

Ondine's Curse in a Patient with Unilateral Medullary and Bilateral Cerebellar Infarctions

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Central sleep apnea (CSA), also known as Ondine's curse (OC), is a phenomenon characterized by episodes of repeated apnea during sleep due to disorders of the central nervous system. We report a patient with CSA/OC due to right dorsolateral medullary and bilateral cerebellar infarctions that occurred in the clinical setting of right vertebral artery stenosis. Polysomnography (PSG) showed repeated episodes of absence of nasal cannula flow accompanying cessation of thoracic and abdominal respiratory movements and a decline in blood oxygen saturation. The duration of apnea was as long as 12 seconds. Brain magnetic resonance (MR) images showed acute infarctions involving the right dorsolateral medulla, bilateral cerebellar vermis and paramedian cerebellar hemispheres. MR angiography showed nonvisualization of the right vertebral artery. Transcranial Doppler sonography showed a high resistance flow profile in the right vertebral artery and normal flow patterns in the basilar artery and left vertebral artery. These findings suggest that the medullary and bilateral cerebellar infarcts were caused by stenosis/pseudo-occlusion of the right vertebral artery. Reduced respiratory afferent inputs to the dorsal respiratory group of medullary neurons, the nucleus tractus solitarius and reduced "automatic" components of the respiratory drive may play a role in the development of CSA/OC. [*J Chin Med Assoc* 2005;68(11):531-534]

Key Words: cerebellar infarction, medullary infarction, Ondine's curse, polysomnography, sleep apnea, vertebral artery stenosis

Introduction

Central sleep apnea or Ondine's curse (CSA/OC) is characterized by episodes of repeated apnea during sleep. CSA/OC has been reported to occur in patients with brainstem strokes such as medullary infarctions, bulbar angioma, pontine glioma, Leigh's disease, Arnold-Chiari malformation, syringobulbia, multi-system degeneration, and cervical cord infarction due to anterior spinal artery occlusion.¹⁻⁹ Bilateral lesions of the lower brainstem are most commonly found regardless of etiology. We herein report a patient with CSA/OC due to right dorsolateral medullary and bilateral cerebellar infarctions that occurred in the clinical setting of right vertebral artery stenosis. The polysomnographic and neuroimaging findings are presented.

Case Report

A 62-year-old hypertensive man developed acute onset of dizziness and occipital headache when he was riding a scooter. Severe vomiting, mild weakness in the left limbs and incoordination in the right limbs brought him to our attention. On arrival, his blood pressure was 240/140 mmHg. His pulse rate was 72 beats per minute, respiration rate was 22/minute (regular), and body temperature was 36°C. His consciousness was clear. He had severe hoarseness, dysarthria, dysphagia, and hiccup. He had right Horner's syndrome (right eye miosis, smaller eye fissure of the right eye with normal extraocular movements, anhidrosis on the right side of the face), multidirectional gazing nystagmus, and mild weakness of the left-side limbs and face. Ataxia of the limbs on the right side, and

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bilateral Babinski's signs were noted. Brain computed tomography (CT) scan was unrevealing a few hours after the onset. Chest radiograph was unremarkable. The patient was soon placed on subcutaneous low-molecular-weight heparin treatment.

Respiratory patterns during awakeness were normal. However, 2 episodes of sudden apnea followed by cardiac asystole developed during the night of the third hospital day and the early morning of hospital day 13. Arterial blood gas analysis showed a pH of 7.283, PaCO₂ of 58.8 mmHg, PaO₂ of 53.4 mmHg, and SaO₂ of 83% on one occasion under nasal cannula with oxygen flow of 3 L per minute, just prior to cardiopulmonary resuscitation (CPR). The patient recovered quickly (within a few hours) from these events following successful CPR, and no additional neurologic deficits were observed. Brain magnetic resonance imaging (MRI) showed acute infarctions in the right dorsolateral medulla oblongata and bilateral cerebellum (Figure 1). MR angiography showed nonvisualization of the right vertebral artery and segmental stenosis of the very proximal part of the basilar artery (Figure 2). Neurosonographic examinations revealed a high-resistance flow profile for the right vertebral artery, with peak systolic flow velocity (PSV) of 36 cm/second, end-diastolic peak flow velocity (EDPV) of 4 cm/second, time-average mean flow velocity (MV) of 14 cm/second, systolic-to-diastolic ratio of 9.0, resistivity index (RI) of 0.89, and pulsatility index (PI) of 0.58. The corresponding values for the left vertebral artery were PSV of 57 cm/second, EDPV of 18 cm/second, MV of 31 cm/second, RI of 0.68, and PI of 0.47.

