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# Acquired Central Alveolar Hypoventilation as a Sequelae of Brainstem Tuberculoma

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## Abstract

Central alveolar hypoventilation (CAH) is a rare condition resulting from brainstem injury, characterised by a loss of automatic breathing. We present a case of a 16-year-old female initially diagnosed with a brainstem glioma based on magnetic resonance imaging brain. Following craniotomy and tumour debulking, she developed episodic apnoea during both wakefulness and sleep. Histopathological analysis of the brainstem specimen unexpectedly revealed a diagnosis of brainstem tuberculoma. Despite the initiation of anti-tuberculous therapy, the patient showed persistent CAH two weeks post-treatment. Management required tracheostomy and long-term pressure-control synchronised intermittent mandatory ventilation (PC-SIMV), which effectively stabilised her respiratory function.

## Subject Areas

Respiratory Medicine

## Keywords

Alveolar Hypoventilation, Tuberculoma, Mechanical Ventilation

## 1. Introduction

Hypoventilation is characterised by elevated arterial carbon dioxide levels due to inadequate gas exchange. Central alveolar hypoventilation (CAH) disorders arise from neurologic impairments affecting respiratory sensors, central control mechanisms, or signal integration. These conditions can lead to insufficient ventilation,

resulting in hypercapnia and hypoxemia. Central hypoventilation is a rare condition, with causes ranging from congenital abnormalities to acquired neurologic insults. In this case report, we present a case of CAH in a young patient, secondary to brainstem tuberculoma, who remained dependent on mechanical ventilation despite appropriate anti-tuberculous therapy.

## 2. Case Report

An adolescent female presented with a three-month history of insidiously progressive symptoms, including restricted visual fields, right-sided facial asymmetry, and left-sided hemiparesis accompanied by numbness and dysphagia. She also reported new-onset choking episodes. There was no history of weight loss, fever, or malaise. Neurological examination revealed muscle power of 4/5 in the left upper and lower limbs with multiple cranial nerve palsies involving cranial nerves III, IV, V, VI, and IX. No café-au-lait spots or freckles were noted. Laboratory investigations showed an elevated erythrocyte sedimentation rate (ESR) of 103 mm/hr and a white cell count of $8.3 \times 10^9$/L.

Magnetic resonance imaging (MRI) with image-guided surgery (IGS) protocol revealed a lobulated mass measuring 2.6 × 3.3 × 2.6 cm at the pontomedullary junction, associated with extensive white matter oedema and obstructive hydrocephalus (**Figure 1(a)**). The mass appeared hypointense on T2-weighted/FLAIR sequences with peripheral enhancement. An initial diagnosis of brainstem glioma was made. The patient underwent craniotomy and tumour debulking. Intraoperatively, the tumour showed a cheese-like appearance and was adherent to the brainstem. Histopathological examination (HPE) revealed chronic granulomatous inflammation without evidence of acid-fast bacilli on Ziehl-Neelsen staining. Tissue culture for Mycobacterium tuberculosis was negative, as were cerebrospinal fluid analyses for Mycobacterium tuberculosis complex and Xpert MTB/RIF assay. However, imaging showed tree-in-bud changes in both upper lobes and mediastinal lymphadenopathy. Bronchoalveolar lavage was positive for Mycobacterium tuberculosis. Given the clinical, radiological, intraoperative, microbiological and histopathological findings, brainstem tuberculoma was considered the likely aetiology. The patient was started on AKURIT-4, a fixed-dose combination of isoniazid, ethambutol, rifampicin, and pyrazinamide, alongside dexamethasone at 0.4 mg/kg/day, which was tapered weekly per guidelines.

Postoperatively, the patient was extubated on the first day but developed generalised tonic-clonic seizures on day three and required reintubation for airway protection. A repeat computed tomography (CT) scan of the brain showed no new changes. She was started on phenytoin for seizure control, with no further recurrence of seizures. The patient was ventilated using pressure-control synchronised intermittent mandatory ventilation (PC-SIMV) with a backup rate of 12 breaths per minute, $FiO_2$ of 40%, and minimal intravenous fentanyl sedation. Serial arterial blood gases (ABG) revealed persistent carbon dioxide ($CO_2$) retention, with a partial pressure of $CO_2$ ($PaCO_2$) of 78 mmHg, $PaO_2$ of 74 mmHg, pH of 7.33, and

bicarbonate of 30 mmol/L. A recurrence of apneic episodes was observed (**Figure 1(b)**). Ventilator settings were adjusted to an inspiratory positive airway pressure (IPAP) of 20 $cmH_2O$, positive end-expiratory pressure (PEEP) of 6 $cmH_2O$, pressure support of 12 $cmH_2O$, and a backup rate increased to 16 breaths per minute, which normalised the arterial $PaCO_2$ to 42 mmHg. A diagnosis of acquired central alveolar hypoventilation secondary to brainstem tuberculoma was made. Due to prolonged ventilation requirements, a tracheostomy was performed.

