

LITERATURE REVIEW

Empty nose syndrome

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ABSTRACT

Empty nose syndrome (ENS) is a clinical entity lacking consensual meaning, illustrating a rare nose surgery complication, particularly of nasal conchae surgery, which results in the destruction of the normal nasal tissue. In severe forms it may become debilitating; the inability in identification and appreciation of this syndrome turns detrimental to the patient. Physiopathology remains controversial, which probably implies disorders caused by excessive nasal permeability, affecting neurosensory receptors as well as the humidification functions and conditioning of inhaled air. Neuropsychological involvement is being suspected. Symptomatology is both variable and changeable, the most evident sign outlining paradoxical nasal obstruction. The diagnosis is based on a series of symptoms that need to be collected precisely, the objective examination that highlights the permeability of nasal fossae.

The management is problematic; there are implemented a complete range of simple hygiene and humidification techniques of the nasal cavity and, for more severe cases, surgery is provided, regardless of technique, the surgery targeting partial filling of the nasal airways. Prevention is the most essential strategy along with basic conservative surgical techniques.

KEYWORDS: empty nose syndrome, nasal obstruction, turbinoplasty.

INTRODUCTION

Empty nose syndrome (ENS) is a clinical entity poorly recognized, but undoubtedly destructive, presenting surgical complication of the nasal conchae. The term appears described for the first time in the specialty literature in 1994 by Dr. Eugene Kern from Minnesota, as being an empty space, which is outlined within the coronary section on CT image, in the conchae region, in certain patients who underwent surgery on inferior or middle nasal conchae¹. These patients complained about dryness and crusts at the level of nasal mucosa, paradoxical nasal obstruction, the feeling of obstructed breathing, significant nasal breathing difficulty, feeling of excessive airflow, discomfort while breathing, irritability, anxiety, asthenia. ENS so far remains a controversial disorder regarding symptomatology, because the majority of patients that undergo surgery on nasal conchae experience an improvement in nasal breathing. The disease may outset from several months to years after the surgery at the nasal conchae level. The incidence of the disease is

not known since there were not published detailed studies, but some authors assume that approximately 20% of patients who suffered turbinoplasties develop ENS². It is difficult to set a diagnosis, as exact objective tests for this do not exist; so, the subjective symptoms of the patient are considered.

ETIOLOGY OF ENS

Chronic nasal obstruction, although not being a pathology with vital risk, may affect patient's quality of life. Patients who do not respond to the medical treatment may benefit from a surgical one. The most important thing to consider in the surgery of nasal conchae is the fact that a wider nasal cavity does not necessarily imply a better functioning as such. The aim of the surgery is to decrease patient's complaints, keeping organ functionality and the volume reduction of the conchae, considering individual anatomical features, preserving at the same time the nasal mucosa as much as possible. There exists a multitude of surgical

methods used in the volume reduction of the nasal conchae. As far as the inferior nasal conchae are involved, surgery is applied in the treatment of compensatory hypertrophy, protrusion of concha bone, isolated hyperplasia of the anterior or posterior part of the nasal conchae (e.g. lateroposition, resection procedures, clotting procedures, cryotherapy, radiofrequency laser surgery, ultrasound).

Concha bulosa, polypoid degeneration of the mucosal middle nasal concha, paradoxical curved middle nasal concha represent pathologies that require surgical treatment through the following methods: temporary septum medialization by means of a suture; volume reduction of the middle nasal concha; resection of the middle nasal concha.

Surgical techniques on nasal conchae are very different; nevertheless, till now, none of these techniques embody the ideal standard.

CLASSIFICATION

Two types of ENS are described: with and without nasal conchae mucosa defect.

