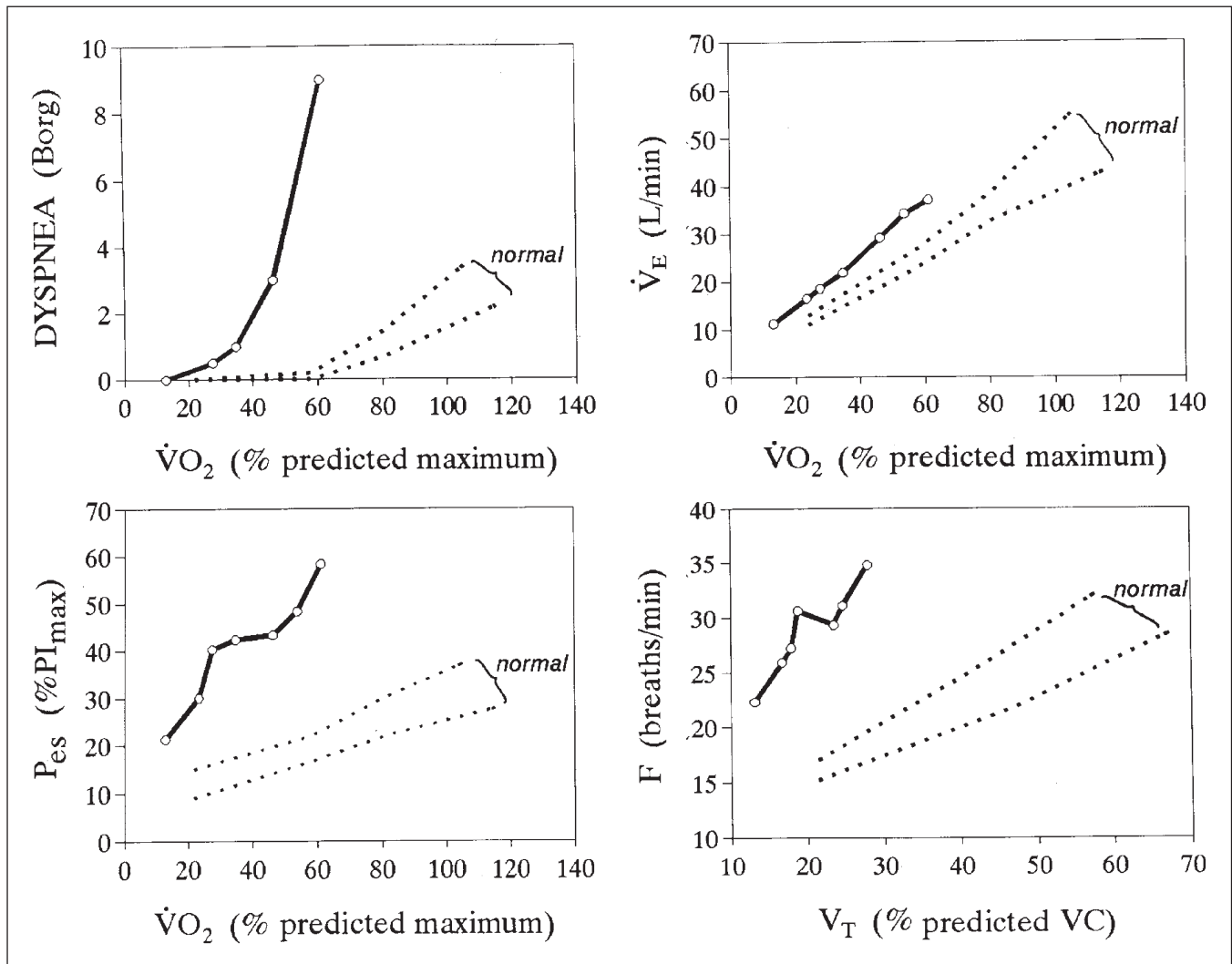


Figure 1 Dyspnea (Borg scale ratings), ventilation (\dot{V}_E), tidal esophageal pressure (P_{es}) swings relative to maximal pressure generating capacity (PI_{max}) and breathing pattern responses are shown in reference to normal (dotted lines indicate the mean normal response \pm SEM). F Breathing frequency; VC Vital capacity; VO_2 Oxygen consumption; V_T Tidal volume

sponding maximal dynamic inspiratory P_{es} curve during an inspiratory capacity manoeuvre at peak exercise (Figure 2) underscored the minimal to zero prevailing force reserve, which was overestimated when P_{es} was expressed as a fraction of static PI_{max} (Figure 1). The tension-time index of the inspiratory muscles, the product of mean inspiratory P_{es} expressed as a fraction of the dynamic PI_{max} and the inspiratory duty cycle (inspiratory time as a fraction of total time of the breath) (1) was 0.17 at peak exercise. This index reflects a high oxygen cost of breathing for these muscles and was significantly elevated compared with the critical level of 0.15, above which fatigue occurs (1).