Gradual weaning from PC-SIMV was achieved over two weeks. Final ventilator settings were IPAP 14 $cmH_2O$, PEEP 6 $cmH_2O$, pressure support 10 $cmH_2O$, and a rate of 16 breaths per minute using a portable ventilator (Trilogy EVO, Philips Respironics). Serial sleep reports from the PC-SIMV ventilator showed no significant reduction in the frequency of central apnea events. The patient underwent regular rehabilitation, including locomotor training, chest wall range of motion exercises, upper extremity ergometer use, and mechanical insufflation-exsufflation for airway secretion clearance. There was no improvement in limb power or cranial nerve deficits, and the patient remained ventilator-dependent.

On outpatient review at 2 months, she remains well with home ventilator support with no pulmonary infection.

## 3. Discussion

Tuberculosis, an airborne disease, primarily affects the lungs but can also involve other organs, including the central nervous system (CNS). CNS manifestations of tuberculosis include tuberculous meningitis, tuberculomas, and cerebral abscesses. Intracranial tuberculomas are rare and represent a severe form of tuberculosis. Tuberculomas involving the brainstem are particularly uncommon, accounting for only 5% of all intracranial tumours [1]. In a case series of 11 patients with brainstem tuberculomas, most had normal chest radiographs, with three patients demonstrating a miliary pattern. All patients showed a reduction or resolution of lesions with treatment [2].

The brainstem, comprising the midbrain, pons, and medulla, houses critical centres for autonomic functions, including respiration. The medulla contains the primary respiratory centre, regulating breathing in response to changes in pH, oxygen, and carbon dioxide levels in the blood and cerebrospinal fluid. The pons, located below the medulla, act as an auxiliary respiratory centre, controlling the rate and rhythm of breathing. Damage to these areas can result in varying degrees of hypoventilation, ranging from intermittent apnoeic episodes to severe apnoea requiring mechanical ventilation. These episodes are often exacerbated during sleep due to the loss of accessory ventilatory muscle tone and the absence of cortical influences. Hypoventilation leads to elevated arterial carbon dioxide ($PaCO_2$) levels, reflecting inadequate gas exchange.

Central alveolar hypoventilation (CAH) can be either congenital or acquired. Acquired CAH may arise from various etiologies, including brainstem stroke,

trauma, infection, anoxic-ischemic damage, and complications following neurosurgical procedures [3]. The onset of CAH may be delayed after an insult to the brainstem. In our patient, CAH manifested three days postoperatively, likely due to ischemia and perilesional oedema affecting the pontomedullary area. The patient experienced apnoea during both wakefulness and sleep, with arterial blood gases demonstrating hypercapnia, indicative of acquired CAH. A tracheostomy was performed to reduce dead space ventilation and assist alveolar ventilation.

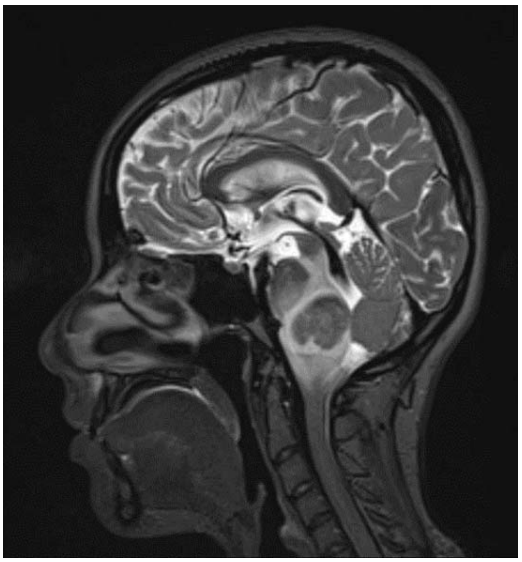
Alveolar hypoventilation is defined by inadequate alveolar ventilation, resulting in elevated $PaCO_2$ levels, particularly evident upon waking. The American Academy of Sleep Medicine defines hypoventilation during sleep as occurring when more than 25% of total sleep time is spent with $PaCO_2$ levels exceeding 50 mmHg, as measured by arterial $PaCO_2$ or surrogates such as transcutaneous $PaCO_2$ ($PtcCO_2$) and end-tidal $PaCO_2$ ($PETCO_2$) [4] [5]. Central apnoea is characterised by the cessation of airflow without respiratory effort for 20 seconds or longer or for a duration of two breaths during baseline breathing, associated with arousal or ≥3% oxygen desaturation [5]. There is no consensus on the diagnostic criteria for acquired CAH. However, proposed criteria include normal arterial $PaO_2$ during wakefulness, hypercapnia during non-REM sleep, alveolar hypoventilation during sleep, and the exclusion of pulmonary diseases [6]. Polysomnography is a valuable tool for evaluating hypoxemia and hypoventilation in CAH [7].

The prognosis of CAH varies depending on the severity and location of the lesion. Treatment focuses on preventing the sequelae of hypoxemia and hypercarbia, which can lead to adverse neurological outcomes, pulmonary hypertension, right-sided heart failure, and death. Pharmacotherapy is generally ineffective, and agents such as opiates and benzodiazepines should be avoided. Metabolic alkalosis should be aggressively corrected, and while oxygen therapy can address hypoxia, it does not correct hypercarbia or the underlying ventilatory dysfunction.

