

## REVIEW SERIES

## The pulmonary physician in critical care • Illustrative case 4: Neuromusculoskeletal disorders

N Hart, A K Simonds

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The case history is presented of a patient admitted to the ICU with ventilatory insufficiency following thoracotomy for thymic resection. The role of non-invasive ventilation for weaning in patients following phrenic nerve injury is discussed.

Congenital or acquired disorders affecting the respiratory muscles and/or causing chest wall deformity can precipitate ventilatory insufficiency either through the development of inspiratory muscle weakness or by a marked increase in the work of breathing due to low thoracic compliance. In some congenital disorders such as Duchenne muscular dystrophy and intermediate spinal muscular atrophy respiratory muscle involvement is almost inevitable; in others such as limb girdle muscular dystrophy and facioscapulohumeral muscular dystrophy respiratory muscle weakness is highly variable. Expiratory muscle weakness reduces cough efficiency and increases the tendency to atelectasis. Bulbar muscle involvement predisposes the individual to aspiration. Risk factors for ventilatory decompensation in patients with idiopathic scoliosis include early onset scoliosis (before the age of 5 years), a high (cephalad) thoracic curve, and a vital capacity of less than 30% predicted. Some acquired neuromuscular disorders—for example, motor neurone disease, Guillain Barré syndrome—may present with ventilatory failure due to respiratory muscle weakness; other patients with a precarious balance between ventilatory load and capacity may decompensate during a chest infection or after surgical intervention. In some neuromuscular disorders—for example, Duchenne muscular dystrophy and acid maltase deficiency—cardiomyopathy may complicate the picture. In addition, it should be remembered that congenital scoliosis is associated with an increased incidence of congenital heart disease. Intensivists should be able to identify patients at high risk of ventilatory failure from neuromusculoskeletal disorders and be prepared for weaning problems. They should also be aware of advances in non-invasive ventilation (NIV) that may be of value in avoiding the need for endotracheal intubation and conventional ventilation, and help facilitate early discharge from the intensive care unit (ICU).

## CASE REPORT

A 40 year old woman was found to be anaemic at a routine blood donor session. Shortly after she

developed joint pains and pruritus, and autoimmune haemolytic anaemia was diagnosed. A mediastinal mass was observed on her chest radiograph which was shown to be a thymoma on needle biopsy. The autoimmune haemolytic anaemia was complicated by red cell aplasia. Following prednisolone therapy the haemoglobin rose from 6.2 to 12.8 g/dl. There were no symptoms of myasthenia such as diplopia, limb weakness or dyspnoea, and the FEV<sub>1</sub>/FVC was 2.39/2.98 litres. The patient underwent a thoracotomy during which the thymic tumour was found to be adherent to the right hilum, right phrenic nerve, and pericardium. The tumour was resected with strips of the right lung at the hilum. Histologically, the tumour was a cortical thymoma. Initially the patient made a good recovery on the ICU and was rapidly extubated. However, over the following 2 weeks she became progressively more breathless and orthopnoeic. The chest radiograph showed elevation of the right hemidiaphragm and bibasal consolidation (fig 1). A ventilation-perfusion scan confirmed matched defects at both lung bases. Little response was seen to several courses of antibiotics and physiotherapy, and the patient reported continued orthopnoea and fragmented sleep. She was therefore referred to the weaning programme at the Royal Brompton Hospital for further assessment.

On arrival, breathing spontaneously she was unable to lie flat and the FEV<sub>1</sub>/FVC while sitting was 1.05/1.2 litres. Arterial blood gas tensions on air were Po<sub>2</sub> 10.6 kPa, Pco<sub>2</sub> 5.9 kPa, HCO<sub>3</sub> 30.3 mmol/l. Overnight monitoring during which the patient slept very lightly showed a rise in transcutaneous (Tc) CO<sub>2</sub> to 12 kPa with dips in arterial oxygen saturation (Sao<sub>2</sub>) to 60% breathing air (fig 2A). A CT scan showed patchy subsegmental atelectasis affecting the right and left lower lobes with marked elevation of the right hemidiaphragm. There was no evidence of thromboembolism. Baseline respiratory muscle test results are shown in table 1 and indicate a marked reduction in inspiratory muscle strength with a modest reduction in expiratory muscle strength. Stimulation of the phrenic nerves generated no transdiaphragmatic pressure spike bilaterally. A tensilon test using the diaphragm as the test muscle was negative (fig 3).