DISCUSSION

Although neuromuscular disease is a well recognized cause of respiratory failure, clinical presentation with respiratory symptoms due to vocal cord paralysis and respiratory muscle weakness with minimal limb symptoms is distinctly unusual. Clinical features, electrophysiological studies and

pathological findings are in keeping with a motor and sensory polyneuropathy. Early onset, long clinical course and nerve biopsy findings indicate a chronic pathological process. The main diagnostic possibilities are hereditary motor and sensory neuropathy (HMSN), also known as Charcot-Marie-Tooth disease, and chronic inflammatory polyneuropathy (2,3). The pes cavus and absence of a fluctuating course favour the diagnosis of HMSN. Absence of a family history makes confirming a diagnosis of HMSN difficult. However, paternal family history was not known in the present case. Dysparemia, an autosomal recessive mode of inheritance, and a de novo mutation are possible explanations for the absence of a family history in cases of HMSN, which is predominantly an autosomal dominant disorder (4,5). Diaphragm weakness has been reported in patients with Charcot-Marie-Tooth disease by Chan et al (6) and Laroche et al (7). In a recent report, Dyck and co-workers (8) documented members of two kindred families with HMSN type II who developed a combination of peroneal muscular atrophy

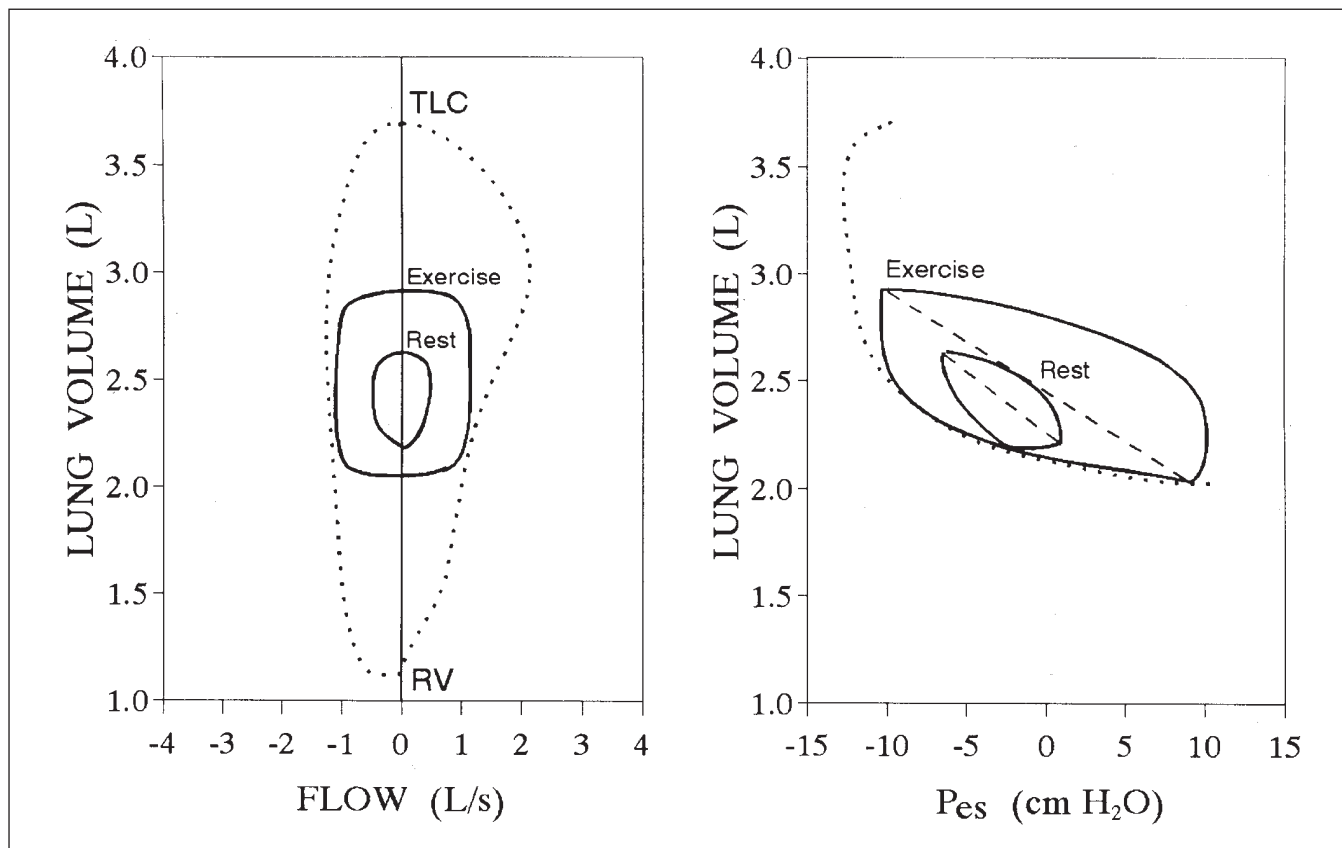


Figure 2) Tidal flow volume (left) and esophageal pressure volume (P_{es}) (right) loops are shown at rest and at peak exercise. Dotted lines indicate the maximal flow-volume envelope (left) and the maximal dynamic P_{es} curve during inspiration at peak exercise (right). Dashed lines within each pressure-volume loop indicate dynamic compliance. RV Residual volume; TLC Total lung capacity

with variable degrees of vocal cord and respiratory muscle involvement. Pulmonary symptoms, such as dyspnea, wheezing or 'asthma', and altered voice were often the presenting symptoms rather than limb muscle weakness. The presenting symptoms of the patient described in the present report – exertional breathlessness and noisy breathing – and the findings of vocal cord paralysis, respiratory muscle dysfunction and normal nerve conduction velocities bear a striking resemblance to those of patients described in a series by Dyck et al (8).

Apart from early childhood respiratory symptoms, which resolved, our patient had minimal symptoms until pregnancy. Pregnancy may have precipitated her symptoms and aggravated her condition in several ways. Geometric distortion of the diaphragm and lower thoracic cage, and elevated intra-abdominal pressure related to the gravid uterus may have resulted in increased functional weakness of the compromised diaphragm. The physiological increase in minute ventilation in pregnancy likely accentuated the sense of breathlessness, which is common even for normal subjects (9). Pregnancy-related hyperemia and mucosal edema of the upper respiratory tract, which are most pronounced in the third trimester, may have further compromised the narrowed glottis and increased the resistive load on the inspiratory muscles (10). Lastly, the underlying polyneuropathic process may have been exacerbated by pregnancy (11,12).

