

Refractory Hypercapnic Respiratory Failure in an Elderly Female

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ABSTRACT

The most common cause of hypercapnic respiratory failure is acute exacerbations of chronic obstructive pulmonary disease (AECOPD). Many other factors can contribute to hypercapnia and may lead to refractory hypercapnia in AECOPD. One of the important causes is electrolyte imbalance. We report a case of refractory hypercapnic respiratory failure in an elderly female due to postthyroidectomy hypocalcemia. The patient responded well after the correction of hypocalcemia.

KEYWORDS: *Acute exacerbations of chronic obstructive pulmonary disease, hypocalcemia, refractory hypercapnic respiratory failure*

A 55-year-old female, homemaker, presented with slowly progressive breathlessness from Grade 1 to Grade 3 for the last 8 months. Her breathlessness suddenly increased to Grade 4 1 day prior to hospital admission. She had no other respiratory symptoms or fever. She did not have any cardiac symptoms. There was no history of leg swelling. She had no past history suggestive of asthma. She did not have any symptoms suggestive of obstructive sleep apnea (OSA). She had undergone total thyroidectomy 12 years back for papillary carcinoma of thyroid. She was on thyroxin 100 mcg daily. She was not on regular follow-up. She had no symptoms suggestive of hypothyroidism. There was no past history of psychiatric medications or psychiatric symptoms. She had no addictions. There was no history of any other illness in the past.

QUESTION 1: WHICH OF THE FOLLOWING IS THE LEAST LIKELY CAUSE FOR BREATHLESSNESS IN THIS PATIENT?

1. Anemia
2. Pulmonary secondaries
3. Congestive cardiac failure
4. Chronic pulmonary thromboembolism
5. Primary pulmonary hypertension.

Answer: 3

She had no cardiac symptoms. There was no history of leg swelling. Hence, congestive cardiac failure is the least likely. Anemia can manifest with slowly progressive breathlessness and is common in Indian females. Lungs

are the most common site for secondaries, and papillary carcinoma of thyroid can recur, and metastasis to lung can occur even after many years of successful treatment of primary.^[1] The most common symptom in lung secondaries is breathlessness. Secondary from thyroid is slow growing, and hence the patient can have chronic symptom.^[1] Chronic pulmonary thromboembolism and primary pulmonary hypertension manifest with breathlessness. Primary pulmonary hypertension is more common in females than in males.

Physical findings: she was conscious, alert, and oriented. Pulse rate was 86/min, regular. Respiratory rate was 28/min. Oxygen saturation was 82% with room air. Body mass index was 21.6 kg/m². Physical appearance was normal. She had no pallor, thyroid swelling, palpable cervical lymph nodes, pedal edema, leg swelling, or calf muscle tenderness. She had no physical feature of hypothyroidism.

QUESTION 2: WHICH OF THE FOLLOWING IS NOT A FEATURE OF HYPOTHYROIDISM?

1. Slowed speech and movements
2. Loss of body hair
3. Periorbital puffiness
4. Microglossia
5. Coarse facial features.

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Answer: 4

Hypothyroidism can lead to macroglossia due to the increased accumulation of mucopolysaccharides because of decreased degradation of these substances.^[2] It is important to know the features of hypothyroidism as it can lead to respiratory complications.

QUESTION 3: WHICH OF THE FOLLOWING IS THE MOST COMMON RESPIRATORY COMPLICATION IN HYPOTHYROIDISM?

1. Pleural effusion
2. OSA
3. Respiratory muscle dysfunction
4. Hypoventilation
5. Hypoxic respiratory failure.

Answer: 2

The most common respiratory complication in hypothyroidism is OSA.^[3] Hypothyroidism is a relatively common condition. Clinical features of hypothyroidism such as lethargy, weight gain, and excess sleepiness overlap with features of OSA. The prevalence of OSA in hypothyroidism is up to 35%. Hence, all patients with hypothyroidism should be screened for OSA. The main cause for OSA in hypothyroidism is due to the narrowing of pharynx due to soft-tissue infiltration by mucopolysaccharides and proteins. Hormone replacement therapy for hypothyroidism cures OSA in majority of these patients.^[3]

Physical examination did not show any chest wall deformities. Respiratory system examination revealed few bilateral scattered rhonchi with prolonged expiration. Cardiovascular system examination was normal. No other abnormalities were detected on clinical examination.

QUESTION 4: WHAT IS THE MOST LIKELY DIAGNOSIS IN THIS PATIENT?

1. Obstructive airway disease
2. Psychogenic hyperventilation
3. Respiratory muscle dysfunction
4. Atrial septal defect
5. Primary pulmonary hypertension.

