Anterior Spinal Artery Syndrome Complicated by the Ondine Curse

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Background: Anterior spinal artery (ASA) syndrome results in motor palsy and dissociated sensory loss below the level of the lesion, accompanied by bladder dysfunction. When the cervical spine is involved, breathing disorders may be observed.

Objective: To describe the polysomnographic findings in a patient with cervical ASA syndrome complicated by a sleep breathing disorder.

Setting: Unit of neurology at a sleep center.

Patient: A 30-year-old man had an ischemic lesion that affected the anterior cervical spinal cord (C2-C6) bilaterally because of an ASA thrombosis. He developed ASA syndrome associated with respiratory impairment during sleep.

Results: The polysomnographic study during sleep showed a severe sleep disruption caused by continuous central apneas that appeared immediately after falling asleep. Treatment by intermittent positive pressure ventilation normalized the respiratory pattern and sleep architecture.

Conclusions: The sleep breathing pattern was compatible with central alveolar hypoventilation due to automatic breathing control failure caused by a lesion of the reticulospinal pathway, which normally activates ventilatory muscles during sleep. This autonomic sleep breathing impairment resembles that found as a complication in patients who undergo spinothalamic tract cervical cordotomy for intractable pain. This surgical complication is known as the Ondine curse.

Arch Neurol. 2003;60:1787-1790

REPORT OF A CASE

A 30-year-old man was admitted to the Neurological Unit–Sleep Centre of St Orsola-Malpighi Hospital (Bologna, Italy) because of ventilatory failure during sleep. Three months before, cerebrospinal magnetic resonance angiography (MRA) revealed an ischemic lesion affecting the anterior spinal cord (C2-C6) as a consequence of ASA thrombosis. He exhibited sudden tetraplegia and respiratory arrest, requiring mechanical ventilation by tracheostomy. In the days following, he recovered motor activity in his legs and distal arms. He experienced complete rehabilitation of breathing while awake but not while asleep and thus required intermittent positive pressure ventilation (IPPV) during sleep. The results of blood tests, including inflammatory markers, coagulation parameters, and an autoantibody profile, were normal. Dynamic cineradioscopy showed a bilateral diaphragmatic palsy. His ventilatory effort while awake was supported by intercostals, other accessory respiratory muscles, and residual diaphragmatic contraction. The spirometry showed a mild restrictive syndrome. At night, IPPV via tracheostomy was required (tidal vol-
volume, 540 mL; respiratory rate, 11/min) because he reported being “unable to fall asleep without it.” Several trials to wean him off the mechanical ventilation during sleep failed. With the diagnosis of idiopathic ASA syndrome, he was referred to our sleep center for a polysomnographic study of breathing patterns. At the time of our examination, no cognitive or cranial nerve deficits were found. There was hypotrophy and flaccid palsy of the bilateral girdle muscles of upper limbs with preserved strength of the distal arms, mild spastic paraparesis predominant on the left side, dissociated sensory loss below C2 to C3, a bilateral Babinski sign, and sphincteric and erectile dysfunction. While awake, his breathing was spontaneous with the closed tracheostomy, respiratory rate was 20/min to 22/min, and the results of a blood gas analysis were normal (PaCO₂, 38.1 mm Hg; PaO₂, 63.8 mm Hg; pH, 7.42). Brainstem evoked potentials were normal.

SLEEP STUDIES

Five nighttime polysomnographic studies were performed in a single-bed room; the following tests were done: electroencephalography (C3/A2, C2/A1, O2/A1); electro-oculography (ROC/A1, LOC/A1); electromyography of submental, right intercostal, rectus abdominis, and left anterior tibialis muscles; airflow (oronasal thermistor during breathing by closed tracheostomy, and thermistor positioned in front of the stoma during breathing by opened tracheostomy); chest and abdominal movements (inductive plethysmography); electrocardiography; finger probe pulse oximetry (SaO₂); and transcutaneous capnography (TCO₂). Each recording was performed in different respiratory conditions: during spontaneous ventilation by closed and by open tracheostomy, during IPPV by tracheostomy nasal mask (respiratory rate, 11/min; tidal volume, 540 mL), and during sleep induction by triazolam (0.25 mg at 11 PM). Furthermore, the flow distribution of IPPV by tracheostomy was manually stopped during slow-wave sleep and during rapid eye movement (REM) sleep to evaluate the functioning of automatic breathing control in consolidated sleep. Sleep was manually scored in 20-second epochs according to the standard criteria of Rechtschaffen and Kales.

