Endoscopic endonasal repair of spontaneous cerebrospinal fluid leaks using multilayer composite graft and vascularized pedicled middle turbinate flap technique

Review Article

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Abstract

Objective: Review of the series of nasosinusal CSF fistulas and evaluation of reconstruction treatment using the multilayer technique and pedicled flap in the middle turbinate by CENS.
Study design: retrospective
Material and Methods: review of the clinical files of the patients submitted
CENS for closure of spontaneous CSF fistulas
Results: Three cases of spontaneous fistulas, females, with a mean age of 48.6 years (range 23-72 years) with unilateral rhinorrhea and a history of meningitis. The presence of glucose and b2-transferrin was investigated in rhinorrhea. The imaging study was performed by cranial CT and sinus CT and RM. The bone defect was identified by imaging in all cases. The cribriform plate and the ethmoid roof were the sites involved. Surgical treatment was performed using the "multilayer" technique with a pedicled flap of the middle turbinate. There were no relapses after a mean follow-up of 30 months.
Conclusions: Surgical correction of spontaneous fistulas is indicated by the risk of intracranial infectious complications. Surgical correction by CENS using the multilayer technique is a safe and effective way to treat these defects.

Keywords: cerebrospinal fluid leak; anterior skull base; spontaneous CSF leak; vascularized flap repair

Introduction

Sinonasal fistulae of cerebrospinal fluid (CSF) result from an anatomic bone defect that results in communication between the subarachnoid space, nasal cavity, and paranasal sinuses[1].

The most frequent cause (70%–80%) is usually accidental head and iatrogenic trauma associated with nasal or skull base surgery.

Fistulae of the CSF can also be secondary to cancer or to congenital defects that involve the base of the skull and they are classified as spontaneous in the absence of a specific cause.

More than one fistula can originate from external fracture of the base of the skull. The most common sites are the ethmoid roof and the cribriform plate because they firmly adhere to the dura mater[2,3,4]. Iatrogenic fistulae often occur in sites of greater anatomic weakness such as the lateral lamella of the cribriform plate, particularly on the right side, as well as the posterior ethmoid roof, the sphenoid sinus, and the posterior wall of the frontal sinus[2]. The risk is greater during significant nasal hemorrhage and revision surgeries[5]. Endoscopic sinonasal surgery is associated with the development of a CSF fistula in 0.5% of patients and hypophysis surgery is associated with a 16% intraoperative, and 5% postoperative risk[2].

Although the etiology of spontaneous fistulae is not completely understood, idiopathic intracranial hypertension (IIH)[6] and obesity with a body mass index (BMI) >30) seem to be frequently associated with their development, especially among middle-aged women[7]. A sustained increase in intracranial pressure (ICP) is associated with bone remodeling and thinning that can lead to bone erosion[2,6], the incidence of which has recently increased from 14% to 55%[6].

Spontaneous fistulae do not respond well to conservative medical therapy and can progress along with intracranial infectious complications such as meningitis (up to 10% of patients annually)[2], subdural empyema, cerebral abscess, and pneumocephalus[1].

Unilateral watery rhinorrhea is the predominant clinical symptom. Headaches, tinnitus, visual changes, and episodes of meningitis can also be associated. A clinical history of head trauma or previous nasal surgery combined with nasal endoscopy and complementary diagnostic tests usually lead to an established diagnosis.

Skull base fractures and CSF rhinorrhea are associated in 15%–30% of patients. Cerebrospinal rhinorrhea can develop within 48 hours (early) or during the first three months (late) in 95% of patients. Patients with head trauma and periorbital hematoma have a higher risk of late CSF rhinorrhea due to late recognition of dura mater rupture[2].

Detecting glucose in nasal discharge using glucose test strips is accessible and routinely applied, but low specificity and sensitivity prevents them from being recommended as a sole diagnostic test[2]. Intracranial infections such as meningitis with reduced glucose concentrations in the CSF are associated with false-negative results[2]. Furthermore, glucose can be detected in airway secretions of patients with diabetes mellitus, hyperglycemia, and inflammation of the nasal mucosa[2]. A CSF fistula is suspected when the concentration of glucose exceeds 30 mg/dL and the fluid is not contaminated with blood[2]. The absence of glucose usually excludes a CSF[2].