The first type, empty nose syndrome with conchae mucosa defect, is represented by three subtypes:

1. ENS of the inferior nasal concha is most commonly met and paradoxical nasal obstruction stands for the most frequent symptom.
2. ENS of the middle nasal concha is rarely met; beside nasal obstruction, pain persists during respiration, induced by the cold airflow that, at its turn, hits the area of the sphenopalatine ganglion, which is no more protected by the middle concha as it was before surgery.
3. Common ENS, which refers to the resection of both inferior and middle nasal conchae.

The second type is characterized by the presence of seemingly enough healthy tissue at the nasal conchae level, but the patient suffers from ENS as a result of nasal conchae surgery³.

ENS PHYSIOPATHOLOGY

Physiopathology of the syndrome stays incompletely elucidated, but in the specialty literature, certain hypotheses may be found. It is well known the fact that the nose represents a lot more than the pathway for the inhaled air. It also serves as air conditioner before it gets to the lungs through filtration, thermal adjustment, as well as humidification⁴. The nose offers more than 50% resistance toward the airflow, and it has the role of air and odor passage to the olfactory grooves. Nasal conchae play a very important role, presenting bony structures from the sidewall of the nasal fossae,

covered with mucosa and submucosa. Inferior nasal conchae direct the airflow toward the middle meatus, acquiring the capacity to modify its size, as well as the airflow. The middle nasal concha has minimum tissue capacity, but it has mucous glands and a small quantity of olfactory nerve endings; in addition to this, it protects the sphenopalatine area.

According to some authors, ENS denotes a combination between structural changes and physiological ones, as a result of surgeries at this level. This combination in structural and physiological changes impacts each other and interferes amongst them leading to: decrease in nasal resistance, a nonphysiological and unnatural airflow, absence of functional mucosa in certain areas and also simultaneous widening of the nasal cavity, temporary contact reduction between air and mucosa⁵.

I. Functional composition of the syndrome may be expressed either by one of the following, or a combination of:

Nerve damage (neuropathy) and mucosa atrophy. Often, ENS patients do not feel the airflow through the nasal cavity. The nasal mucosa is richly innervated by multiple sympathetic and parasympathetic nerve fibers (autonomic nervous system), nociceptive fibers that can be damaged during surgery, resulting in insensitivity and atrophy. Through its sympathetic and parasympathetic fibers, the autonomic nervous system controls several involuntary functions in the body, such as blood pressure, heart rate, breathing frequency. At the nose level, the autonomic nervous system controls the conditioning of inhaled air, nasal resistance, mucus secretion, cilia function and mucus layer, having an important vascular and glandular role⁶. Surgery often unbalances the autonomic nervous system, in some cases causing neuropathy; certain areas of the mucosa change their sensitivity to airflow, and the patient may experience pain or burning sensation that may occur in response to stimuli that normally do not cause pain.

Cold thermoreceptors. According to Zhao et al.⁷, the primary physiological mechanism that explains the production of nasal airflow sensation is the activation of cold thermoreceptors, TRPM8, located at the level of the inferior nasal conchae mucosa. These receptors are activated by the airflow, which moves rapidly as it penetrates through the nostril and induces water evaporation from the fluid that covers the epithelium. The remaining fluid has a lower temperature, which leads to a decrease in the fluidity of the phospholipid membrane. This change in membrane rigidity is perceived by TRPM8 receptors, causing neuron depolarization that contacts the respiratory center⁷. The cold message is interpreted as nostril permeability and open airway, leading to a decrease in the activity of intercostal and

accessory respiratory muscles. The lack of stimulation is interpreted by the brain as uncool signal and causes apnea, increases the activity of respiratory muscles or falsely increases the sensations, which is interpreted as nasal obstruction. In response, thickening of the nasal mucosa or excessive production of mucus can also occur, which may also partially occlude the airways and limit evaporation; thereby, the degree of mucosal cooling is reduced, which consequently reduces the feeling of permeability. The permeability sensation is dependent on adequate mucosal cooling as well as a sufficient number of TRPM8 receptors that function properly.