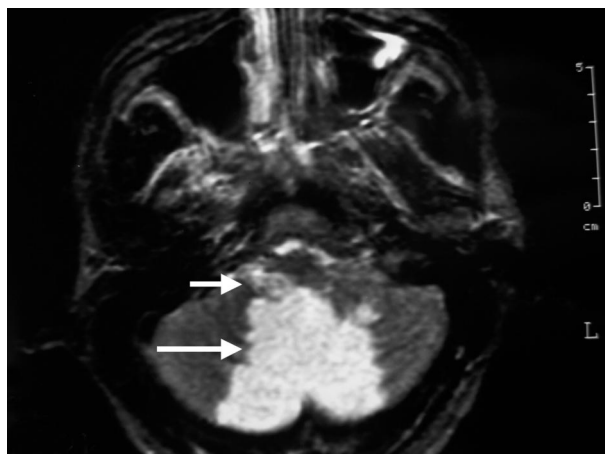


Figure 1. Magnetic resonance imaging (T2-weighted image; TR/TE: 2800/100) shows lesions of high signal intensity in the right dorsolateral part of the right medulla oblongata (short arrow) and bilateral cerebellum (long arrow), suggesting acute brain infarctions.

Polysomnography (PSG) showed repeated occurrence of the absence of nasal cannula flow during the episodes of apnea, with the apnea period lasting as long as 12 seconds (Figure 3). Oxygen saturation declined during the apnea episodes. The respiratory disturbance index was 11.9 per hour. The PSG findings were consistent with CSA/OC. Orotracheal intubation was performed, and assisted mechanical ventilation continued for the subsequent 2 days. The patient was successfully weaned off the ventilator thereafter. Theophylline was added for CSA/OC. Following the second episode of apnea and cardiac asystole, he was placed on bilevel positive airway pressure for the ensuing 2 months to prevent unpredictable episodes of apnea and cardiac asystole at night during sleep. The patient was well in a nursing home 3 months later, and he continued on ticlopidine therapy for secondary stroke prevention.

Discussion

CSA/OC frequently leads to mortality because of the unpredictable and unnoticed episodes of apnea during sleep. The neural mechanism of the apnea episodes in CSA/OC has long been investigated. In essence, 2 components of the neural control of the respiratory system while awake and during sleep have been elucidated. They are anatomically distinct but functionally integrated elements, referred to as the central neural network for control of respiration and the peripheral neurochemical respiration control network. The former consists of the “automatic” and



Figure 2. Magnetic resonance angiography reveals nonvisualization of the right vertebral artery (arrow).