The sensitivity and specificity of b2 transferrin tests are 94%–100% and 98%–100%, respectively, and it is thus considered the gold standard for detecting CSF in rhinorrhea[2]. High-resolution computed tomography (CT) and magnetic resonance imaging (MRI) can reveal common characteristics in patients with IIH and spontaneous CSF fistulae that are not usually associated with fistulae of other etiologies8. Thinning of the base of the skull and multiple defects can be visualized by CT with 83%–88% sensitivity for bone detail in up to 31% of patients[2]. Intranasal masses, suspected meningoencephalic herniation, tumors, and an empty sella turcica can be discerned by MRI. Finding an empty sella turcica on MRI images is associated with increased ICP in IIH and spontaneous CSF fistulae[8].

Cisternography can accurately locate active fistulae. Surgical exploration with preoperative intrathecal fluorescein injection is an alternative when fistulae cannot be precisely located by imaging[2,4,5].

Understanding the etiology of fistulae allows planning for a more appropriate therapeutic approach. Conservative treatment consists

of bed rest with the head elevated, restricted water intake, diuretics, antihistamines, and prophylactic antibiotic therapy for 2–4 weeks. This can be an initial approach to resolving small traumatic and iatrogenic fistulae[2].

An endonasal surgical approach to correct fistulae was first applied in 1981. Since then, the continuous development of endoscopic techniques has led to excellent visualization of fistulae, precise flap placement, and shorter surgeries. Thus, endoscopic sinonasal surgery has become the technique of choice for the minimally invasive repair of fistulae with success rates of 87%–100%, which exceed those of external approaches[2]. Defects can be closed using overlay, underlay, or a combination of both types of grafts. Overlay grafts are placed over a bone defect outside the cranial cavity. Underlay grafts are placed inside the cranial cavity and consist of an epidural type that is placed between the bone and the dura mater, and an intradural type that is placed in the subdural space. The closing rates of these techniques are similar. Combining them can increase flap stability and maximize surgical outcomes[2].

Perioperative antibiotic therapy is associated with a low incidence of postoperative meningitis. Postoperative antibiotic therapy should be administered to prevent toxic shock syndrome, usually caused by *Staphylococcus aureus* and *S. epidermidis*.

The present study reviews spontaneous sinonasal CSF fistulae and the effects of multilayer (underlay and overlay) grafts reinforced with a pedicled flap from the middle turbinate to repair these defects.

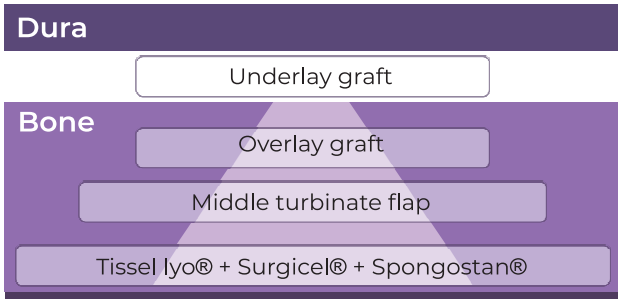
Material and Methods

Three spontaneous CSF fistulas were corrected by the authors through endoscopic sinonasal surgery at the otorhinolaryngology department of the Hospital Senhora da Oliveira, between January 2018 and January 2020.

The following parameters were assessed: age, sex, BMI, comorbidities, history of nasal/skull base surgery, clinical presentation, defect location, meningoencephalic herniation, length of hospital stay, peri- and postoperative morbidity, and need for revision.

