



Disease in a Nutshell

Empty nose syndrome and atrophic rhinitis

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ARTICLE INFO

Article history:

Received for publication May 17, 2016.

Received in revised form June 30, 2016.

Accepted for publication July 5, 2016.

Introduction

Nasal congestion, nasal obstruction, and sensations of dyspnea are concerns commonly presenting to the practicing allergist. Although in many cases these represent rhinitis (allergic or vasomotor), several other disorders need to be considered. Among these disorders are atrophic rhinitis and the empty nose syndrome (ENS). The term ENS was first used by Eugene Kern and Monika Stenkvis at the Mayo Clinic in 1994.¹ ENS as is currently used refers to a disorder associated with symptoms that arise from iatrogenic nasal tissue loss and often present radiologically with a paucity of normal nasal anatomical structures (Fig 1A and B).¹ The condition develops months to years in a small subset of patients undergoing turbinate resection and results from progressive nasal tissue atrophy.² Similarities exist between ENS and the disease referred to as atrophic rhinitis, and the literature is often rife with confusion.

Atrophic Rhinitis

ENS needs to be differentiated from a related disorder, atrophic rhinitis (or ozena), a syndrome of chronic rhinosinusitis, thick adherent crusts, foul odor (feter), and nasal congestion (Table 1). Both primary and secondary forms of atrophic rhinitis have been described, with the latter often following surgical trauma, granulomatous inflammation, or irradiation. Nasal biopsy if performed reveals glandular atrophy, endarteritis obliterans, and inflammatory cell infiltration.^{1,3} Paradoxical congestion (sensation of nasal congestion or obstruction despite large nasal cavities), dryness, and crusting are features, much as in ENS. The dryness and crusting represent loss of glandular function and humidification of the inspired air. Atrophic rhinitis can be a crippling disease, and the patient can be disabled by the chronic, unrelenting nature of

the symptoms and airflow limitation.¹ Endoscopy reveals partial or total absence of the inferior and/or middle turbinate in many cases. Histopathologic analysis of biopsy tissue reveals typical findings, including atrophy of serous and mucinous glands, loss of cilia and goblet cells, and sporadic inflammatory cell infiltration.^{1,3} Bacterial infection is common, setting this disorder apart from ENS, and nasal cultures often yield pathogenic organisms, including *Klebsiella ozaenae*, *Staphylococcus species*, *Proteus mirabilis*, and *Escherichia coli*. Computed tomography of the paranasal sinuses reveals a variety of abnormalities, including mucosal thickening of the sinuses, nasal cavity enlargement, and bony destruction/loss of the inferior and/or middle turbinate. The management includes nasal saline irrigation, antibiotics, and surgical techniques that restore nasal mucosal function and narrow the airway using a variety of implants.

Empty Nose Syndrome

ENS usually develops after turbinate resection and is divided into 3 subtypes. ENS–inferior turbinate (ENS-IT) refers to ENS encountered after resection of IT tissue. This is the most common subtype and might develop in 20% (estimated) of patients undergoing IT surgery.¹ Scheithauer,⁴ on the other hand, estimates the incidence at 16% after IT surgery. In these patients, a combination of tissue resection by surgery and poor nerve regeneration has been hypothesized as contributors to the development of the syndrome.¹ Typically, the patient presents with paradoxical nasal congestion, dryness, and crusting months or years after surgery, sometimes making it difficult to differentiate from atrophic rhinitis.¹ ENS–middle turbinate (ENS-MT), although much more common after IT surgery, may develop in patients after MT excision.^{1,5} The incidence of ENS after MT resection is unknown. Nasal congestion symptoms may be accompanied by nasal pain, which is thought to be secondary to altered nasal airflow over mucosa overlying the sphenopalatine ganglion.^{1,6} ENS–both refers to patients who have had a resection of both IT and MT tissue. Crippling and severe symptoms are likely along with loss of olfactory sensation, with

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Disclosures: Authors have nothing to declare.

