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A 62-year-old man with sudden onset of orthopnea and left shoulder weakness and pain

He is using
his accessory
muscles while
supine

A 62-YEAR-OLD MAN is admitted with sudden onset of severe dyspnea when lying supine. One day ago he developed dull pain in the left shoulder and could not abduct his left arm more than 45 degrees owing to weakness. He has noted mild exertional dyspnea for the past year and experienced several episodes of dyspnea while leaning forward to tie his shoes, shovel snow, or wash his car.

He denies wheezing, cough, pleurisy, chest pain, palpitations, nocturia, or lower extremity edema. He is semiretired and is an avid golfer.

Past medical history

- Left rotator cuff tear, repaired 4 years ago
- Gastric esophageal reflux disease, currently treated with lansoprazole (Prevacid)
- Elective endoscopic dilation of a benign esophageal stricture, performed 4 months ago. The procedure was complicated by aspiration pneumonia, resulting in a 5-day hospitalization. An elevated right hemidiaphragm was noted on a chest radiograph at that time. There were no prior radiographs to compare.
- Cigarette smoking—2 packs per day for 15 years, after which the patient quit and has been abstinent for the past 30 years
- Asbestos exposure. The patient owns an auto and towing shop and he estimates he had 30 years of exposure to asbestos in brakes and clutches and did not wear a protective mask.

Physical examination

The patient is afebrile; respirations are 18 per minute, heart rate 80, blood pressure 120/71 mm Hg. He has no jugular venous distension, normal S1 and S2 heart sounds, and no lower

extremity edema. His lungs are clear, but he has poor diaphragmatic excursion and paradoxical thoracoabdominal breathing and uses his accessory muscles while supine.

His strength is 4 on a scale of 5 in the distribution of the axillary nerve on the left side, and there is loss of pinprick sensation in the C4 distribution on the left.

Laboratory and test data

- White blood cell count $11.6 \times 10^9/L$ (normal 4.0–11.0)
- Monocytes 11% (normal 2%–10%)
- Hemoglobin 15.9 g/dL (normal 13.7–17.5)
- Platelet count $230 \times 10^9/L$ (normal 150–400)
- Alanine aminotransferase 80 U/L (normal 0–30)
- Aspartate aminotransferase 40 U/L (normal 7–40)
- Alkaline phosphatase 140 U/L (normal 20–120)
- Electrolytes, blood urea nitrogen, creatinine within normal limits.

Posterior-anterior and lateral chest radiograph. Bilateral reduction of lung volumes and elevation of both hemidiaphragms. The lung parenchyma is clear.

An echocardiogram is normal.

BLOOD GAS ABNORMALITIES

1 When sitting upright, this patient is likely to be which of the following?

- ☐ Hypercapnic
- ☐ Hypocapnic
- ☐ Eucapnic
- ☐ Hypoxic



This man's symptoms consist primarily of exertional dyspnea and orthopnea. When resting upright, he has no symptoms and is likely to be eucapnic.

Patients with respiratory muscle weakness, such as this patient, commonly adopt a rapid shallow breathing pattern that is accentuated at rest; tachypnea is probably related to diffuse microatelectasis and stimulation of vagal afferent fibers. Thus, in the early stages of disease, patients are most likely to have a normal or slightly low PCO_2 .

This prediction is borne out by his arterial blood gas values:

- pH 7.37 (normal 7.35–7.45)
- PCO_2 43 mm Hg (normal 34–46)
- PO_2 73 mm Hg (normal 85–95)
- HCO_3 24 mmol/L (normal 22–26).

When ventilation demand is increased, however, as in fever or pneumonia, patients may be unable to maintain eucapnia, and respiratory failure may ensue. When diaphragm muscle weakness becomes severe, patients progress to chronic hypercapnic respiratory failure.

■ DO BLOOD GASES PREDICT DIAPHRAGM WEAKNESS?

