Case report

Do all breathless smokers have a COLD?

Rajendram R*, Parker R, Joseph A

Email: rajkumarrajendram@doctors.org.uk

Abstract

Ventilatory failure may result from dysfunction of any part of the respiratory pathway. Muscle weakness pre-existing or acquired should be considered in all patients. **Case Report:** A 52-year-old smoker presented *in extremis* with type II respiratory failure. She was treated with bronchodilators, steroids and antibiotics. Weaning ventilatory support was difficult and so a tracheostomy was performed.. Two weeks later, she was transferred to a respiratory ward where she was decannulated before discharge home. After discharge, her breathlessness and weakness progressed until she was readmitted *in extremis* 1 week later. On readmission, she deteriorated despite treatment for COPD. Mandatory ventilation was initiated after recannulation of the tracheostomy. The patient gradually improved over the next few days and was transferred to a respiratory ward where she was weaned onto nocturnal NIV and the tracheostomy was decannulated. Flow volume loops excluded air flow obstruction but spirometry confirmed severe inspiratory muscle weakness. The patient reported progressive weakness over several years. On examination all muscle groups were weak and deep tendon reflexes were absent but there was no fatigability or fasciculation. Sensation was intact. The diagnosis of acid maltase deficiency (AMD) was confirmed by analysis of peripheral blood lymphocytes, muscle biopsy and enzyme assay.

Keywords: Acid maltase deficiency, muscle weakness, type II respiratory failure.

Case Report

A 52-year-old woman with a 38 pack-year cigarette smoking history was brought to hospital in extremis. After a similar presentation, one month earlier she had required ventilation on the intensive care unit (ICU) for type II respiratory failure. Computed tomography (CT) pulmonary angiogram showed collapse and consolidation of both lung bases. She improved with nebulised bronchodilators, steroids and antibiotics. Weaning from mechanical ventilation was difficult and required a tracheostomy. Two weeks later, she was decannulated and she was discharged home with a diagnosis of chronic obstructive pulmonary disease (COPD).

After discharge her breathlessness, cough and malaise had increased together with a new complaint of progressive muscle weakness. One week later she was found by her husband on the floor, unable to stand, breathing with difficulty and cyanosed. Her general practitioner (GP) called in for a home visit and immediately had the patient 'blue-lighted' into hospital.

On this readmission, she was tachypnoeic, hypotensive and tachycardic but afebrile. Oxygen saturations were 98% on high flow oxygen. Speaking only single words and using her accessory muscles, she was mildly confused and had a carbon dioxide (CO_2) retention flap. Chest expansion was reduced, breath sounds were diminished and a mild expiratory wheeze was audible. Nebulised bronchodilators, intravenous hydrocortisone and antibiotics were administered.

Rajkumar Rajendram, AKC BSc (hons), MBBS (dist), MRCP, FRCA, EDIC, FFICM

Locum Consultant in Anaesthesia, Intensive Care and Perioperative Medicine, Royal Free London NHS Trust, Barnet and Chase Farm Hospitals, Wellhouse Lane, Barnet, UK

Robert Parker, MBBS, MRCP, FFICM

Consultant in Respiratory and Intensive Care Medicine, Aintree University Hospital, Liverpool, UK

Alex Joseph, MD, FRCA

Consultant, Department of Anaesthesia and Surgical Intensive Care, Changi General Hospital, Singapore

How to cite this article: Rajendram R, Parker R, Joseph A. Do all breathless smokers have a COLD? Ind J Resp Care 2015; 4:572-4.

Routine blood tests were normal apart from raised alanine transaminase (104 IU/L) and creatine kinase (224 IU/L). However, the electrocardiograph showed only sinus tachycardia and the troponin I was <0.2 μg/L.