<http://dx.doi.org/10.1016/j.anai.2016.07.006>

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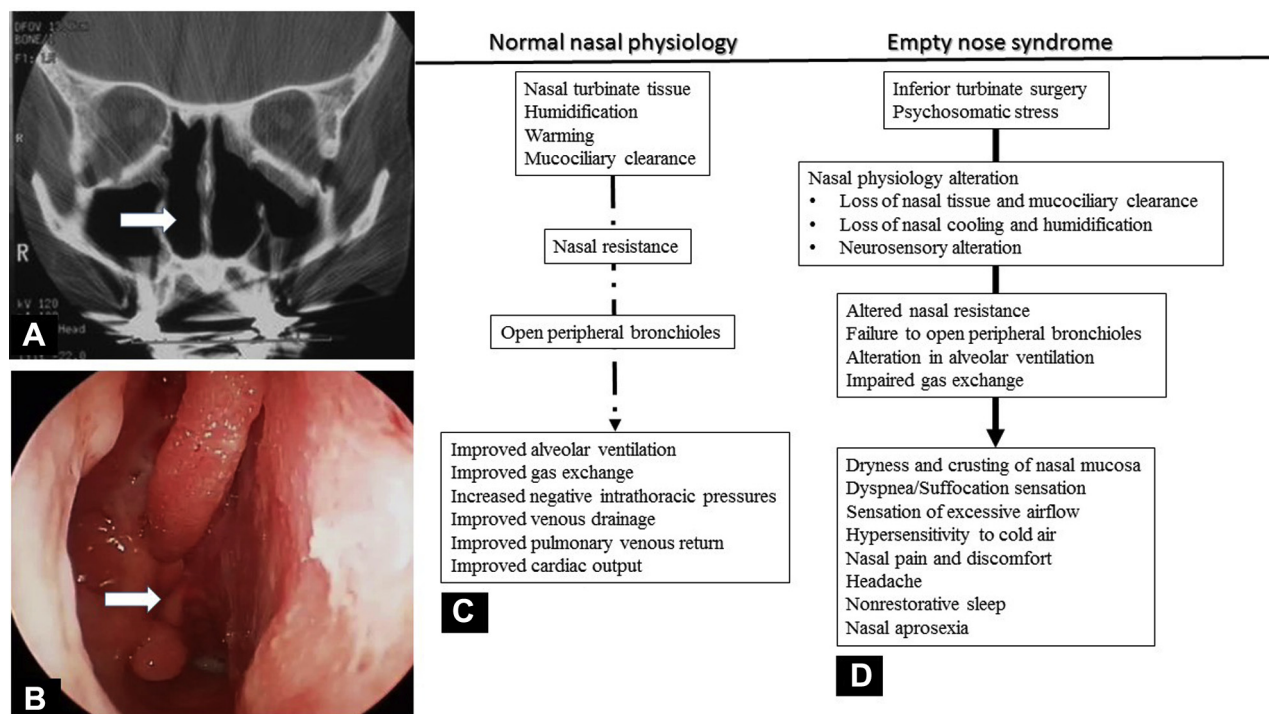


Figure 1. Radiologic (computed tomogram) (A) and nasal endoscopic (B) findings in empty nose syndrome. Open nasal cavities with turbinate loss are observed in these patients. Patients often are concerned about a “paradoxical” nasal congestion, obstruction, and sense of suffocation. Normal nasal physiologic features (C) and presumed alterations in empty nose syndrome (D) that lead to the clinical symptoms associated with the disease. White arrows on panels A and B indicate radiological and endoscopic demonstration of tissue loss and open nasal cavity.

some developing depression attributable to the recalcitrant nature of the symptoms.⁶ Middle turbinectomy is performed more frequently in patients with rhinosinusitis with polyposis, when there is disease such as an inverted papilloma or when the access to the ostium of the maxillary sinus is limited. Inferior turbinectomy is indicated in patients with persistent airway obstruction or turbinate hypertrophy that has not responded to medical therapy.

Extensive turbinectomy also can occur in patients with refractory sinus headaches, patients with malignant tumors, and at times during transsphenoidal pituitary surgery.