2 True or false? Arterial blood gas data accurately predict the degree of diaphragm weakness.

- ☐ True
- ☐ False

False. It is difficult to predict the degree of diaphragm weakness on the basis of arterial blood gas data alone, for several reasons:

- Many patients with severe diaphragm weakness can maintain eucapnia if they are upright and maintain an adequate rate of ventilation.
- Body habitus (abdominal girth, weight on the chest wall, chest wall stiffness) can have a profound effect on a patient's ability to ventilate if he has bilateral diaphragmatic paralysis.
- Patients with bulbar muscle weakness (typically due to multiple sclerosis or amyotrophic lateral sclerosis [ALS]) tend to have upper airway obstruction during sleep and therefore may be hypercapnic at night due to obstructive sleep apnea.

- Patients with infections (particularly pneumonia and sepsis) may become hypercapnic as their ventilation demand outweighs their ability to ventilate.

■ DIAGNOSTIC WORKUP

3 Which of the following should be part of this patient's diagnostic workup?

- ☐ Chest radiography
- ☐ Transdiaphragmatic pressure gradient measurement
- ☐ Sitting and supine pulmonary function tests
- ☐ Diaphragmatic electromyography
- ☐ "Sniff" fluoroscopy

All of the above are appropriate.

Chest radiography can be useful in ruling out parenchymal lung disease, and, as in this patient, comparing current and previous radiographs may prove helpful in determining a temporal relationship (eg, chronic paralysis of one diaphragm with acute loss of the other).

Transdiaphragmatic pressure gradient measurement is the gold standard for diagnosing bilateral diaphragmatic paralysis. Esophageal and gastric pressures are recorded with a balloon catheter system while the seated patient performs a "sniff maneuver."

A normal gradient is greater than 98 cm H_2O . Patients with a gradient less than 30 cm H_2O are orthopneic and exhibit paradoxical thoracoabdominal breathing.¹ This is presumably because 30 cm H_2O is the approximate pressure needed to overcome the hydrostatic pressure of the abdominal contents.

Pulmonary function testing. The peak inspiratory pressure and the forced vital capacity, measured sitting and supine, are useful noninvasive tests that correlate with the transdiaphragmatic pressure gradient and can therefore quantify diaphragmatic paralysis.¹ A fall in forced vital capacity of 30% when supine suggests diaphragmatic paralysis.

Diaphragmatic electromyography can be performed with an intraesophageal or surface electrode and is helpful for distinguishing a neuropathic pattern of paralysis from a myopathic pattern. Phrenic nerve conduction velocity is measured to determine whether the phrenic nerve is intact.

A normal gradient across the diaphragm is > 98 cm H_2O

TABLE 1

The patient's pulmonary function test results

	SITTING	% OF PREDICTED	SUPINE	% FALL WHEN SUPINE
FVC	1.72 L	42%	1.03 L	−40%
FEV ₁	1.20 L	37%	0.48 L	−60%
FEV ₁ /FVC ratio	69.7		46.3	
FEF _{25%–75%}	0.54 L/sec	17%	0.10 L/sec	−82%

FVC = forced vital capacity; FEV₁ = forced expiratory volume in 1 second; FEF_{25%–75%} = forced expiratory flow, midexpiratory phase

“Sniff” fluoroscopy is most useful for differentiating unilateral diaphragmatic paralysis from bilateral diaphragmatic paralysis. While lying supine, the patient is asked to breathe in, and the diaphragm's motion is observed under fluoroscopy.

In unilateral diaphragmatic paralysis, the intact side of the diaphragm should move downward while the paralyzed side should paradoxically move upward as the intrathoracic pressure is decreased. In bilateral paralysis, one would expect to see a small amount of symmetrical downward motion, as accessory muscles expand the lung symmetrically and force the diaphragm downward on both sides.

Case continued

The patient undergoes further testing.

Pulmonary function testing is consistent with a restrictive pattern. The tests reveal a 40% fall in forced vital capacity in the supine position compared with the sitting position (TABLE 1). This finding is consistent with severe bilateral diaphragmatic paralysis, which is expected in the setting of severe orthopnea and paradoxical thoracoabdominal breathing. He can maintain eucapnia while upright because his accessory muscles of inspiration are relatively intact.