Answer: 1

The patient had progressive dyspnea over 8 months. Respiratory system examination showed features of airway obstruction, i.e., few bilateral scattered rhonchi with prolonged expiration. The patient had no history or symptoms suggestive of psychiatric illness. The patient had no symptoms or physical findings suggestive of

respiratory muscle dysfunction. In atrial septal defect, a left-to-right shunt or reversal of shunt will lead to breathlessness. By this time, the patient will have signs of pulmonary hypertension which this patient does not have. Normal cardiovascular examination findings exclude primary pulmonary hypertension and atrial septal defect.

QUESTION 5: WHAT IS THE NEXT INVESTIGATION IN THIS PATIENT?

1. Chest X-ray
2. Two-dimensional (2D) echo
3. Arterial blood gas analysis (ABG)
4. Electrocardiography (ECG)
5. Spirometry.

Answer: 3

The next investigation of choice in a patient with features suggestive of respiratory failure is ABG. This will help to determine the severity of the condition and may give a clue for possible cause and help to plan further evaluation and management.

ABG showed respiratory acidosis with hypercapnic respiratory failure. PO_2 was 56 mmHg, PCO_2 was 78 mmHg, and pH was 7.31.

Investigations: Chest X-ray was normal. ECG and 2D echo were normal. T3, T4, and thyroid-stimulating hormone were normal.

QUESTION 6: WHAT IS THE MOST COMMON CAUSE FOR HYPERCAPNIC RESPIRATORY FAILURE?

1. Kyphoscoliosis
2. Neuromuscular diseases
3. Obesity hypoventilation syndrome
4. Acute exacerbation of chronic obstructive pulmonary disease (COPD)
5. Hypothyroidism.

Answer: 4

The most common cause of hypercapnic respiratory failure is acute exacerbations of chronic obstructive pulmonary disease (AECOPD).^[4]

Causes for hypercapnic respiratory failure include as follows:^[4]

- AECOPD
- OSA, obesity hypoventilation syndrome
- Chest wall deformities – kyphoscoliosis
- Drug overdose – barbiturates, suxamethonium, and benzodiazepines.
- Tetanus
- Central hypoventilation syndromes.

Respiratory muscle dysfunctions were neuropathies, muscular dystrophies, myopathies, myasthenia gravis, and Lambert–Eaton syndrome

QUESTION 7: WHICH OF THE FOLLOWING IS NOT A TREATMENT STRATEGY FOR THIS PATIENT?

1. Short-acting nebulized bronchodilators
2. Noninvasive ventilation (NIV) for correction of hypercapnia
3. Intubation and mechanical ventilation
4. Supplemental oxygen
5. Nebulized steroid.

Answer: 3

The patient was conscious and alert with adequate respiratory drive. ABG parameters also do not warrant intubation and mechanical ventilation at this stage.

Treatment: The patient was diagnosed with hypercapnic respiratory failure due to AECOPD.

Despite adequate bronchodilators, antibiotics, and NIV, the patient did not show any improvement. ABG after 2 and 6 h after NIV remained the same with PCO_2 76 mmHg and PO_2 was 74 mmHg despite making ventilatory adjustments.

QUESTION 8: WHICH OF THE FOLLOWING VENTILATORY CHANGE IS NOT USEFUL TO TREAT HYPERCAPNIA?

1. Increase positive end-expiratory pressure
2. Decrease inspiratory time
3. Increase respiratory rate
4. Increase FiO_2
5. Decrease expiratory time.

Answer: 5

Expiratory time should be increased to treat hypercapnia.^[5]

QUESTION 9: WHICH OF THE FOLLOWING IS NOT A CAUSE FOR PERSISTENT HYPERCAPNIA IN A PATIENT ON NONINVASIVE VENTILATION?

1. Inadequate bronchodilators
2. Patient-ventilator asynchrony
3. Improper ventilatory settings
4. High respiratory rate
5. Improperly fitting mask.

Answer: 4

High respiratory rate will wash out carbon dioxide and may even lead to hypocapnia.^[5]

She developed focal seizures of right upper limb lasting for 1 min a day after admission in the intensive care unit (ICU), witnessed by the intensivist. The patient was conscious, alert during and after the seizure. There was no focal neurological deficit.

QUESTION 10: WHICH OF THE FOLLOWING IS LEAST LIKELY TO CAUSE SEIZURE IN THIS PATIENT?

1. Electrolyte imbalance
2. Carbon dioxide narcosis
3. Transient ischemic attack
4. Cerebral secondaries from thyroid
5. Medications.

Answer: 2

The patient was conscious, alert during and after the seizure. Hence, carbon dioxide narcosis leading to seizure is unlikely. ABG immediately after seizure showed PCO_2 of 72 mmHg and PO_2 was 167 mmHg. Certain medications such as quinolones can lead to seizure.