Pathophysiologic Mechanisms

The pathophysiologic mechanisms of ENS remains unclear, and many hypotheses have been suggested. A schematic of the normal

Table 1
Distinguishing Aspects of Allergic Rhinitis, Atrophic Rhinitis, and the Empty Nose Syndrome

Feature	Allergic rhinitis	Atrophic rhinitis	Empty nose syndrome
Definition	IgE-mediated inflammatory disease	Inflammatory atrophic disorder with loss of turbinate and mucosal tissue	Paradoxical nasal obstruction after turbinate surgery; iatrogenic disease
Crusting	No	Thick, adherent	++
Nasal dryness	No	++	+++
Foul odor	No	+++	No
Anosmia	No	+++; Loss of olfactory, pain, temperature receptors?	Hyposmia or anosmia
Dyspnea or suffocation	No unless underlying asthma	No	+++
Nasal obstruction Or congestion	+++	+++ Paradoxical (enlarged nasal cavity)	++ Paradoxical (enlarged nasal cavity)
Depression	No	No	++
Etiology	Atopy; genetic	Primary or secondary to trauma, radiation, surgery or granulomatous disease	Iatrogenic secondary to turbinate surgery
Histopathology	Inflammatory cell infiltration; inflammation; edema; Goblet cell hyperplasia	Mucus gland atrophy; loss of cilia and goblet cells; inflammatory cell infiltration	Loss of turbinate and mucosal tissue; no inflammation
Infection	No	<i>Klebsiella ozenae</i> , <i>Proteus mirabilis</i> , <i>Staphylococcus aureus</i> and <i>Escherichia coli</i>	No
Management	Nasal steroids, antihistamines, leukotriene antagonists, allergy immunotherapy	Nasal hygiene, irrigation?; antibiotics; treat primary disease; surgical therapy: implantation	Nasal hygiene; irrigation; surgical implantation

++, moderate; +++, severe.

nasal physiologic process and the aberrant responses seen in ENS are shown in [Figure 1](#). Humidification and warming of the inspired air, mucociliary activity, and removal of particulate material are essential nasal functions that are greatly impaired in disorders such as atrophic rhinitis and ENS.⁴ It is presumed that turbinatectomy leads to a loss of sensorineural receptors, some essential for pain and temperature sensation.^{2,4} Loss of turbinate tissue and enlargement of the nasal cavities might also lead to altered and turbulent airflow, whereas lack of humidification and glandular destruction leads to mucosal dryness and crusting.^{1,4} An additional mechanism is discussed in [Figure 1C](#) and [D](#) and involves alterations in nasal airway resistance function.^{1,2,7} Nasal airway resistance is presumed essential to keep bronchioles open and thus to improve ventilation and gas exchange. These effects also decrease intrathoracic pressure, resulting in improved venous return, pulmonary blood flow, and cardiac output. Alterations of these physiologic aspects might lead to dyspnea, paradoxical congestion, and the sense of suffocation, as discussed previously.^{1,2,5} Radical resection of the turbinates may decrease the surface area stimulated by mucosal cooling. Partial resection of the anterior part of the turbinate may result in loss of valve function and lead to the disease. Dayal et al⁸ used simulated 3-dimensional models and virtual surgery to demonstrate that nasal airway resistance decreased while airflow increased. They also found that total inferior turbinate surgery led to greater increases in nasal airflow but also impaired nasal air-conditioning capacity much more so than with middle turbinate resection, which might explain the differences in incidence of ENS after inferior vs middle turbinate surgery. Although the symptoms are secondary to changes in normal nasal physiologic functions after loss of turbinate tissue, neuropsychiatric mechanisms may also be at play. Accordingly, these patients experience a higher incidence of other functional syndromes, such as fibromyalgia, migraine, and irritable bowel syndrome.⁹

Clinical Presentation

The term *ENS* was initially used to describe the radiologic findings in patients after surgical resection of turbinate tissue. The diagnosis requires a strong clinical suspicion and demonstration of widely patent nasal passages in patients with nasal obstruction. The mucosa appears pale, dry, and crusty. The finding of an absent inferior or middle turbinate endoscopically is suggestive of the diagnosis.