No specific diagnostic algorithm was applied. In general, a detailed medical history was obtained from all patients with suspected CSF fistulae. They underwent a complete otorhinolaryngological (ORL) physical examination with endoscopic rhinoscopy and an evaluation of glucose and beta-2 transferrin in rhinorrhea. Defect locations in the skull base were confirmed and other etiologies were excluded by CT and/or MRI. Endoscopic rhinoscopy proceeded exclusively by sinonasal endoscopy using rigid 0 and 30° endoscopes under general anesthesia. The entire mucosa of the nasal cavity was vasoconstricted using a cotton swab soaked in phenylephrine (Neo-Synephrine® 5 mg/mL) and the nasal cavity was thoroughly assessed to identify normal structures and any anatomical variations such as nasal septum deviation and concha bullosa. A nasal procedure was applied to correct such variations when required to improve surgical access. Anatomical defects were identified and the surrounding mucosa was removed to expose their borders. Thereafter, autologous grafts were placed between the septal mucoperichondrium and middle or superior turbinate, then reinforced with a pedicled flap from the middle turbinate in all patients. Grafts were always placed using the epidural underlay technique, complemented with an overlay graft and secured using Fibrin Sealant Tisseel Lyo® (Baxter Healthcare Corp., Deerfield, UL, USA). This was further reinforced with absorbable hemostatic Surgicel® and Spongostan® (Ethicon Inc., Raritan, NJ, USA) and nasal packing with Merocel® (Medtronic Inc., Minneapolis, MN, USA). Intact dura mater was separated from the margin of the defect in the skull base during epidural underlay to allow enough support to stabilize the graft. The free graft was molded to remain a few millimeters between the bone and the dura on all sides of the defect. Figure 1 shows the interposed grafts. Figures 2, 3, and 4 show repairs of the bone defects.

Figure 1
Interposition of multilayered grafts



Postoperative care included general measures of ICP reduction and prophylactic antibiotic therapy with ceftriaxone (1 g every 12 hours).

Results

All patients were women, with a mean age of 48.6 years (range: 23–72 years). The mean BMI was 28 kg/m2 (minimum of 24 kg/m2 and maximum of 32 kg/m2). Only one patient had diabetes mellitus. No patient had a history of concomitant sinonasal surgery, traumatic brain injury, or chronic rhinosinusitis.

The clinical presentation of all patients was unilateral watery rhinorrhea and a history of meningitis. Headache was the main symptom in two of them and none had symptoms of nasal obstruction. Beta-2 transferrin and glucose were detected in rhinorrhea from all patients. Four defects of the skull base were identified, as one patient had two distinct

Figure 2
Spontaneous CSF fistulae on right and left ethmoid roof. View after anterior and posterior ethmoidectomy.

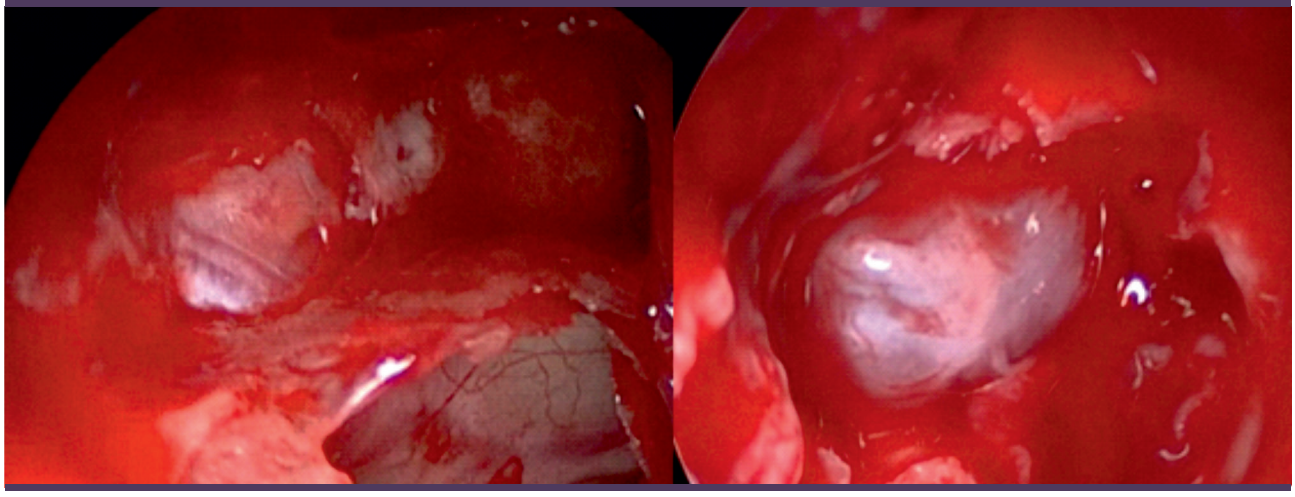


Figure 3
Multilayer technique with interposition of graft in epidural underlay position

