Fluoroscopy-Assisted Transnasal Onyx Occlusion of the Eustachian Tube for Lateral Skull Base Cerebrospinal Fluid Leak Repair

Neil S. Patel¹ Matthew L. Carlson^{1,2}

¹ Department of Otolaryngology-Head and Neck Surgery, Mayo Clinic, Rochester, Minnesota, United States

² Department of Neurologic Surgery, Mayo Clinic, Rochester, Minnesota, United States

Address for correspondence Matthew L. Carlson, MD, Department of Otolaryngology-Head and Neck Surgery, Mayo Clinic, 200 1st St SW, Rochester, MN 55905, United States (e-mail: carlson.matthew@mayo.edu).

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Abstract

Objectives To describe transnasal Eustachian tube (ET) occlusion with a liquid embolic solution for lateral skull base cerebrospinal fluid (CSF) leaks.

Design A lateral skull base CSF fistula model was developed by the authors using fresh cadaveric heads. Using a transtympanic needle, regulated pressurized pigmented saline was continuously instilled into the middle ear space and visualized endoscopically in the nasopharynx. An angioembolization catheter was then placed through the cartilaginous ET orifice just medial to the bony ET. Under endoscopic and fluoroscopic guidance, a column of liquid embolic agent was deployed into the bony ET segment up to the middle ear space.

Setting Tertiary care academic center.

Participants Cadaveric specimens.

Main Outcome Measures Cessation of CSF flow after occlusion at supraphysiologic pressures.

Results In two cadavers, a CSF fistula model was developed and endoscopic visualization of irrigant flow into the nasopharynx was confirmed. Fluoroscopy provided adequate anatomic views of the ET and middle ear, in addition to dynamic views of embolization. Cessation of flow after occlusion was successfully achieved with pressures up to 25 mm Hg, which exceeds normal physiological intracranial pressure.

Conclusion Eustachian tube occlusion with a liquid embolic solution is feasible in a novel cadaveric CSF leak model. In the future, this relatively short, straightforward procedure may become an outpatient alternative to manage intermittent or low-flow CSF fistulae following lateral skull base surgery.

Keywords

- cerebrospinal fluid leak
- vestibular schwannoma
- onyx
- fluoroscopy
- lateral skull base surgery

Introduction

Microsurgical resection remains the most common treatment for vestibular schwannoma (VS) in the United States and carries a relatively low incidence of neurologic complications when performed by an experienced team.¹ By definition, all surgical approaches to the internal auditory canal and cerebellopontine

angle create a potential conduit between the subarachnoid space and air cells within the temporal bone, thereby exposing the patient to the risk of cerebrospinal fluid (CSF) fistula. In a review of over 5,000 cases of retrosigmoid (RS) and translabyrinthine (TL) craniotomy for VS, the rate of CSF leak was roughly 10% regardless of approach.² The avenue for CSF fistula formation varies depending upon patient factors and intraoperative

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findings. While the dura can usually be primarily closed in RS craniotomy, meatal drilling often results in opening of perilyabyrinthine air cells that are most commonly managed with bone wax. In the TL approach, the dura of the posterior fossa can rarely be closed in a watertight manner and thus free abdominal fat is used to obliterate the pathway from the posterior fossa to the middle ear space.

Postoperative CSF leak following lateral skull base surgery rarely resolves spontaneously or with conservative measures. In most cases, patients are treated either with admission and multiple days of CSF diversion via lumbar drain and/or reoperation with blind-sac closure of the ear canal and obliteration of the middle ear space. Without timely recognition and intervention, CSF leaks can expose patients to significant postoperative morbidity. The risk of developing postoperative meningitis is roughly 10 times higher in patients with a CSF fistula. This devastating complication results in an extended hospital stay, the need for monitoring in an intensive care setting, parenteral antibiotics, and the attendant risks and costs associated with each.³ Though less common, tension pneumocephalus secondary to a conduit between the middle ear or Eustachian tube (ET) and intracranial space can result in brain herniation and severe neurologic morbidity.⁴

In most cases of CSF fistula with an intact tympanic membrane, the ET serves as the final common pathway for CSF drainage into the nasopharynx and exposure to bacteria. Apart from middle ear obliteration using autologous tissue during TL craniotomy, few attempts have been made to surgically occlude the ET from the middle ear or transnasally with permanent materials. In spite of the development of advanced endoscopic equipment for rhinologic and anterior skull base surgery, the nasopharynx remains a relatively challenging anatomic location to instrument. Furthermore, a model whereby lateral skull base CSF rhinorrhea can be studied has yet to be developed. In this report, the authors describe the development and use of a cadaveric CSF fistula model to demonstrate successful treatment of low-flow CSF leaks using an established liquid embolic agent (Onyx 18 LES, Medtronic; Minneapolis, MN, United States).