Arterial blood gas (ABG) 1 *(Table 1)* was taken. In response, the intensivists were contacted and the inspired oxygen concentration was reduced. ABG 2 *(Table 1)* was taken 30 minutes later. Although the FiO_2 was increased, oxygen saturations of only 65% were achieved. The tracheostomy was recannulated and pressure support ventilation was started and at 16:00 hours, ABG 3 *(Table 1)* was achieved. Ventilatory support was weaned over 4 weeks and when the patient was stable on nocturnal NIV, the tracheostomy was decannulated.

A neurologist then noted weakness of neck flexion and the upper and lower limbs (4+/5) but could not demonstrate fatiguability or elicit deep tendon reflexes. Sensation was intact and no fasciculations were seen. The cranial nerves were normal. History of progressive muscle weakness over several years could be elicited. She also had a waddling 'myopathic' gait.

Despite her 38 pack-year smoking history, the flow volume loop excluded air flow obstruction. Spirometry and sniff nasal inspiratory pressure *(Table 2 and Figure 1)* confirmed severe inspiratory muscle weakness. Analysis of peripheral blood lymphocytes *(Figure 2)*, muscle biopsy *(Figure 3)* and enzyme assay led to the diagnosis of acid maltase deficiency (AMD).

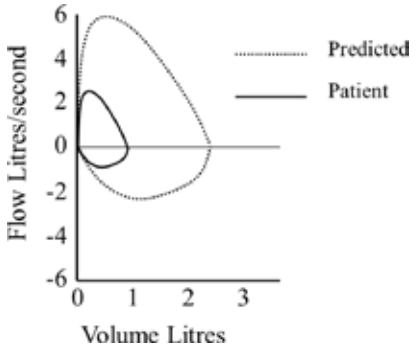

Figure 1: The flow volume loop prior to discharge from the Chest Unit.

The patient was discharged home 7 weeks after readmission. Six months after discharge she was tolerating the nocturnal NIV well with controlled daytime arterial blood gases ($PaCO_2$ 6.5 kPa; base excess 5.1 mmol/l). She had not required hospital

Table 1: Arterial Blood Gas Results: Arterial blood gas 1 was taken on admission, arterial blood gas 2 was taken 30 minutes later after reduction of inspired oxygen concentration to 24%. Arterial blood gas 3 was taken on BiPAP after optimisation of the ventilator settings. Arterial blood gas 4 was taken on air after decannulation of the tracheostomy prior to discharge. Abbreviations: Bilevel positive airway pressure (BiPAP), Expiratory positive airway pressure (EPAP), Inspiratory positive airway pressure (IPAP), Oxygen (O_2), partial pressure of oxygen (PO_2), partial pressure of carbon dioxide (PCO_2).

Arterial Blood gas	**1**	**2**	**3**	**4**
Inspired Oxygen	15 Litres O_2	2 Litres O_2	4 Litres O_2	Air
Method of delivery	Non-rebreathing mask & reservoir bag	24% Venturi mask	BiPAP IPAP 20 cm H_2O EPAP 5 cm H_2O	
Respiratory Rate	25	9	12	14
pH	7.07	7.16	7.38	7.40
PO_2 (kPa)	33	4	14	8
PCO_2 (kPa)	11	15	8	8
Bicarbonate (mmol/L)	25	28	31	32
Base Excess (mmol/L)	+4	+6	+7	+8
Oxygen Saturations	98%	43%	98%	94%

Table 2: Spirometry prior to discharge from the Chest Unit.

Forced expiratory volume in one second (FEV_1)	0.9 litres	42 % predicted
Standing Vital Capacity	1.0 litres	37 % predicted
Lying Vital Capacity	0.6 litres	40% fall compared to standing
Sniff nasal inspiratory pressure (SNIP)	16 cmH_2O	Normal > 70 cmH_2O

admission in that time but unfortunately had to stop work due to physical incapacity.