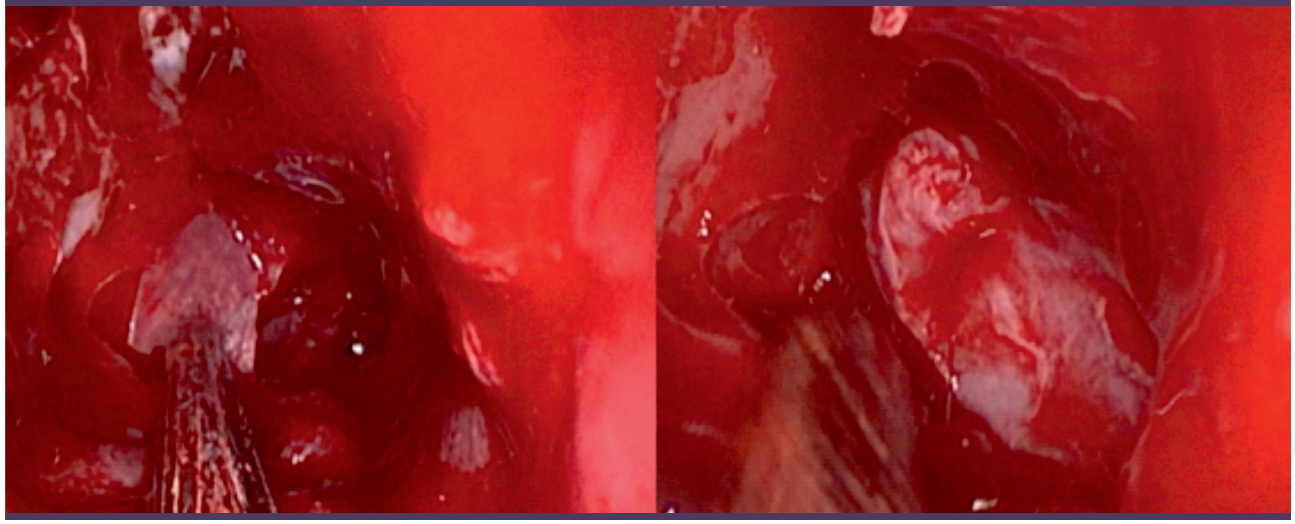


Figure 4
Multilayer technique with perichondrium and septal cartilage in overlay position