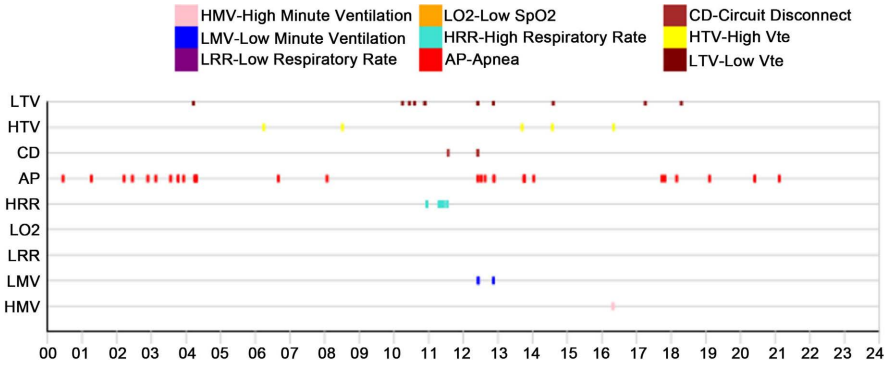
There is no established consensus on respiratory rehabilitation and ventilator weaning in acquired CAH. The primary goal is to achieve adequate ventilation and oxygenation during both sleep and wakefulness. Adult patients with acquired CAH may achieve adequate ventilation during wakefulness due to the maturity of the respiratory system and circadian rhythm. Treatment options include non-invasive positive pressure ventilation (NiPPV), positive pressure ventilation (PPV) via tracheostomy, or diaphragmatic pacing. NiPPV can be delivered via nasal, oronasal, or full-face interfaces using a bilevel positive airway pressure ventilator. PPV via tracheostomy requires more intensive family education, training, and nursing support. Treatment should be individualised, with goals typically including maintaining oxygen saturation above 95% and end-tidal $CO_2$ between 35 and 45 mmHg [7]. Due to the diminished ability to sense and respond to hypercarbia and hypoxemia, oxygen saturation should be closely monitored during sleep.

This case report highlights a rare neurological complication of brainstem tuberculoma, resulting in CAH. Early identification and appropriate ventilation strategies are crucial for improving outcomes associated with chronic hypercapnic

respiratory failure. Ventilation titration should be individualised, taking into account the clinical pathway and time required for ventilation.



(a)




(b)

**Figure 1.** (a): MRI sagittal view shows lobulated mass at the pontomedullary junction with extensive white matter oedema and obstructive hydrocephalus. (b): A sleep report generated from the PC-SIMV ventilator shows significant apnoeic episodes.

## Authors' Contribution Statement

The work conducted and presented in this manuscript has not been published or submitted for publication in another journal. All authors named in the manuscript have made substantial contributions to qualify for authorship according to BIMJ authorship criteria and have approved of the content of the manuscript. We have disclosed all financial support for our work and other potential conflicts of interest.

## Ethics Statement

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

## Conflicts of Interest

The authors declare no conflicts of interest.

## References

[1] Das, M., Dooley, K., Gupta, A. and Thakur, K. (2018) The Global Neurological Burden of Tuberculosis. *Seminars in Neurology*, **38**, 226-237. https://doi.org/10.1055/s-0038-1651500

[2] Talamás, O. (1989) Brain-Stem Tuberculoma. *Archives of Neurology*, **46**, 529-535. https://doi.org/10.1001/archneur.1989.00520410063025

[3] Randerath, W., Verbraecken, J., Andreas, S., Arzt, M., Bloch, K.E., Brack, T., *et al.* (2016) Definition, Discrimination, Diagnosis and Treatment of Central Breathing Disturbances during Sleep. *European Respiratory Journal*, **49**, 1600959. https://doi.org/10.1183/13993003.00959-2016

[4] Grigg-Damberger, M.M. (2012) The AASM Scoring Manual Four Years Later. *Journal of Clinical Sleep Medicine*, **8**, 323-332. https://doi.org/10.5664/jcsm.1928

[5] Berry, R.B., Budhiraja, R., Gottlieb, D.J., Gozal, D., Iber, C., Kapur, V.K., *et al.* (2012) Rules for Scoring Respiratory Events in Sleep: Update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. *Journal of Clinical Sleep Medicine*, **8**, 597-619. https://doi.org/10.5664/jcsm.2172

[6] Kuhn, M., Lütolf, M. and Reinhart, W.H. (1999) Ondine's Curse. *Respiration*, **66**, 265-265. https://doi.org/10.1159/000029388

[7] Berry RB, Chediak A, Brown LK, Finder J, Gozal D, Iber C, *et al.* (2010) Best Clinical Practices for the Sleep Center Adjustment of Noninvasive Positive Pressure Ventilation (NPPV) in Stable Chronic Alveolar Hypoventilation Syndromes. *Journal of Clinical Sleep Medicine*, **6**, 491-509. https://doi.org/10.5664/jcsm.27941