Electromyography of his left arm reveals evidence of a left axillary neuropathy with moderate axon loss and a left musculo-cutaneous neuropathy with mild axon loss.

Magnetic resonance imaging of the cervical spine is performed under sedation with noninvasive positive pressure ventilation. This shows mild spondylosis with mild spinal

canal narrowing, insufficient to produce diaphragmatic paralysis.

DIFFERENTIAL DIAGNOSIS

4 The differential diagnosis includes all of the following except which one?

- ☐ Asbestosis
- ☐ Amyotrophic lateral sclerosis (ALS)
- ☐ Systemic lupus erythematosus (SLE)
- ☐ Myasthenia gravis
- ☐ Neuralgic amyotrophy

Although this patient's asbestos exposure is significant enough to produce asbestos-related disease, he would be unlikely to present with sudden onset of orthopnea. Moreover, asbestosis does not typically cause diaphragmatic paralysis.

The differential diagnosis for bilateral diaphragmatic paralysis can be divided into disorders of the cervical spinal cord (C3–C5), disorders of the anterior horn cells, phrenic neuropathies, disorders of the neuromuscular junction, and disorders of the respiratory muscles (TABLE 2).^{2–8} The most common causes include cervical cord injury, phrenic nerve injury during cardiac surgery, multiple sclerosis, anterior horn cell disease (eg, ALS), and muscular dystrophy.³

ALS. Respiratory muscle weakness is usually a late complication of ALS, though patients can present with orthopnea (usually accompanied by bulbar symptoms).

SLE has been known to cause the “shrinking lung syndrome,” which is postulated to be due to deposition of immune complexes or ischemic injury to the phrenic nerves; the process can respond to steroids.⁴

Myasthenia gravis crises can cause rapidly progressing diaphragmatic weakness accompanied by weakness in the eye muscles and bulbar muscles, with classic fatigue with exertion and improvement with rest.

Neuralgic amyotrophy is an oligoneuropathy involving the upper trunk of the brachial plexus and sometimes the phrenic nerve as well. The disease always follows some antecedent event (infection or surgical procedure). It is painful and causes axonal destruction, which leads to weakness and muscle atrophy.

A supine fall in FVC is consistent with severe bilateral diaphragm paralysis



■ TREATMENT

5 What is the best initial treatment strategy for a patient with bilateral diaphragmatic paralysis?

- ☐ Diaphragmatic pacing
- ☐ Surgical plication
- ☐ Noninvasive positive-pressure ventilation
- ☐ Negative-pressure ventilation
- ☐ Tracheostomy and mechanical ventilation
- ☐ Abdominal displacement ventilation

Noninvasive positive-pressure ventilation is the mainstay of therapy for bilateral diaphragmatic paralysis and would be the best initial treatment.³

The postural muscles are inhibited during rapid eye movement (REM) sleep, making the diaphragm the sole muscle of inspiration. Therefore, patients with bilateral diaphragmatic paralysis are particularly prone to alveolar hypoventilation during sleep and to sleep apnea. While they may be eucapnic during the day, they can be profoundly hypercapnic and hypoxic at night; this may result in frequent arousals, excessive daytime sleepiness, and morning headaches.

Negative-pressure ventilation (the “iron lung”) may be needed if the patient cannot adapt to noninvasive positive-pressure ventilation, although it is rarely used today. Subatmospheric pressure is intermittently applied to the chest wall and abdomen by means of a thoracic cuirass (a rigid thoracoabdominal shell with tight-fitting seals at the neck, trunk, and arms), increasing transpulmonary pressure.

Proper positioning of the patient within the device can be difficult, especially for those with neuromuscular dysfunction. Patients must lay supine and may suffer from back and shoulder pain, while claustrophobic patients may find the device intolerable. Moreover, the delivered negative inspiratory pressure may exacerbate obstructive sleep apnea, especially in those with bulbar neurologic dysfunction.