Methods

Lateral Skull Base CSF Fistula Model

Two fresh, lightly embalmed human cadaveric heads were procured using internal departmental funding in accordance with institutional policies. Preservation was achieved with 7% formaldehyde-37, 55% reagent alcohol, 10% phenol, 25% glycol, and 3% water, diluted to 50% strength and injected until the desired level of light preservation was achieved. Rigid and angled sinus endoscopes were utilized to visualize the nasopharynx and confirm the presence of normal anatomy of the torus tubarius (►Fig. 1). A 22-gauge spinal needle was placed transcanal through the tympanic membrane and connected to a pressure infusion bag containing normal saline with blue food coloring. The external auditory canal was packed with occlusive putty to prevent retrograde fluid flow (►Fig. 2). The pressure bag was fitted with a blood pressure cuff to apply and measure fluid pressure in mm Hg.

Fig. 1 Normal appearance of left torus tubarius and ET orifice with a 0-degree rigid endoscope. ET, eustachian tube.

Fig. 2 Pressure infusion bag with colored saline (panel A) and transtympanic needle with external auditory canal packing (panel B).

Once pressurized, fluid flow into the nasopharynx was confirmed endoscopically (see ►Video 1).

Video 1

Endoscopic visualization of fluid flow from Eustachian tube orifice in nasopharynx. Online content including video sequences viewable at: www.thieme-connect.com/products/ejournals/html/10.1055/s-0038-1625975.

Fluoroscopy

To visualize the location of planned ET embolization, a conventional C-arm was utilized for fluoroscopic visualization of the ET. Landmarks were marked with the tip of the transtympanic needle against the cochlear promontory and the tip of the endoscope at the torus tubarius. Two-dimensional oblique X-rays were obtained to visualize both structures. An angioplasty wire was passed transnasally into the middle ear space to confirm that no bony or cartilaginous stenoses were present along the ET.

Preparation of Onyx Liquid Embolic Solution

A sample of Onyx nonadhesive LES was obtained and prepared according to the manufacturer's instructions with the assistance of a representative from the manufacturer. The agent (comprised of ethylene vinyl alcohol copolymer, totaling 1.5 mL volume) is dissolved in an equal volume of dimethyl sulfoxide (DMSO) and agitated until suspended. The agent is then loaded in DMSO-compatible syringes. While liquid when prepared, Onyx becomes solid upon contact with blood or saline.

Embolization Technique

The DMSO-compatible delivery catheter is passed over the wire transnasally using endoscopic and fluoroscopic guidance (►Fig. 3). Once positioned within the bony ET, the wire

is withdrawn and fluoroscopy is changed from conventional single-shot fluoroscopy to digital subtraction angiography (DSA) mode. Under combined endoscopic and fluoroscopic visualization, the material is injected first by forming a "plug" around the injection catheter tip and subsequently by filling the target lumen (i.e., bony ET) distally. Injection is stopped immediately after material is visualized fluoroscopically in the middle ear cleft. The catheter is slowly withdrawn from the nasopharynx, leaving the endoscope in place. Any reflux of Onyx is suctioned out of the nasopharynx with conventional sinus suction, and if required, material can be retrieved from the ET with endoscopic forceps or curved suction.

CSF Fistula Testing

Prior to injection of Onyx, the pressure of saline in the infusion bag is kept at 20 to 25 mm Hg to simulate supra-physiologic CSF pressure as may be present in patients with meningitis or benign intracranial hypertension. This, however, represents a surrogate for intracranial pressure as fluid is being directly instilled in the middle ear space and not transmitted from the larger subarachnoid space. While viewing the torus tubarius endoscopically, the pressure is gradually increased until CSF flow is visualized.

Results

Lateral Skull Base CSF Fistula Model Testing

Two cadaveric heads were examined and used for CSF fistula model development and occlusion testing. One side in one cadaver exhibited ET narrowing that prevented successful passage of the angioplasty wire. The remaining three sides (75%) were successfully instrumented, and clear passage of saline in the simulated model was achieved without difficulty.

Embolization with Cessation of CSF Flow

As seen in ►Fig. 3 and ►Video 2, successful occlusion of the proximal bony ET was achieved in the cadaveric CSF models.

Fig. 3 Standard projection fluoroscopic visualization (panel A) of transtympanic needle (white arrow), tip of endoscope in nasopharynx (white arrowhead), and wire in ET (asterisks). Digital subtraction angiography (panel B) demonstrating Onyx within bony ET and middle ear space (large white arrow). ET, eustachian tube.