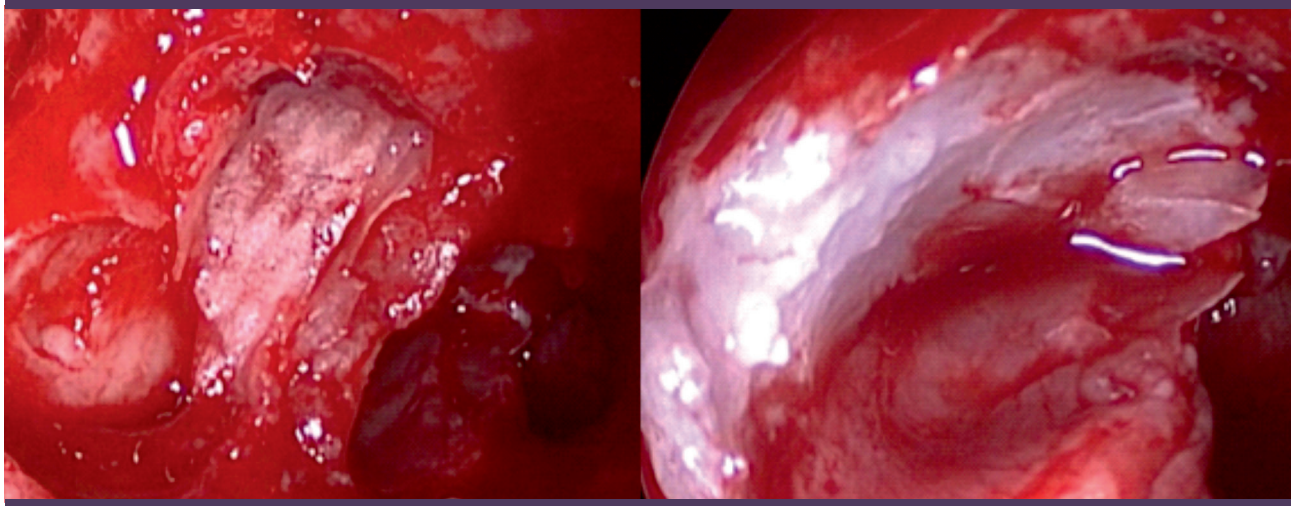
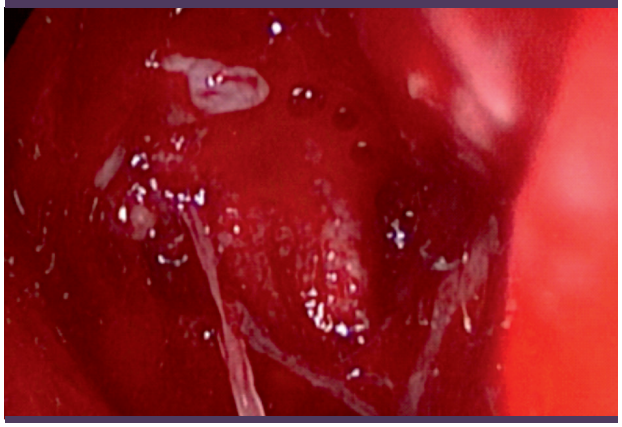


Figure 5
Multilayer technique with rotated flap from middle turbinate



bone defects on the ethmoid roof that were simultaneously repaired. Two fistulae each were located at the level of the cribriform plate and the roof of the ethmoid sinus, and three were on the right side (75%). None of the patients had herniated brain tissue at the time of the surgery or received a lumbar drain (LD) as adjuvant treatment. Nasal packing was removed on postoperative day 3, and the patients were discharged on postoperative day 5.66 after hospitalization for 5–6 days.

None of the patients developed neurological complications, meningitis, or any associated morbidities. The mean follow-up was 30 months with no evidence of relapse.

Discussion

The therapeutic approach to spontaneous CSF fistulae is challenging because of its increasing prevalence, undefined etiology, and higher surgical failure rates when they are associated with IIH. The initial approach using only conservative treatment (lifestyle changes, diuretics, bed rest, with or without PL) is insufficient for the treatment of most spontaneous fistulae[7]. Surgery is indicated when conservative therapy fails. A fistula that persists for > 7 days is associated with a significantly higher risk of intracranial infections, including meningitis[2].

The predominant clinical presentation in our patients was unilateral watery rhinorrhea as described in the literature, and all had a history of bacterial meningitis.

Fistulae can occur in any location of the base of the skull; however, some areas are more susceptible and thus have a higher risk of bone dehiscence. The more prevalent involved sites are the cribriform plate and the ethmoid and sphenoid bones[7]. Among the defects corrected herein, 50% each were located on the cribriform plate, and ethmoid bone, respectively.

The bone defects were small and precisely located in all patients. Surgical repair proceeded without the need for lumbar drainage due to the defects being small. Intrathecal fluorescein was not applied

immediately before surgery to locate bone defects as advocated by many surgeons.

Mucosa around a bone defect should be completely removed (at least 5 mm in all directions). Prominent bone adjacent to a defect should also be removed to facilitate graft application.

Meningoencephalic herniation should be reduced by cauterization with a bipolar device at the level of the pedicle to reduce the risk of retraction toward the intracranial compartment[2].