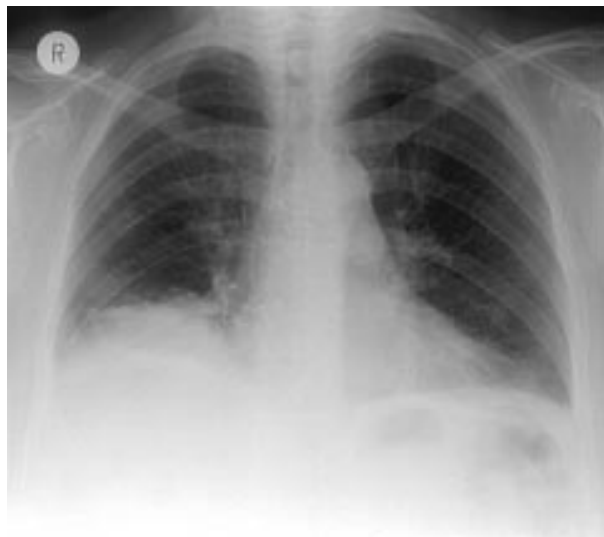
Thyroid function tests demonstrated hypothyroidism (free thyroxine 7.6 pmol/l (NR 9–23), thyroid stimulating hormone 17.7 mU/l (NR 0.32–5)).

## Diagnosis

The patient had developed bilateral basal atelectasis and consolidation after thoracotomy for

See end of article for authors' affiliations

Correspondence to:  
Dr A K Simonds, Royal Brompton & Harefield NHS Trust, Sydney Street, London SW3 6NP, UK; a.simonds@rbh.nthames.nhs.uk

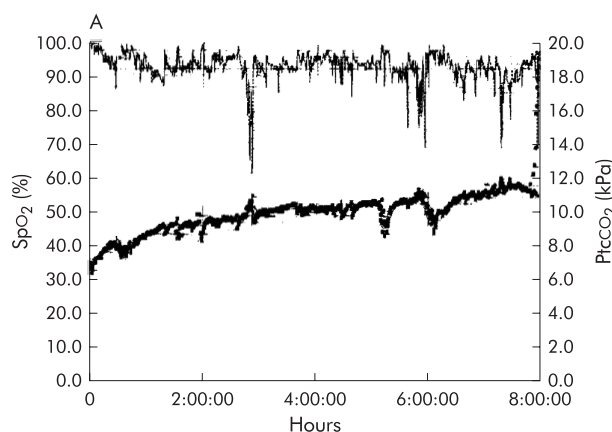


**Figure 1** Chest radiograph showing elevated right hemidiaphragm and bibasal atelectasis, more marked at the right lung base.

thymic resection because of marked diaphragmatic weakness. Ventilatory decompensation occurred during sleep due to loss of intercostal muscle tone in REM sleep leaving ventilation dependent on the already weak diaphragm. Ventilation is further compromised during sleep by a reduction in central drive and basal ventilation-perfusion mismatch. In this patient the differential diagnosis of respiratory muscle weakness lies between:

- myasthenia gravis;
- phrenic nerve injury caused by thymic tumour involvement and/or surgery;
- a combination of myasthenia and phrenic palsy;
- respiratory muscle weakness associated with hypothyroidism.<sup>1</sup>

The tensilon test was negative and respiratory muscle tests showed absent conduction down both phrenic nerves indicating that the main problem was phrenic nerve injury. The situation was probably exacerbated by hypothyroidism induced myopathy. Acetylcholinesterase (ACh) antibody was subsequently shown to be positive in this patient, but the combination of red cell aplasia, thymoma and ACh antibodies *without* clinical features of myasthenia has been reported previously. In a Japanese series of 17 cases of red cell aplasia and thymoma, only two patients had myasthenia.<sup>2</sup>