Maximum CSF pressure achieved prior to breakthrough of CSF flow was 25 mm Hg. In spite of higher pressures, the Onyx material did not migrate within the ET nor did it expel from the ET into the nasopharynx. In one model, the mastoid was exenterated to visualize the middle ear space, and Onyx material was visualized within the middle ear cleft with minimal filling of the mastoid antrum (►Fig. 4).

Video 2

Fluoroscopic visualization of Onyx within proximal Eustachian tube. Online content including video sequences viewable at: www.thieme-connect.com/products/ejournals/html/10.1055/s-0038-1625975.

Discussion

In this report assessing feasibility, the authors demonstrate the successful development of a cadaveric CSF fistula model and transnasal occlusion of the ET for a simulated lateral skull base CSF fistula. Successful cessation of flow was achieved with simulated CSF pressures of up to 25 mm Hg. While further in vitro testing is required prior to clinical implementation, the authors foresee the potential use of Onyx administered transnasally for the treatment of CSF fistula following lateral skull base surgery.

Interventions for lateral skull base CSF fistulae aim at stopping the flow of CSF into spaces colonized with bacteria such as the nasopharynx. The goal of each is to minimize patient morbidity, avoid extended hospitalization, and mitigate the risk of meningitis, pneumocephalus, or other intracranial complications. To date, the most definitive strategy for repairing CSF leak following lateral skull base surgery involves middle ear obliteration and blind-sac closure of the

external auditory canal. Under general anesthesia, a postauricular incision is either reopened or a new incision is made and the middle ear space and mastoidectomy cavity are entered. The skin of the external auditory canal, tympanic membrane, malleus, and incus is removed, and the middle ear is packed with muscle, fascia, fat, and/or synthetic materials such as bone wax or hemostatic matrices such as oxidized cellulose. Removal of residual mucosa within the middle ear is thought to improve the likelihood of adipose graft obliteration.⁵ The lateral portion of the external auditory canal skin is everted and closed in a blind sac. At present, the authors utilize this technique for the treatment of CSF fistula following TL craniotomy either primarily or in cases where trial lumbar drainage failed.

Following RS craniotomy with hearing preservation, more conservative approaches are often selected to avoid placing residual hearing at risk. Lumbar subarachnoid drainage is commonly used in this situation. Typically, patients undergo drainage for 3 to 5 days, requiring inpatient hospitalization, prophylactic parenteral antibiotics, and limited activity. A recent review estimates success of lumbar drainage alone in postoperative CSF fistula following RS craniotomy to be only 50%.⁶

Several reports of successful transnasal closure of the ET for lateral skull base CSF fistula exist. Kwartler et al described a case of endoscopic closure utilizing incision and eversion of torus tubarius mucosa with cauterization to induce scarring at the ET orifice.⁷ Orlandi and Shelton reported three cases of CSF otorrhorrhea where closure without packing of the ET orifice successfully aborted the CSF fistula.⁸ More recently, Lemonnier et al reported 6 of 7 patients undergoing successful endoscopic closure of the ET orifice over a 17-year period.⁹

The method described in this report offers several advantages over presently available techniques. In contrast to EAC overclosure, reopening of a preexisting craniotomy incision is not required, nor is the permanent creation of a blind-ended external auditory canal. In a temporal bone histology study, Saim et al demonstrated that peritubal pneumatization was present in 78 of 120 (65%) specimens, and described a case of persistent CSF leak from air cells anterior to the tympanic orifice of the ET. Furthermore, 13 of the temporal bones with peritubal cells had a communication with the ET greater than 5 mm from the protympanic orifice.¹⁰ The method described in this study has the potential advantage of effectively occluding the ET in a situation where open peritubal air cells may be responsible for a persistent CSF fistula.

In addition, the currently proposed method overcomes many of the challenges encountered with complex instrumentation of the nasopharynx described in other reports. In our experience, eversion of torus tubarius mucosa, placement of absorbable materials, and suturing or stapling of the torus endoscopically are often frustrating procedures with presently available instrumentation and lack published data to support the use of one technique over another. Furthermore, such techniques may require extended access or several days of posterior nasal packing.⁷ With minimal

Fig. 4 Mastoidectomy with visualization of Onyx within middle ear space. Malleus head (black arrow) and lateral semicircular canal (black arrowhead) are visible for orientation.

repetition, transnasal fluoroscopic-assisted occlusion of the ET with a liquid embolic solution was performed quickly and could potentially be accomplished with topical anesthesia alone or a short general anesthetic in an interventional radiology suite. As an analog of this procedure, Cavallo et al performed nine fibrin glue injections in awake patients under endoscopic guidance to seal sphenoid sinus CSF leaks, avoiding a lumbar drain in four patients.¹¹ While not specifically examined in this study, the theoretical risk of carotid artery injury from ET instrumentation is low, given that Onyx and the delivery catheter are pliable and do not appear to exert pressure sufficient to deform the walls of the ET. Furthermore, the material can be readily suctioned out should concern for over injection be present.