Poor nerve regeneration. Importantly, the nasal conchae are a source of nerve growth factor⁸. However, it is known that sensory nerves regenerate poorly. Therefore, damage to nasal conchae or the removal of any part of them, the surface of which is rich in receptors, can cause poor nerve regeneration. It can induce a feeling of insufficient airflow, a general impediment to the nasal function, significant disturbances in the perception of nasal signals, the transmission of contradictory information at the brain level and the autonomic nervous system, with a successive incorrect system response⁹.

Atrophy and destruction of the mucosa. Atrophy of the nasal mucosa is a common sign in patients suffering from ENS. Often, the mucosa of these patients is pale, dry due to nerve damage; scarring, deterioration of nasal air conditioning function, lack of mucosal stimulation and blood flow changes, caused by surgery, may be also present. Deterioration of mucosal regeneration due to atrophy and mucosal dysfunction leads to the increase in nasal epithelium vulnerability and damage of the mucociliary transport mechanism. Shortage of muciparous glands produces a humidity decrease in the nasal cavity and a decline in nasal secretions. Moreover, the nasal mucosa contains mechanoreceptors, proprioceptors and thermoreceptors of the nasopulmonary reflex. Additionally, there exist pulmonary C-fiber receptors and quickly adapting receptors located on the bronchial wall, the larynx and the nasal cavity, multimodal responsiveness to mechanical stimuli, chemical stimuli, and to the inflammatory and immunological mediators responsible for the secretion of mucus at the level of the respiratory tract and cardiovascular reflex. It is discussed the possible existence of a reflex arc between the lungs and the capacity of the blood from the nose vessels that come from extensive pulmonary receptors. The reflex arc starts from the extensive pulmonary receptors in the vagus nerve to the central nervous system and contacts the blood from the vessels of the nasal mucosa through the efferent nerves of the vidian one. Finally, studies have demonstrated that the absence, inappropriate stimulation of any receptor group can reflex-

ively cause changes in breathing, bronchomotor tone, mucus secretion, laryngeal caliber, spinal reflexes.

II. Structural modifications

Nasal resistance. Nasal conchae have an important role in nasal breathing. The nasal meatuses being the spaces through which the airflow passes, formed between the nasal conchae, the nasal septum and the floor of the nasal cavity are very narrow and create airflow resistance. Normally, nasal airway resistance constitutes more than 50% of the total respiratory tract resistance. This resistance offers an average velocity of nasal flow, still laminar. As a result, there is a mucosal air-conducting interface that provides the right breathing sensation. Additionally, the nasal valve redirects the flow of air coming from the front and the sides to create a laminar airflow, thus prolonging its contact with the nasal mucosa, appropriately achieving olfaction, retaining foreign particles, humidifying and heating the inhaled air¹⁰. Tissue loss of nasal conchae destroys and damages meatus structures causing airflow disruption. This airflow transformation from laminar to turbulent decreases the velocity of the inhaled air, facilitating at the same time the heat and the evaporation transfer. Moreover, a significant decrease in nasal resistance can substantially affect the balance of resistance required for deep pulmonary inspiration and may lead to breathlessness. In order to apprehend a sufficient airflow, the nasal mucosa must experience aerodynamics.

In the ENS patient, the nasal cavity becomes unphysiological and abnormally wide, leading to stress reduction over the nasal mechanoreceptors and thus reducing the sensation of airflow and nasal regulation mechanisms⁵.

Air conditioning. During inspiration, the air is filtered, heated and humidified. The air conditioning function is mainly performed by the nasal airways. The healthy nose provides about 90% of the humidity and heating required for conditioning the surrounding air.

