Abstract. – Central sleep apnea is a breathing disorder that manifests as repetitive cessation of the breath during the sleep. The occurrence of breathing disorders after cervical laminectomy has been exceptionally described as a complication after cervical decompressive laminectomy for cervical stenotic myelopathy.

In 1994, Naim-ur-Rahman reported the first case of postoperative central sleep apnea following C3-C6 laminectomy, occurring right after surgery and associated with spyncterial incontinence, that spontaneously recovered three weeks after onset. Recently we described a rare complication of cervical laminectomy for cervical stenotic myelopathy: the onset was delayed from surgery (nearly two weeks later) and cervical stenotic myelopathy was not associated to any other neurological sign of spinal cord damage as demonstrated by the neurophysiological assessment. Possible familiar predisposition can be matter of discussion.

No definite interpretation of pathophysiological mechanisms can ultimately explain the occurrence of delayed and isolated central sleep apnea after laminectomy for the treatment of cervical stenotic myelopathy. Such a reversible and benign complication remain unpredictable in the best surgical hands.

Key Words: Ondine curse, Central sleep apnea syndrome, Spinal cord diseases, Spine, Laminectomy.

Introduction

Breathing disorders following decompressive laminectomy for cervical stenotic myelopathy (CSM) are rare1-2 Central sleep apnea (CSA) is a breathing disorder that manifests as repetitive cessation of the breath during the sleep3. The occurrence of breathing disorders after cervical laminectomy has been exceptionally described as a complication after cervical decompressive laminectomy for cervical stenotic myelopathy (CSM)2. CSA, also known as Ondine’ Curse, is a potentially life threatening condition in which, during sleep, breathing stops at intervals for 10 s or more4. It has been rarely reported in patients with upper cervical lesions associated with: rheumatoid arthritis, Arnold-Chiari type 1 malformation, anterior C1-C2 osteochondroma and os odontoideum2,5.

The aim of this paper is to highlight the possibility of CSA presenting as isolated and delayed complication occurring after laminectomy for the treatment of CSM.

CSA After Cervical Laminectomy for CSM: Myth or Truth?

The evidence

Sleep apnea is a clinical symptom in sleep-related breathing disorders that are divided into obstructive sleep apnea, CSA and mixed apnea by analysis using polysomnography6 (Figure 1). The event is obstructive if during apnea there is effort to breathe. On the other hand, in CSA there is no effort to breathe during sleep, which is a less common clinical problem. The prevalence of primary CSA is reported to be 9-28% of the general population throughout the world7,8.

Obesity in middle-aged males and shortening of the mandible and/or maxilla are the predisposing factors of CSA8. It has been also reported that diseases such as hypothyroidism, acromegaly, myotonic dystrophy and Ehlers-Danlos syn-
drome are risk factors for Obstructive Sleep Apnea/Hypopnea Syndrome (OSAHS)\textsuperscript{1,9}.

As we have already reported in the Introduction, CSA has been rarely reported in some class of patients as rheumatoid arthritis, Arnold-Chiari type 1 malformation, anterior C1-C2 osteochondroma and os odontoideum\textsuperscript{2,3}. The occurrence of breathing disorders after cervical laminectomy is considered exceptional as a complication after cervical decompressive laminectomy for the treatment of CSM\textsuperscript{2}.

In 1994, Naim-ur-Rahman reported the first case of postoperative CSA following C3-C6 laminectomy, occurring right after surgery (8 hrs later) and associated with spyncterial incontinence, that spontaneously recovered three weeks after the onset\textsuperscript{4}.

Recently we have described a case similar but different in the delayed occurrence of CSA without spyncterial incontinence\textsuperscript{15}. In this case, neurological examination showed hyporeflexia of the upper limbs and paraparesis at the admission. Bilateral Achilles clonus and lower limbs hyperreflexia were present with a light spasticity. Magnetic resonance (MR) and computerized tomography (CT) examinations showed a cervical stenosis at C3-C6 level, associated with multiple cervical intervertebral disc herniations, osteophytes and calcified ligamentum flavum. A cervical C3-C6 (partial C7) decompressive laminectomy was performed according to standard procedures. After a midline incision, the laminae were exposed bilaterally and the spinous processes were then removed. Facetectomy was not performed.

Nearly two weeks later from surgery, the CSA become evident and not associated to any other postsurgical neurological signs of spinal cord postsurgical damage as demonstrated by the negativity of the neuroradiological and neurophysiological assessment. To the best of our knowledge, no previous report has been published on the topic.

### The Breathing Anatomy and Physiology

Breathing is a rhythmic motor behavior generated and controlled by hindbrain neuronal networks. Neural circuits controlling breathing in mammals are organized within serially arrayed and functionally interacting brainstem compartments extending from the pons to the lower medulla. The core circuit components that constitute the neural machinery for generating respiratory rhythm and shaping inspiratory and expiratory motor patterns are distributed among three adjacent structural compartments in the ventrolateral medulla: the Bötzinger complex (BötC), pre-Bötzinger complex (pre-BötC) and rostral ventral respiratory group (rVRG). The respiratory rhythm and inspiratory-expiratory patterns emerge from dynamic interactions between: (i) excitatory neuron populations in the pre-BötC and rVRG active during inspiration that form inspiratory motor output; (ii) inhibitory neuron populations in the pre-BötC that provide inspiratory inhibition within the network; and (iii) inhibitory populations in the BötC active during expiration that generate expiratory inhibition\textsuperscript{10-11}.