While this work primarily represents a “proof of concept” study, the safety profile of Onyx deserves further discussion. Elhammady et al describe their experience with 43 patients who underwent Onyx embolization of head, neck, and spinal lesions, including paragangliomas, juvenile nasopharyngeal angiofibromas, and other vascular tumors. The authors reported no neurological complications related to the embolization procedures.¹² Li et al and Natarajan et al documented two instances of microcatheter tip breakage in a total of 78 patients treated for dural arteriovenous fistulae.^{13,14} The United States Food and Drug Administration safety warnings document does discuss the potential for vessel wall compromise, extravasation of the material, and subsequent increased intracranial pressure in animal models. The most direct correlate of this risk is entry of the material into the subarachnoid space through middle or posterior fossa durotomies created during the initial tumor resection. Theoretically, with direct fluoroscopic visualization of the middle ear cleft and the minimum volume of agent used, the risk of intracranial entry of a substantial amount of embolic material should be very low. Frequently, cost of materials utilized in a new surgical technique plays a significant role in its adoption. While a detailed cost analysis is beyond the scope of this publication, we are confident that avoiding a lengthy hospitalization would justify material costs.

Limitations to this study and the proposed method of occlusion warrant mention. As opposed to using a completely formaldehyde-fixed cadaver specimen, we opted to use fresh, lightly embalmed cadaveric heads to maintain tissue qualities similar to living tissue. Therefore, specimens could not be reexamined days or weeks after embolization was performed to assess for leak recurrence. It is possible that usage of even a lightly embalmed cadaveric specimen rather than a fresh, unprepared specimen could affect results, insofar as the ability for fluid to pass around the Onyx material may be greater in the unprepared specimen. However, given that the majority of the material occupies the bony and not cartilaginous ET, the deformability of the space in question is likely similar between fresh and fixed specimens. This may warrant further investigation in future studies. One specimen had a very narrow bony ET that precluded passage of the wire and catheter for Onyx administration. This could be encoun-

tered in vivo and would represent a contraindication to use. In theory, preoperative computed tomography imaging could be utilized to examine the caliber of the ET, in a manner similar to the use of imaging prior to balloon dilation of the ET for ET dysfunction. The CSF leak model created for this study involves direct irrigation of fluid into the middle ear cleft. To facilitate objective analysis of occlusion results, the assumption that the pressure of irrigation represents a surrogate for intracranial pressure was made. In a clinical situation, even an opening pressure via lumbar puncture with an active CSF leak is not truly representative of intracranial pressure. Thus, this limitation may be difficult to overcome experimentally even in an animal model. Therefore, we expect that early in vivo trials would initially involve only low-flow or intermittent leaks. While it has proven biocompatibility in intravascular embolization, Onyx has not been studied in contaminated environments such as the nasopharynx and ET. The potential for and effects of bacterial colonization of the material cannot be determined from this study. While an animal model of a lateral skull base CSF leak may be challenging to develop, testing of the material in vivo will be crucial to determine the risk of subarachnoid space entry and subsequent chemical meningitis, infectious complications, and material migration or displacement into the middle ear or nasopharynx.

Conclusion

Occlusion of the ET is feasible using Onyx LES in a novel cadaveric CSF fistula model. Once the biocompatibility and longevity of the material within the ET is determined, this technique may serve as the basis for a rapid, outpatient treatment of low-flow or intermittent lateral skull base CSF fistula causing otorrhorrhea.

Funding

Internal departmental funding was utilized without commercial sponsorship.

Conflict of Interest

M.L.C. is a consultant for Advanced Bionics Corp., Cochlear Corp., and MED-EL GmbH.

Institutional Review Board Approval

Not applicable (cadaver study).

Off-Label Use

Onyx 18 LES (Medtronic; Minneapolis, MN, United States) is not FDA approved for the indications discussed in this study.

Note

This manuscript was presented in part as a poster at the Combined Otolaryngology Spring Meeting (COSM), American Neurotology Society (ANS), San Diego, CA, 2017. This material has not been previously published in part or whole, and is not currently under consideration for publication elsewhere.

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