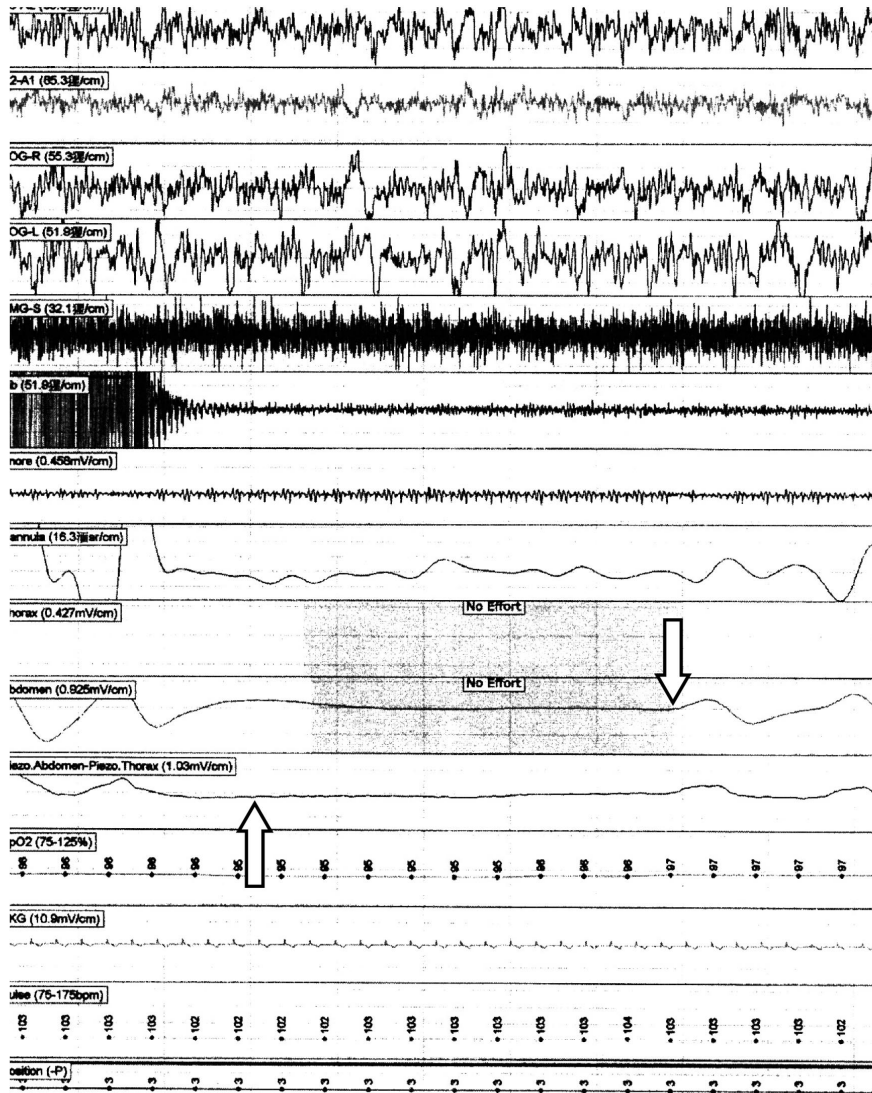


Figure 3. Polysomnography shows cessation of the thoracic and abdominal movements for 12 seconds (arrows). No nasal cannula flow can be detected during this period. Oxygen saturation declined to 85%.

“behavioral” respiratory control systems.¹⁰ The automatic respiratory control system has its central autonomic network in the brainstem that comprises the dorsal respiratory group (DRG) of medullary neurons, the nucleus tractus solitarius (NTS), and the reciprocally connected ascending and descending projections.¹¹ The DRG and NTS in the dorsomedial part of the medulla oblongata receive not only the important afferents from the cardiovascular and respiratory tracts, but also the efferents that are necessary for the autonomic control of cardiac rhythm, circulation and respiration.¹¹ The DRG and NTS in the dorsolateral part of the medulla oblongata were involved in our patient (Figure 1). We speculate that reduced afferent input from the target organs, reduced “automatic” respiratory drive and efferents during sleep due to ischemic injury to these neurons may have played a role in the development of CSA/OC in our patient.

CSA/OC is different from a more common, yet nonspecific, condition called Cheyne-Stokes respiration (CSR). The latter is characterized by irregular periods of apnea alternating with phases of hyperpnea. The breathing waxes and wanes in amplitude. CSR has been found in comatose patients with deep bilateral cerebral hemispheric lesions (rather than medullary lesions), and in patients with a prolongation of the circulation time, such as congestive heart failure.¹² Furthermore, CSR has nothing to do with the sleep-wake cycle, whereas CSA/OC is an abnormal respiratory phenomenon that occurs during sleep. Therefore, drugs that suppress the central nervous system (such as benzodiazepine), or other sedatives that may alter the cortical voluntary and behavioral component of respiratory control must be avoided in patients with suspected CSA/OC.

It is well known that Wallenberg syndrome can be caused by infarction of the lateral medulla oblongata due to either thrombotic occlusion of the ipsilateral posterior inferior cerebellar artery (PICA) or stenosis/occlusion in the proximal vertebral artery or its branch.¹³ A benign course¹⁴ is more common than a malignant one. The latter may lead to sudden death, and the terminology of “malignant” Wallenberg syndrome was coined. CSA/OC might be one possible explanation for such a situation when the apnea episodes at night during sleep go unnoticed or are ignored by the physicians who take care of these patients. Moreover, agitation and sleep disturbance are common in patients who have suffered from acute brainstem stroke.

CSA/OC is more common in patients with bilateral lesions of the medulla oblongata.¹³ Unilateral medullary lesions may also cause CSA/OC in some instances.^{6,9,13} Infarction of bilateral cerebellum and unilateral dorsolateral medulla due to stenosis/occlusion of the unilateral vertebral artery is intriguing. A variation in the extent of vascular supply to the cerebellum and brainstem regions by the unilateral vertebral artery and its major branch, the PICA, is one possible explanation.

In conclusion, repeated apnea and cardiac asystole may occur in patients who are in the acute stage of infarction/ischemia of the unilateral dorsolateral medulla oblongata involving the DRG and NTS. These life-threatening conditions are preventable, treatable, and reversible. Close surveillance and avoidance of sleeping pills are important to prevent sudden death at night during sleep due to CSA/OC.

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