On further inquiry, patient relatives admitted that she had three episodes of focal seizures for the last 3 months. She had no other neurological symptoms. She did not develop any other new symptoms after the seizure.

QUESTION 11: WHAT IS THE NEXT INVESTIGATION FOR THIS PATIENT WITH FOCAL SEIZURE?

1. Magnetic resonance imaging (MRI) of the head
2. Nerve conduction study of the right upper limb
3. Electroencephalogram
4. X-ray skull
5. Psychiatric evaluation.

Answer: 1

Focal seizure usually indicates local cerebral pathology. Hence, MRI of head is the next investigation.^[6] Psychiatric disease does not manifest with focal witnessed seizure.

MRI head was normal. On further inquiry, she admitted having numbness and paresthesia of extremities for the

last 3 months. Nerve conduction study showed mild asymmetrical sensory-motor axonal peripheral neuropathy.

QUESTION 12: WHAT COULD BE THE MOST LIKELY CAUSE FOR REFRACTORY HYPERCAPNIC RESPIRATORY FAILURE, FOCAL SEIZURES, AND PARESTHESIA IN THIS PATIENT WHO HAD TOTAL THYROIDECTOMY?

1. Hypothyroidism
2. Hypocalcemia
3. Hyponatremia
4. Hypomagnesemia
5. Hypokalemia.

Answer: 2

The most common electrolyte imbalance after total thyroidectomy is hypocalcemia.^[7] Hypocalcemia can manifest with all the above features.

QUESTION 13: WHAT IS THE NEXT DIAGNOSTIC INVESTIGATION?

Answer: estimation of serum calcium and magnesium level.

Serum calcium level was 4.4 mg/dl (9–11 mg/dL). Magnesium level was 2.6 mg/dL (1.8–3.6 mg/dL). Serum albumin level was 4.1 mg/dL (normal). Serum phosphate level was 10 mg/dl (3–4.5 mg/dL). Vitamin D3 level was 13.65 ng/ml (20–100 ng/mL). Parathormone level was 139.7 pg/ml (10–65 pg/mL). Urine calcium was 4.1 mg (20–275 mg). Serum calcium level was <8.5 mg/dL or an ionized calcium level <1.0 mmol/L is considered hypocalcemia. Inadequate dietary magnesium intake leads to hypomagnesemia, hypophosphatemia, and hypocalcemia.

Causes for hypocalcemia in ICU patients:^[7]

- Hypoxemia
- Hypercapnia
- Metabolic acidosis
- Pulmonary congestion
- Adult respiratory distress syndrome.
- Malnutrition
- Electrolyte abnormalities – hypophosphatemia, hypokalemia, hypocalcemia, and hypomagnesemia
- Hypoglycemia
- Steroid use
- Drugs
- Thyroid disorders
- Congestive cardiac failure.

Differential diagnosis for hypocalcemia:^[8]

- Hyperventilation
- Hypoalbuminemia

- Conn's syndrome
- Vitamin D deficiency
- Pseudohypoparathyroidism
- Chronic renal failure
- Hypoparathyroidism
- Acute pancreatitis
- Hypomagnesemia.

Final diagnosis: Postthyroidectomy hypocalcemia, pseudohypoparathyroidism, and AECOPD with refractory hypercapnic respiratory failure due to hypocalcemia.

Why the diagnosis?

- Decreased levels of serum calcium
- Increased levels of parathormone
- Increased levels of serum phosphate.

HOW HYPOCALCEMIA LEADS TO HYPERCAPNIA?

Hypocalcemia causes respiratory muscle fatigue and poor effort of breathing.^[9] This leads to hypercapnic respiratory failure. This needs to be distinguished from other lung abnormalities. Hypocalcemia is a reversible cause of hypercapnic respiratory failure. Severe hypocalcemia can lead to laryngeal spasm and respiratory arrest. Hypocalcemia can lead to seizures and tetany.

HYPOPARATHYROIDISM

The most common cause of hypoparathyroidism is following total thyroidectomy. This occurs in 1%–2% of patients after total thyroidectomy.

COURSE IN HOSPITAL

She was treated with intravenous calcium gluconate, followed by oral calcium supplements and vitamin D3. Next day, PCO₂ was normal. She was weaned slowly from NIV after 48 h of calcium supplement. She had uneventful recovery.

This case aims to highlight the fact that neuromuscular weakness secondary to electrolyte imbalance which can lead to refractory hypercapnic respiratory failure. Electrolyte imbalance should be considered in the differential diagnosis of causes for refractory hypercapnic respiratory failure. Most often, electrolyte imbalance contributes to hypercapnia in ICU due to respiratory muscle dysfunction.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/

her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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