POLYSOMNOGRAPHIC RESULTS

During spontaneous breathing, the sleep respiratory pattern was characterized by continuous central apneas that appeared immediately after falling asleep and persisted throughout the entire sleep period. These episodes lasted 10 to 30 seconds and were associated with mild oxygen desaturation (3%-6%). The apneas ended with arousal or awakening, leading to severe sleep disruption (Figure 1). The total bed time for the first night was 6 hours 41 minutes, and the total sleep time was 3 hours 55 minutes, completely constituted by stage 1 and 2 non-REM. Slow-wave and REM sleep were absent. During wakefulness, the respiratory rate was 20/min, with regu-
lar electromyographic intercostal activity. The administration of 0.25 mg of triazolam did not change the breathing pattern except for a mild lengthening of the apneas. The IPPV supply led to a regular respiratory pattern during a complete sleep cycle, with a constant respiratory rate of 11/min, no intercostal activity, and no SaO₂ fluctuations (Figure 2). With IPPV by tracheostomy, the ventilation was manually stopped during slow-wave sleep (3 times) and REM sleep (3 times). On each occasion, central apneas reappeared immediately after discontinuation of assisted ventilation, with the same respiratory pattern.

**FOLLOW-UP**

At the 1-year follow-up, polysomnography was performed during spontaneous breathing with a closed tracheostomy, confirming a central sleep apnea pattern associated with severe sleep disruption. The following year, IPPV by nasal mask was successful, yielding the same good respiratory and sleep results obtained during ventilation by stoma. The tracheostomy has since been removed, and the patient has been breathing with an IPPV nasal mask every night. After 4 years, repeated cerebrospinal MRA revealed the anterior spinal cord lesion extending from C2 to C6, with no brainstem involvement (Figure 3).

**COMMENT**

The sleep breathing disorder in this patient was characterized by continuous central apneas associated with severe sleep disruption. The apneas appeared immediately after falling asleep and were followed by arousal or complete