To carry out this task properly, the anatomical and morphological conditions must operate in an equivalent way; the geometry of the nasal structures and the sufficient quantity of the functional mucosa must be kept intact⁵. Fulfillment of the nasal air conditioning function is required for the exchange of undiluted alveolar gas to avoid dehydration and adhesion of the alveolar capillary bed¹¹. The mucociliary nasal clearance is very important for nasal drainage. Extracellular nucleotides (adenosine and uridine) can stimulate the mucociliary clearance in several ways. These nucleotides are released by the local epithelium and act in a paracrine way. Furthermore, an altered histological structure, such as cilia loss after surgery on nasal conchae, disturbs the normal mucociliary flow in the anterior sinuses (the frontal, anterior ethmoid, and

the maxillary sinuses), which occur along the uncinat process and the inferior nasal conchae toward the nasopharynx in the posterior. Thus, nasal secretions are accompanied by insufficient mucociliary clearance in ENS patients due to deteriorated and reduced inferior conchae tissue.

Cognitive function. After nasal conchae resection, the nasal passage becomes much wider than it should physiologically be. Intranasal pressure decreases, the airflow rate diminishes during inspiration and expiration. However, because of a low airflow rate (within the same inspiring effort) as well as a lack of airflow sensation, an ENS patient begins to experience a feeling of suffocation and other physical and cognitive symptoms, forcing the activation of the sympathetic nervous system, anxiety and forced breakout of breathing, which becomes unstable. This leads to the inability to relax, concentrate or think clearly (nasal apoplexy)⁴.

POSITIVE AND DIFFERENTIAL DIAGNOSIS OF THE EMPTY NOSE SYNDROME

The diagnosis is difficult to assess because of the lack of a precise clinical definition, symptom variability and psychological stress that gets associated frequently. Ultimately, a number of ENS patients are not diagnosed, as most often the physicians search for physical signs of dryness and atrophy - a result of turbinoplasties as long-term complications. The subjective complaints of nasal obstruction or the breathing difficulty get to be ignored as much as many other otolaryngological disorders (e.g. tinnitus, throat lumps), since the symptoms are subjective and cannot be objectively kept under control. And yet the diagnosis is based on the patient's complaints and the objective clinical examination performed during consultation.

The **signs and the symptoms** of the empty nose syndrome may be structured into several categories: respiratory, nasal, cognitive, emotional, sleep disorders.

The *respiratory* signs and symptoms can be represented by paradoxical nasal obstruction, empty nose sensation, shortness of breath, tachypnea or dyspnea. The paradoxical nasal obstruction is the most common complaint, a subjective feeling of nasal "stiffness"; during physical examination of the nasal fossae, the permeability of the nasal fossae is noted because of the nasal conchae tissue absence¹². The feeling of nasal obstruction may be associated with the feeling of "emptiness", patients referring to this term to depict the subjective incapacity to perceive the airflow, mainly noted due to total inferior turbinectomy. The excessive flow of air, the lack of nasal resistance and the difficulty in complete breathing can lead to breathing difficulties like shortness of breath, tachypnea and

dyspnea. Because of the subjective absence of airflow, these patients tend to become tachypneic and often slip into hyperventilation because they feel a relentless feeling of dyspnea. Dyspnea may be accompanied by compensatory hyperventilation. Although the air that enters the nose in ENS patients fails to stimulate the thermoreceptors of the nasal mucous membrane, the air gets into the lungs and activates the pulmonary tissue stretching receptors, indicating the brain that a proper ventilation is taking place. The possibility of this conflicting message could explain the stress associated with breathing in ENS patients. This condition is probably the most severe form of paradoxical obstruction and can aggravate patient's physical activity.

Nasal symptoms can be represented by nasal dryness, facial and nasal pain, sneezing, anosmia/hyposmia, hoarseness and cough (due to inadequate air purification and humidification. A healthy nose can provide 90% of the heat and water flows necessary to condition the inspired air in a constantly changing environment. After conchae reduction surgery, a relatively large volume of inspired air passes through a wide pathway without any chance for a proper conditioned air. Naftali et al.¹³ have demonstrated that the middle and inferior conchae control up to 90% of the total nasal conditioned air, its efficacy being reduced by almost 23% without an adequate conchae surface (resection of both inferior and middle turbinates).