Nevertheless more recent models describe interacting populations of respiratory neurons spatially distributed within the BötC and pre-BötC and rostral ventrolateral medulla that contain core circuits of the respiratory central pattern generator (CPG). Network interactions within these circuits along with intrinsic rhythmonic properties of neurons form a hierarchy of multiple rhythm generation mechanisms. The functional expression of these mechanisms is controlled by input drives from other brainstem components, including the retrotrapezoid nucleus and pons, which regulate the dynamic behavior of the core circuitry. The emerging view is that the brainstem respiratory network has rhythmic capabilities at multiple levels of circuit organization. This allows flexible, state-dependent expression of different neural pattern-generation mechanisms under various physiological conditions, enabling a wide repertoire of respiratory behaviors. Some models consider control of the respiratory CPG by pulmonary feedback and network reconfiguration during defensive behaviors such as cough\textsuperscript{16}.

The location and fiber arrangement of the descending respiratory pathways (involuntary respiratory pathway) in the ventral reticulospinal tract is close to the descending micturition pathways within the upper cervical cord\textsuperscript{2}.

### Looking for the Pathophysiology

A disturbance to the respiratory center, in or adjacent to the pre-Bötzinger complex in lower medulla oblongata, would be postulated to determine a loss of normal autonomic response to chemical changes in the blood; nevertheless, in our case CSM was anatomically far for the lower medulla to hypothesize a direct compressive-traumatic mechanism determining a disturbance to the pre-Bötzinger area respiratory centers, definitely\textsuperscript{10,11}.  

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\textsuperscript{1} G.M. Della Pepa, G. La Rocca, G. Barbagallo, A. Spallone, M. Visocchi
We have also critically analyzed whether, after posterior decompression, the spinal cord was displaced posteriorly thus determining an angular deformation of the lower medulla oblongata that could possibly explain the patient’s symptoms. However, postoperative neuroradiological assessments of the cases described so far did not display any deformation that could justify such a mechanism.

Diaphragm paralysis has not been recorded in the cases published. In light of this, we are able to rule out a dysfunction of the phrenic nerve nuclei, focusing our interest on a possible transient nocturnal sleep-related transmission dysfunction of the reticulo-spinal fibers directed to these nuclear targets. A transient central neural limitation to hypercapnic ventilation could be an explanation. The delayed modalit of presentation could be related to “time related” neural transmission dysfunction. In fact, decompressive laminectomy provides an immediate decompressive effect on the spinal cord, as seen by the light dorsal migration of the cord, possibly associated with accompanying spasm of the radicular vessels, producing a transient ischaemia of the cord, perhaps triggered by neck movements after one week from collar removal.

The mechanism of central cord syndrome with CSM is thought to be caused by the inward bucking of the ligamentum flavum along with shortening and thickening of the spinal cord while the cervical spine is in extension. Interestingly animals undergone decompressive laminectomies with removal of the epidural ligaments had significant spinal cord deformation with subsequent reduction in blood flow and in MEP when placed in cervical flexion. Does the cervical epidural ligament provide the same protective effect in human beings?

As stated before, the location and fiber arrangement of the descending respiratory pathways (involuntary respiratory pathway) in the ventral reticulospinal tract and its proximity to the descending micturition pathways within the upper cervical cord explain the common concurrence of the sleep apnoea and urinary incontinence. Such an association as been described in the first paper dealing with reversible CSA after cervical laminectomy in CSM. On the contrary urinary incontinence due to upper cervical cord lesions may thus be a warning of the possibility of postoperative apnoea.

In conclusion and unfortunately, the exact biomechanics of the cervical spine and the spinal cord after decompressive laminectomy remain uncertain and, in our opinion, possible related risk factors need better investigations by preoperative evaluation of respiratory functions, intraoperative neurophysiological monitoring.

What to do?

Out of the risk factors group, as described in the literature, the CSA after cervical laminectomy for CSM is absolutely unpredictable in the best surgical hands.

When the CSA is reversible without permanent breath assistance procedures, CPAP is strongly recommended. Although not typical nor ordinary for the pathophysiological mechanisms and the modality of presentation, the application of standard protocols for obstructive sleep apnea syndrome, which includes CPAP overnight support, can be suggested in similar cases.

Otherwise, the mortality in patients with non-treated CSA is much higher than in those treated using CPAP. None of the two patients described in the literature, had one of the predisposing factors summarized before; they underwent CPAP successfully, obtaining complete and stable recovery within one month. Moreover the delayed onset of the phenomenon (nearly two weeks after the operation) in our patient still remain unclear concerning the mechanism (postoperative MR without lesional patterns with clear decompression signs; postoperative neurophysiological assessment negative) and unpredictable from the epidemiologic point of view. The choice anterior vs posterior approach for CSM for sure is strictly related to the type and the number of levels of compression and should be absolutely independent from the risk of CSA. Nevertheless it need to be stressed that the anterior cervical approach has no less incidence of CSA, since the location and fiber arrangement of the descending respiratory pathways (involuntary respiratory pathway) in the reticulospinal tract is ventral along with the descending micturition pathways within the upper cervical cord.

CPAP is the gold standard and can totally and permanently recover this complication.

Conclusions

Only two cases dealing with CSA as transient complication of a cervical decompressive laminectomy have been described for the treatment of CSM.
No definite interpretation of pathophysiological mechanisms can ultimately explain the occurrence of delayed and isolated CSA. Patients who are at risk or have already developed CSA are worthy of an accurate preoperative and operative clinical-neurophysiological (SEP and MEP) assessment.

For the others out of the already identified risk groups, no prevision nor prevention are available so far.

Conflict of Interest
The Authors declare that they have no conflict of interests.

References
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