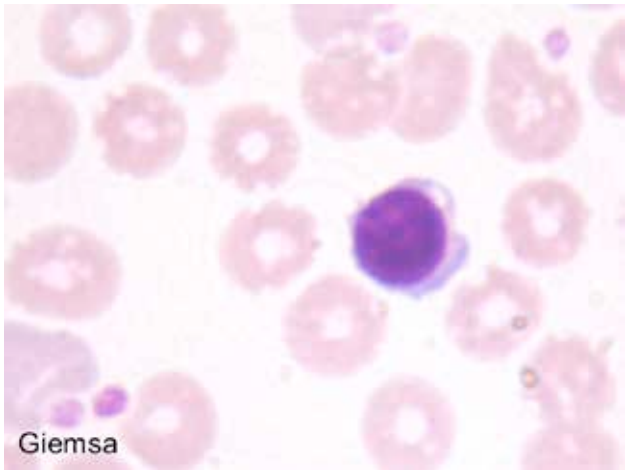

Figure 2: Blood Film - Peripheral blood lymphocytes show vacuolation.

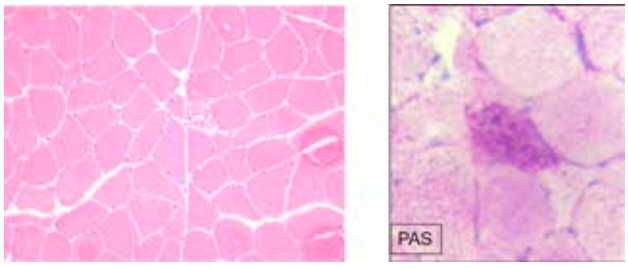

Figure 3: Muscle Biopsy: Periodic acid Schiff staining reveals glycogen stored within some myocytes

Discussion

Type II respiratory failure is a ventilatory pump failure causing alveolar hypoventilation. The PaO_2 falls and the $PaCO_2$ rises. Whilst COPD is a common cause, it is not the only one. Any point of the pathway from the brainstem, through the nerves, *via* the neuromuscular junction to the respiratory muscles can be responsible. Respiratory muscle weakness both pre-existing and acquired as a result of prolonged ITU stay should be considered in all 'slow to wean' patients.

Clues include symptoms or signs of peripheral muscle and/or diaphragm weakness (orthopnoea and paradoxical abdominal movements). The vital capacity is reduced and falls > 20% on lying flat. Mouth and sniff nasal inspiratory pressures are reduced. Alveolar hypoventilation increases at night especially during rapid eye movement sleep. Sleep fragmentation can cause daytime symptoms of headache, lethargy, sleepiness and dyspnoea. These symptoms can be controlled with nocturnal NIV.

Adult onset AMD is an autosomal recessive disorder with a frequency of approximately 1:40000.[1] There is a deficiency of the enzyme 1,4 glucosidase which breaks down glycogen in cell lysosomes. Glycogen accumulates and disrupts cellular function. This affects skeletal muscle including the diaphragm. The presentation is often insidious. Patients can present with respiratory failure rather than peripheral muscle weakness. Prognosis is highly variable and depends on the gene mutation and enzyme activity. As no cure is currently available, supportive therapies and genetic screening of family members are the cornerstones of management. However, enzyme replacement therapies are under development and the results of initial studies are promising.[2]

In conclusion, although COLD would be the commonest diagnosis in all breathless smokers, attempts must be made to evaluate for other concomitant even if rare diseases such as acid maltase deficiency when the patients do not respond to conventional treatment and the objective tests do not show features of significant airway obstruction.

References

1. Martiniuk F, Chen A, Arvanitopoulos E, Chen Y, Rom WN, Codd WJ, *et al.* Carrier frequency for glycogen storage disease type II in New York and estimates of affected individuals born with the disease. *Am J Med Genet* 1998; **79**: 69-72.
2. Winkel LP, Van Den Hout JM, Kamphoven JH, Disseldorp JA, Remmerswaal M, Arts WF, *et al.* Enzyme replacement therapy in late-onset Pompe's disease: a three-year follow-up. *Ann Neurol* 2004; ***55***: 495-502.