Tests of respiratory muscle strength	Predicted value (cm H <sub>2</sub> O)	Baseline (cm H <sub>2</sub> O)	6 months (cm H <sub>2</sub> O)
Sniff Poes	>70	20.6	29.8
Sniff Pdi	>70	2.4	13.8
Cough Pgas	>120	77.3	143.1
Bilateral TwPdi	>20	0.0	5.0
Right TwPdi	>7	0.0	0.0
Left TwPdi	>8	0.0	5.0

Sniff Poes=maximum sniff oesophageal pressure; sniff Pdi=maximum sniff transdiaphragmatic pressure; cough Pgas=maximum cough gastric pressure; TwPdi=twitch transdiaphragmatic pressure following unilateral and bilateral magnetic stimulation of the phrenic nerve.

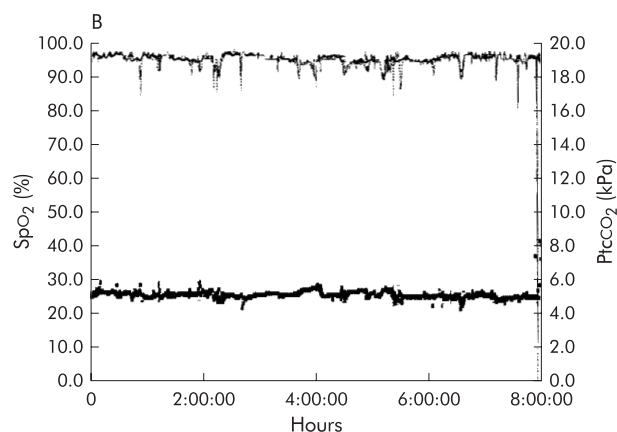
## Management

The patient was started on nocturnal NIV via a nasal mask and thyroxine replacement therapy. She also received physiotherapy during NIV to facilitate coughing and secretion clearance. Theoretically, in this situation bilevel non-invasive positive pressure support may be more beneficial in addressing atelectasis than volume preset ventilation or inspiratory pressure support alone.<sup>3</sup> The patient's sleep quality improved, and overnight monitoring on NIV showed improvements in  $\text{SaO}_2$  and  $\text{Tcco}_2$  (fig 2B). Persistent anaemia was treated by transfusion to raise the haemoglobin above 8 g/dl. Basal atelectasis resolved over 1 week but the right hemidiaphragm remained elevated. The patient was discharged home after 16 days and continued to use nocturnal NIV.

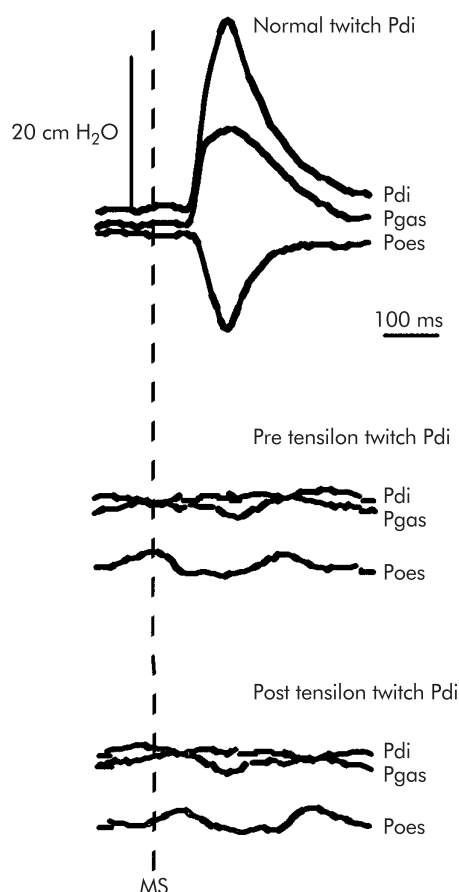
Two months later the sniff inspiratory pressure was 27.6 cm H<sub>2</sub>O compared with a value of 16.2 cm H<sub>2</sub>O on arrival, and the patient had returned to work having completed a course of radiotherapy. Respiratory muscle test results obtained 6 months after surgery are given in table 1. These show a further improvement in inspiratory muscle strength with some recovery in conduction down the left phrenic nerve (fig 4), indicating that it was probably traumatised during the difficult surgical resection. There was no recovery in right phrenic nerve function, presumably because of partial resection. A sleep study with the patient breathing spontaneously showed normal  $\text{Tcco}_2$  and  $\text{SaO}_2$  values, so the patient was weaned from nocturnal ventilatory support.