The performed studies have shown a correlation between turbinoplasties and dryness sensation. According to the histological structure of glands at the level of inferior conchae, the acini of the mucous glands are most often embedded deep in the lamina propria, and these glands grow progressively in number from the anterior region to the posterior one of the inferior conchae. Thus, 70% of the mucous membranes are found in the posterior portion. Hence, it is easy to attest that after conchae reduction surgery, especially on the posterior part of the inferior nasal concha, the number of mucous glands is reduced, resulting in nasal dryness. Difficulties in thickened mucus removal, evident crusts on clinical examination, are the result of insufficient mucociliary clearance due to deterioration and reduction of the inferior conchae tissue.

It is not known exactly the pathophysiology that would explain the facial and nasal pain, but it was speculated that increased pain in ENS patients may be related to the disturbances of the sensory innervation of the anterior nasal cavity. The general sensory nasal innervation is provided by trigeminal nerve branches (V1 and V2). In particular, the internal lateral branch of the anterior ethmoid nerve feeds the anterior end of the inferior nasal concha, which deals with pressure and pain. Nasal sensory receptors are responsible for the airflow sensation, and these receptors are sensitive

to temperature. We suspect that more sensory defects will occur if several anterior conchae tissues are damaged. If there is no nerve and receptor regeneration, the nose could present hypersensitivity responses to the inhaled air; moreover, this response is more likely to be worsened by the uncontrolled and disrupted air flow caused by the reduced nasal conchae.

From the *cognitive* point of view, ENS patients present a loss of concentration because they find themselves in a permanent state of dyspnea, become very concerned about their breathing, which has a bad impact on productivity. This phenomenon is known as “nasal apoplexy”.

The *emotional* status can be characterized by irritability, frustration, depression, panic attacks, anxiety or chronic asthenia.

All the above symptoms can lead to *sleep disorders*, like: sleeping difficulties, nocturnal awakenings, insomnia, general asthenia.

SNOT-20 (Sino-Nasal Outcome Test 20) questionnaires or the modified version, customized with 5 additional questions that relate directly to ENS (SNOT-25), are the most used tools in assessing the quality of life in patients with nasopharyngeal problems, in ENS diagnosis and appreciation of subsequent treatment. It encloses 25 questions marked from 0 to 5, divided into 4 subscales - rhinologic, otological-facial, sleep and cognitive disturbances¹⁴.

The **clinical and paraclinical examination** are also an important step in diagnosing an empty nose syndrome. Nasal endoscopy can reveal large nasal cavities, with the lack or considerable reduction of the inferior nasal conchae and / or post-surgery mediums. The mucous membrane is pale, dry, presenting crusts at the mucosa level.

Objective tests, like the cotton bud test, can validate an empty nose syndrome. During the cotton bud test, a piece of cotton wool moistened in isotonic solution is inserted in the nasal cavity for 20-30 minutes; if symptoms improvement is recorded, the test is considered positive for ENS (because the symptomatology is associated with excessive lumen enlargement)⁹.

Usually, the diagnosis is clinically established, but it can be supplemented with a few signs that can be observed on CT images (but not pathognomonic): thickening of the sinus mucosa, clarity loss of the osteomeatal complex secondary to damaging the ethmoidal bubble and the uncinate process, opacity of the maxillary sinus, enlargement of the nasal fossae, osteodestruction of the inferior and middle nasal conchae¹⁵.

There are authors who state that rhinomanometry is not useful for the diagnose approval of ENS, the test confirming the absence of any anatomical obstruction⁴. Rhinomanometry results cannot be correlated with the subjective sensation of the patient's permea-

bility because it only focuses on the obstruction attributed to certain anatomical factors. However, the test can objectively demonstrate a difference between the subjective perception of nasal patency and the objective air resistance, results that can deter the ENT surgeon in performing other resections of the nasal conchae.