Endoscopic sinonasal surgery is more appropriate for the repair of small defects located on the cribriform plate and ethmoid and sphenoid sinuses. Comparisons among surgical techniques are hampered because of the variety and availability of materials, as well as the preferences of surgeons. Fat, bone, muscle, fascia, perichondrium, cartilage, pedicle flaps, and synthetic materials such as underlay and/or overlay grafts can all be applied. Vascular nasoseptal pedicled flaps have several advantages such as ease of elevation, rotation ability, and coverage of a larger area to include a defect, which justifies their use as a first approach. Vascular pedicled flaps from the inferior turbinate can be an alternative, especially for larger defects, but their application is technically more challenging. However, the middle turbinate is an excellent source of repair material for practically all procedures[2], as shown herein. Viability is an advantage of flaps over grafts because they theoretically increase healing rates. Free grafts can be combined to reinforce repairs of defects[2], as described herein. The skeletal support provided by the composite graft allows addressing pressure exerted by the SCF[2]. The overlay, rather than the underlay technique, is recommended in the event of risk of lesions to the nerve or vascular structures, or when the method is not technically feasible. A vascular nasoseptal flap is indicated to correct larger defects and high-output fistulae[7].

Most investigations into the correction of spontaneous CSF fistulae have not used a standard approach. However, Elmorsy and Khafagy[9] described patients with CSF fistulae repaired with septal cartilage or periosteum and reinforced with a flap from the mucosa of the middle turbinate without consistent application of an LD. The surgical success rate was 27 (87.1%) of 31 patients and the mean follow-up was 32.4 months.

Deenadayal *et al.*[10] similarly described a series of seven patients with spontaneous CSF fistulae that were repaired with a fascia lata graft using the multilayer technique with LD. Their patients remained recurrence-free after the primary surgery and for a mean follow-up of 14.9 months.

Gunaratne and Singh[11] described a series of three patients with spontaneous CSF fistulae that were repaired using septal cartilage or bone from the middle turbinate overlaid with a unilateral/bilateral nasoseptal flap and DuraGen® (Integra Life Sciences, Princeton, NJ, USA) without placement of an LD. None of these patients relapsed after a mean follow-up of 30 months.

Risk factors associated with the failure of surgical repair and a higher rate of recurrence comprise BMI > 30[2,12], defects in the lateral wall of the sphenoid and lateral extension in the frontal sinus, larger and/or multiple defects, and diabetes mellitus[2]. High-output fistulae and prior radiotherapy are also risk factors for relapse. Recurrence rates are higher for spontaneous CSF fistulae than for those with other etiologies (≤ 38% vs. <10%)[2,8]. Patients with IIH can experience recurrence at the same or a different site if elevated ICP is not treated, even after successful surgical repair[7]. Planning the surgical repair of this type of lesion involves vascular pedicled flaps, as applied to our patients. Some limitations must be considered in the selection of the surgical approach. Endoscopic sinonasal surgery is contraindicated for traumatic fistulae associated with intracranial lesions, comminuted fractures in the base of the skull, the orbit roof, and the posterior or lateral wall of the frontal sinus; hence an intracranial approach is favored[1]. A single intraoperative dose and maintenance of antibiotics for

patients at risk is an option, particularly for those with a history of meningitis or multiple interventions to close a fistula. We treated all our patients with intravenous antibiotic therapy for five days during their hospitalization, as recommended[1,3,4]. An LD can be placed and maintained for 24–120 hours[1,4] for spontaneous high-output and large fistulae, as well as those associated with revision surgery. This confers the advantage of stabilizing repairs, thereby avoiding increased pressure on the defect and promoting healing. Nasal packing is recommended to support grafts and most surgeons suggest its removal between postoperative days 3 and 5[2]. None of our patients experienced recurrence after a mean follow-up of 30 months. However, recurrence can happen even at a mean of 80 months[2].

Conclusion

The present results showed that repairing CSF fistulae using multilayer autologous grafts is in line with the favorable success rates reported in the literature, despite a short follow-up. Endoscopic sinonasal surgery is a safe, effective, and minimally invasive approach associated with reduced morbidity. Therefore, it has now become the technique of choice for the repair of CSF fistulae.

Conflicts of Interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

Data Confidentiality

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

Protection of humans and animals

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the 2013 Helsinki Declaration of the World Medical Association.

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Availability of scientific data

There are no datasets available, publicly related to this work.

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