Cardiopulmonary exercise testing has not been reported

in patients with the combination of vocal cord paralysis and respiratory muscle weakness due to chronic polyneuropathy. Results of the patient's exercise test were markedly abnormal and provided clear insight into the etiology of her exercise intolerance and incapacitating dyspnea. The cause of her extreme dyspnea at low work rates was multifactorial: ventilatory demand was increased relative to normal; static ventilatory muscle strength was reduced, with further dynamic functional inspiratory muscle weakness resulting from increased velocity of shortening of these muscles in the setting of an accelerated breathing frequency (13); and the ventilatory muscles were burdened by substantial resistive loading due to fixed upper airway obstruction and by increased dynamic elastance. The combination of neuromuscular weakness and increased impedance to inspiratory muscle action resulted in severe ventilatory limitation early in exercise. Thus, the patient generated inspiratory and expiratory flows that represented the maximal flows that could be generated at the corresponding operating lung volumes. The corollary of this is that the patient was obliged to generate inordinately high inspiratory pleural pressure relative to the reduced maximal force-generating capacity (Figure 2), despite a smaller than normal tidal volume response (Figure 1).

Inspiratory muscle fatigue may have contributed further to the patient's reduced ventilatory capacity because the measured tension-time index exceeded the fatigue threshold of 0.15. The patient had lower limb weakness on ex-

amination, and severe leg effort and fatigue at the break-point of exercise compared with normal individuals at a similar work load. Although this was not the primary exercise-limiting symptom, it likely contributed to reduced exercise tolerance.

SUMMARY

Exercise testing identified true ventilatory limitation as the major cause of the exercise intolerance. We speculate that in physiological terms, the sensation of severe exertional dyspnea is explained by the conscious awareness of the disproportionately high inspiratory muscle contractile effort expended (as reflected by the $P_{es}:P_{I_{max}}$ ratio) (14) and of the simultaneously impaired mechanical response in the setting of the increased ventilatory demand of exercise.

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