Many studies have presented the feeling of obstruction without any proven anatomical cause; for example, local application of an anesthetic in the nasal cavity produces an artificial sensation of nasal obstruction with unchanged permeability measured objectively, while topical application of menthol produces a feeling of decongestion without altering the current nasal morphology¹⁶.

The **differential diagnosis** of the empty nose syndrome is done primarily with atrophic rhinitis. It is important to note that the two distinct conditions were widely highlighted in the specialty literature: primary and secondary atrophic rhinitis. Primary atrophic rhinitis is often spontaneous at onset and, of course, slowly progressively debilitating. Often, no distinct etiology is identified, although the causes of successive or infectious diseases are proposed. Although spontaneous at onset, primary atrophic rhinitis reflects an insignificant blood flow disorder at microvascular level, which continues for a prolonged period of time. Secondary atrophic rhinitis is more commonly encountered and specifically after proper injuries, such as traumas, irradiation, reductive rhinosinus surgery or granulomatous pathology in secondary entities. The clinical examination reveals nasal crusts, enlarged nasal cavities, conchae resorption, mucosal atrophy and paradoxical nasal congestion. Less frequent reported symptoms include facial pain and pressure, anosmia and intermittent epistaxis¹⁷.

TREATMENT STRATEGIES IN THE EMPTY NOSE SYNDROME

Prevention can be the first step to take into consideration. As the nasal mucosa is the functional entity involved in the conditioning of the inhaled air, the minimal invasive surgical procedure of the nasal conchae with maximum preservation of the mucosa and thermoreceptors is the key to obtaining the optimal outcome and reducing the risk of ENS development.

Drug treatment includes nasal hygiene with regular intranasal irrigations, which remains the standard conservative therapy to minimize crust formation and restoring nasal hydration; one can also use vitamin therapy associated with vitamin A and E topically applied, oils locally, aerosols and corticosteroids applied locally as well. The addition of menthol activates thermoreceptors at the conchae mucosa level, those responsible for

inspiration; thus, without causing morphological changes, they transmit the brain a permeability airway signal; hyaluronic acid injected locally produces an increased thickness in the conchae mucosa, but the symptoms return after various periods of time; “disposable silicone” prostheses to redirect the airflow are also used.

Surgical treatment includes reconstruction of the nasal conchae. However, before performing a nasal conchae implant, it must be determined whether the lumen reduction of the nasal fossae would be beneficial to the patient. By cotton wool testing or local injections of hyaluronic acid, the need for a transplant can be determined if the patient responds positively to them. The surgical technique involves the transnasal approach, with implant material fixed in a submucosa pocket. The amount and thickness of the implant material is arbitrarily determined depending on how the reconstruction of the inferior conchae was required during surgery. Implant locations are multiple – on the lateral nasal wall, at the level of the inferior conchae remains or the septal area adjacent to the resected concha –, normally performed to restrict the region of the nasal valve. Materials of different origins may be used: biological – cartilage graft at the auricular pavillion or costal level, bone graft, muscle or adipose tissue; synthetic – teflon, hydroxyapatite (mineral from bones and teeth), acellular dermis.

CONCLUSIONS

The empty nose syndrome may emerge as a result of surgery on nasal conchae, but can still occur on conchae with normal morphological structure. It is not clear why some patients develop this syndrome and others do not. In a sense, it is often associated with psychiatric disturbances and psychosomatic pathologies that indicate the role of psychosocial stress in some patients. The most striking symptom is the paradoxical nasal obstruction. Patients are preoccupied with their breathing and nasal sensations, leading to the inability to concentrate, chronic fatigue, irritability, anxiety, depression, associated with a major impact on the patient’s quality of life. Diagnosis is based on patient’s complaints and clinical examination. ENS measures of prevention are very important by keeping as much as possible the mucosa of the middle and inferior nasal conchae. Patient’s life quality suffering from this syndrome can be improved by restoring the nasal volume.

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