## DISCUSSION

Phrenic nerve injury occurs variably after cardiothoracic surgery<sup>4</sup> and ranges from complete nerve ablation to the "frostbitten phrenic" seen after procedures involving topical cooling to produce cardioplegia.<sup>5</sup> If the nerve is not



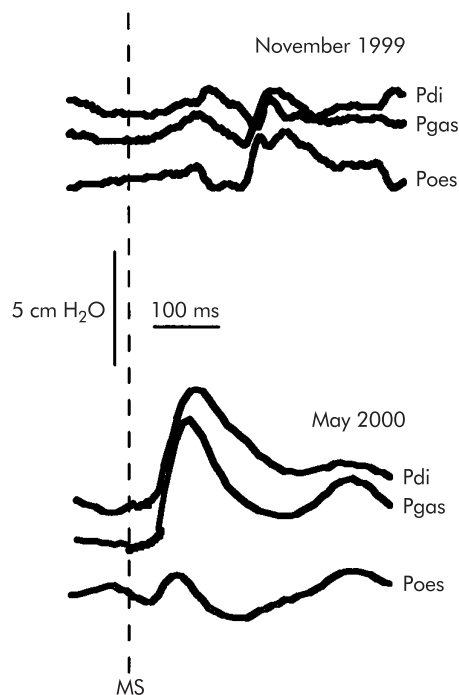
**Figure 2** Overnight monitoring of arterial oxygen saturation ( $\text{SpO}_2$ ) and transcutaneous  $\text{CO}_2$  ( $\text{PtCO}_2$ ) (A) after surgery breathing spontaneously and (B) during NIV.



**Figure 3** Twitch transdiaphragmatic pressure before and after the tensilon test. Pdi=transdiaphragmatic pressure; Pgas=gastric pressure; MS=magnetic stimulation. A normal twitch Pdi is given above for reference.

irretrievably damaged, recovery is usually seen over a number of months.<sup>6</sup> Patients with bilateral phrenic nerve injury often present with bibasal atelectasis. In those with underlying respiratory compromise overt ventilatory failure is precipitated.<sup>7</sup> In this non-smoker, ventilatory decompensation only occurred at night due to the effects of sleep on respiration, but sleep fragmentation exacerbated her daytime symptoms. Respiratory muscle tests<sup>8</sup> were used to help differentiate a true myasthenic syndrome from phrenic nerve damage.

NIV is a useful weaning tool. A randomised trial comparing rapid extubation on to NIV with continued intubation and pressure support ventilation in COPD patients showed more rapid weaning with fewer complications in the NIV group.<sup>9</sup> In patients with restrictive ventilatory defects due to neuromuscular or chest wall disease, case series data<sup>10</sup> suggest that NIV can shorten weaning and reduce the time spent on the ICU. NIV can also be used to prevent the need for reintubation if ventilatory failure recurs after extubation.<sup>11</sup> In the case presented here, reintroduction of invasive ventilation following extubation was not indicated but NIV is likely to have facilitated recovery from basal atelectasis. NIV was successfully carried out on a high dependency unit and subsequently



**Figure 4** Recovery of left twitch transdiaphragmatic pressure after 6 months. Pdi=transdiaphragmatic pressure; Poes=oesophageal pressure; Pgas=gastric pressure; MS=magnetic stimulation.

on a general respiratory ward, thereby eliminating the need for continued ICU bed occupancy.

#### Authors' affiliations

N Hart, A K Simonds, Sleep & Ventilation Unit, Royal Brompton & Harefield NHS Trust, London SW3 6NP, UK

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