Abdominal displacement ventilation is done via a rocking bed or pneumobelt.

The rocking bed tilts on a fulcrum at the hip level and rocks from Trendelenburg to reverse-Trendelenburg positions at a rate of 12 to 24 times per minute. As the bed rocks up,

TABLE 2

Causes of bilateral diaphragmatic paralysis

Cervical spinal cord disease (C3–C5)

Trauma
Spinal cord tumors
Ischemic myelopathy
Syringomyelia
Arnold-Chiari deformity
Transverse myelitis
Multiple sclerosis

Anterior horn cell disease (C3–C5)

Amyotrophic lateral sclerosis (ALS)
Spinal muscular atrophies
Postpolio syndrome
Tetanus

Phrenic neuropathies

Guillain-Barré syndrome
Charcot-Marie-Tooth disease
Herpes simplex virus infection, diphtheria, infectious mononucleosis
Neuralgic amyotrophy
Systemic lupus erythematosus–shrinking lung syndrome
Neuroborreliosis (Lyme disease)
Surgical trauma (section or cooling during cardiac surgery or scalenectomy)
Chiropractic manipulation (trauma to phrenic nerve)

Disorders of neuromuscular junction

Myasthenia gravis
Eaton-Lambert syndrome
Botulism
Drugs (aminoglycosides, penicillamine, chloroquine)
Toxins (spider, tick, snake bites)
Cholinesterase deficiency

Disorders of respiratory muscles

Muscular dystrophies (Duchenne, Becker, limb-girdle)
Myotonic dystrophy
Polymyositis
Myxedema, thyrotoxicosis
Oculocraniosomatic (Kearns-Sayre) syndrome
Acid maltase deficiency

Miscellaneous

Paraneoplastic syndrome (renal cell carcinoma)

abdominal contents are displaced downward, allowing for inspiration.

The pneumobelt straps around the waist and contains an inflatable bladder; as it inflates it forces the abdominal contents downward. Patients sleep semirecumbent while wearing the device.



These options are rarely used because of poor synchronization with spontaneous respiration and lack of benefit in those with severe disease.

Tracheostomy and mechanical ventilation. Some patients with late-stage neuromuscular disease require a permanent tracheostomy and continuous mechanical ventilation. This is a permanent solution, but is disfiguring and requires significant maintenance by the patient.

Phrenic nerve pacing may benefit patients with intact phrenic nerves (typically those with traumatic cervical cord injury). A radiofrequency transmitter is implanted in the supraclavicular area and is programmed to stimulate the phrenic nerve 12 to 18 times per minute.

The device allows patients to be free of mechanical ventilation during the day, but more than 90% need a permanent tracheostomy for mechanical ventilation at night because the device can become out of sync with the bulbar muscles during sleep, leading to apnea.

Surgical plication is primarily useful for unilateral diaphragmatic paralysis, but it also has been used in small numbers of patients with bilateral diaphragmatic paralysis, with some success.⁹

The procedure involves suturing the

diaphragm to the chest wall to flatten it and force the abdominal contents downward. This results in an increased functional residual capacity (lessening the chance for desaturation) and decreased work of breathing because paradoxical diaphragmatic movement is eliminated.

■ CASE CONTINUED

Given this patient's physical examination and diagnostic evaluation, the findings are most consistent with neuralgic amyotrophy.

Therapy for neuralgic amyotrophy centers on pain control and physical therapy to preserve joint mobility in his left shoulder and arm. Recovery of nerve function is expected within 2 to 3 years; however, as with any cause of axonal injury, there is a chance the nerves will never recover.¹⁰

While awaiting possible nerve recovery from neuralgic amyotrophy, he is using noninvasive positive-pressure ventilation at home at night, which has produced a marked improvement in daytime fatigue. He remains unable to sleep or lie in the supine position, however. If he should develop pneumonia, sepsis, or any illness that increases his ventilation requirement, he should be admitted for observation and may need short-term intubation for mechanical ventilation.



Diagnosis: neuralgic amyotrophy

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