Such patients may present to the allergist with a plethora of symptoms, including nasal congestion, decreased ability to sense airflow, nasal dryness and crusting. In some patients, hyposmia, epistaxis, and dyspnea/suffocation or shortness of breath may be the most dominant symptoms.^{1,5,10} It is important to exclude asthma or vocal cord dysfunction in such patients because these disorders may coexist. Spirometry and examination of the flow volume loop may be helpful in this regard. Preoccupation with the nasal disease can lead to anger, frustration, and inability to concentrate (referred to as nasal aprosexia) or perform work-related activities, resulting in other disabling psychosomatic manifestations.⁷ The Beck Inventory Depression II and the Beck Anxiety Index scores are often abnormal, and in the study by Lee and co-workers,¹¹ abnormal values of these indexes predict a better outcome from surgery. Females performed worse preoperatively on the Beck Inventory Depression II and the Beck Anxiety Index and improved considerably postoperatively. Patients with inoperable conditions, who refuse further surgery, or in whom surgery is contraindicated may benefit from counseling, cognitive behavioral therapy, and antidepressant therapy.⁹

The Houser modification of the traditional Sino-Nasal Outcome Test form includes 5 additional questions about nasal dryness, difficulty with nasal breathing, suffocation, feeling that “nose is too

open,” and presence of nasal crusting.^{6,7} The nasal examination reveals dryness, crusting, and large, patent nasal fossae, which contrast with the sensations of paradoxical congestion and dyspnea the patients seem to be preoccupied with. Nasal endoscopy findings in a patient with ENS are shown in [Figure 1A](#) and an example of a computed tomogram in [Figure 1B](#). The white thick arrow in [Figure 1A](#) points to a significant widening of the nasal passage and loss of turbinate tissue, considered pathognomonic of the disease (particularly in the setting of paradoxical nasal congestion or obstruction).

Pivotal aspects that differentiate ENS from allergic and atrophic rhinitis are summarized in [Table 1](#). The diagnosis is mainly clinical based on the constellation of signs and symptoms mentioned above in a patient with a history of turbinatectomy or nasal-sinus surgery.^{1,2,7,12} Another test sometimes recommended for diagnosis is the cotton test.⁷ Isotonic saline–moistened cotton is placed in the nasal cavity for 20 to 30 minutes, and resolution of symptoms is consistent with the diagnosis and suggests success of surgical intervention.^{2,7} No age, sex, or racial differences have been reported that predict the development of disorders. It is unclear whether hormonal or neuroimmunologic factors play any role. Allergic rhinitis can happen at any age, with a higher prevalence in the young. Atrophic rhinitis is more likely to be diagnosed in the elderly patient, especially those living in drier climates. ENS too tends to be diagnosed more frequently in the older population.

Management

Prevention is essential because once the disease becomes manifest management options become limited. A careful evaluation of the need for turbinatectomy and the use of alternative strategies to minimize tissue loss and allow rapid restoration of nasal physiologic mechanisms is essential. A thorough evaluation for allergy and other reversible factors for turbinate swelling and inflammation by an allergist might lead to the discovery of medically treatable factors and avoid the requirement for radical turbinatectomy. Although the incidence of the syndrome after turbinatectomy is low, it can be the source of great disability to the patient and frustration for the clinician.^{3,4} Alternative approaches that have been used to decrease the incidence of ENS include laser surgery, electrical cauterization, partial turbinatectomy, submucosal turbinoplasty, and submucosal resection by specialized techniques, including radiofrequency surgery.² A careful neuropsychological evaluation is required preoperatively because of the effect of surgical failure on the patient's psychological well-being.² In a systematic review, Leong¹³ concluded that corrective surgery not only improved ENS symptoms but also nasal symptoms, sleep function, and psychopathologic conditions.¹³ In some patients, the greatest improvement was observed in the symptoms associated with ENS and in the psychological status of the patient.

The medical management includes mucosal moisturization, hydration using saline or oil-based lubricants, increased fluid intake, intermittent nostril closure (to retain humidity), liberal use of cool mist humidifiers, and an aggressive regimen of nasal saline irrigations.⁵ For patients with somatic symptoms, cognitive behavior therapy may help, and the careful use of newer-generation antidepressants might complement therapy.⁹ A multidisciplinary approach with allergists, ear, nose, and throat surgeons, and psychiatrists might be required in some patients to get a handle on this difficult disease. Surgical approaches are usually attempted only after an adequate trial of medical management, counseling, and education have failed to result in improvement.⁷ The general concept behind surgical intervention is to restore nasal physiologic function, and turbinate reconstruction surgery has been reported using a variety of implanted materials.^{1,5,7} These techniques are beyond the scope of the current review but are adequately reviewed in literature.

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