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**Figure 3.** Sagittal (A) and axial (B) T2-weighted magnetic resonance images show linear hyperintensity in the anterior spinal cord, extending from C2 to C6, suggesting infarction in the territory of the anterior spinal artery. Note that the cervicobulbar junction is normal. ECG indicates electrocardiogram; EMG, electromyogram; EOG, electro-oculogram; Interc, intercostal; NREM, non-rapid eye movement; Resp, respirations; and Thor, thoracic.
awakening. During IPPV, the sleep architecture and respiratory pattern were regular. While awake, the patient breathed spontaneously by residual diaphragmatic activity and intercostal and accessory respiratory muscles, in line with the integrity of the direct pyramidal tracts. The fact that triazolam taken before sleep did not change the respiratory pattern, together with the immediate reappearance of central apneas in slow-wave sleep and REM after stopping IPPV, the possibility that psychological dependency on mechanical ventilation could influence the breathing pattern ruled out. The persistence of the breathing disorder during spontaneous ventilation with opened tracheostomy excluded any obstructive mechanism in the pathogenesis of the apneas. This pattern cannot be explained on the basis of the diaphragmatic palsy. The diaphragmatic hypomobility falls within the restrictive forms of respiratory failure, which could cause REM hypventilation via the inhibition of accessory muscles, which is typical of REM atonia. Further, no electromyographic intercostal activity was found during each episode of apnea, as evidenced by inactivated lower intercostal motor neurons. The breathing pattern described is compatible with central alveolar hypventilation, an impairment of autonomic control of respiration. Central alveolar hypventilation secondary to a lesion of the bulbar respiratory center is very uncommon but well documented in the literature. In our patient, brainstem lesions were excluded by the results of cerebrospinal MRA and brainstem evoked potentials, but autonomic ventilatory control was impaired by lesions of descending reticulospinal axons, which activate breathing muscles during sleep. The reticulospinal tract runs bilaterally along the anterolateral spinal cord neurons and behind the spinothalamic pathways, close to paths subserving micturition and in proximity to ventral horns. The sleep breathing pattern observed in this patient resembles that found as a complication in patients who undergo cervical cordotomy for intractable pain. This surgical complication was first described in 1962 by Severinghaus and Mitchell, who called this kind of sleep hypventilation the Ondine curse. In the last few years, a topographic analysis, performed on a series of cases of Ondine curse secondary to cervical cordotomy, has permitted easier identification of reticulospinal tract localization in the shelter of the spinothalamic pathway. Similarly, the ischemic lesion in our patient involved the spinothalamic tracts, causing dissociated sensory loss and, as a result of the tight nearness, the interruption of the reticulospinal tract subserving autonomic ventilation. We believe ours is the first report of polysomnographic demonstration of Ondine curse in ASA syndrome and other diseases and locations of spinal cord lesions, except for surgical cordotomy. A detailed study, using standard laboratory polysomnography, should always be performed if breathing dysfunction associated with a cervical lesion occurs in the absence of bulbar respiratory center injury. Results of nocturnal oximetry monitoring or polygraphic portable recording do not provide an accurate diagnosis of this condition. Based on our findings, we recommend nasal mask IPPV to resolve breathing dysfunctions and normalize the sleep architecture in these patients.

Accepted for publication July 18, 2003.

Author contributions: Study concept and design (Drs Manconi, Mondini, and Cirignotta); acquisition of data (Drs Fabiani, Rossi, Mondini, and Cirignotta); analysis and interpretation of data (Drs Manconi, Ambrosetto, Mondini, and Cirignotta); drafting of the manuscript (Drs Manconi, Fabiani, Rossi, Mondini, and Cirignotta); critical revision of the manuscript for important intellectual content (Drs Ambrosetto and Cirignotta); obtained funding (Dr Cirignotta).

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mer, Abou-Chebl, and Nadzam and Mr Hixson); study supervision (Drs Furlan and Nadzam).

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Correction

Errors in Figure Legends. In the Observation titled “Anterior Spinal Artery Syndrome Complicated by the Ondine Curse,” published in the December issue of the ARCHIVES (2003;60:1787-1790), the legends to Figures 1, 2, and 3 were incorrect. The legends are reprinted correctly as follows. Figure 1. Axial T2-weighted magnetic resonance image shows linear hyperintensity in the anterior spinal cord, extending from C2 to C6, suggesting infarction in the territory of the anterior spinal artery. Note that the cervicobulbar junction is normal. Figure 2. Continuous central apneas in stage 2 of non–rapid eye movement sleep during spontaneous respiration. During the apneas, no thoracic or abdominal movements or intercostal muscle activity were observed. Abdom Resp indicates abdominal respirations; ECG, electrocardiogram; EMG, electromyogram; EOG, electro-oculogram; Interc, intercostal; Mylo, myloidoideus muscle; Oral Nasal Resp, oral nasal respirations; and Thor Resp, thoracic respirations. Figure 3. Normal sleep architecture with slow-wave sleep and rapid eye movement sleep during mechanical ventilation. ECG indicates electrocardiogram; EMG, electromyogram; EOG, electro-oculogram; Interc, intercostal; Oral Nasal Resp, oral nasal respirations; REM, rapid eye movement; NREM, non–rapid eye movement; Thor Resp, thoracic respirations.