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Abstract

Objectives: Local reconstruction of central skull base defects may be inadequate for large defects or reoperative cases; free tissue transfer may be necessary. Inset of the flap and management of the pedicle can be challenging. We report our experience and approach.

Methods: Retrospective review identifying seven patients with central skull base defects who underwent free flap reconstruction from 2016-2020.

Results: Four patients with recurrent nasopharyngeal carcinoma, one with recurrent craniopharyngioma, one with clival-cervical chordoma, and one with meningioma of the middle cranial fossa were analyzed. Six defects were closed with an anterolateral thigh free flap and one with a radial forearm free flap. In two patients, the flap was secured in an onlay fashion to the defect via a Caldwell-Luc transmaxillary approach. In one patient, the flap was passed transorally, and the pedicle was delivered into the neck via Penrose drain. In two patients, a parapharyngeal technique and in two others, a retropharyngeal was used for nasopharyngeal inset with endoscopic assistance. There were no flap failures, with an average follow-up time of 20.1 (range 3.2 - 47.1) months. One patient required flap repositioning on postoperative day three due to midline shift and intracranial contents compression. The transoral inset flap necessitated flap repositioning on postoperative day 13 to improve the nasopharyngeal airway.

Conclusion: Free flap reconstruction of the central skull base is challenging, but transmaxillary, transoral, parapharyngeal, and retropharyngeal approaches can be used with endoscopic assistance to ensure secure inset flap and avoid airway obstruction.

Introduction

The development of the endonasal approach and advancements in endoscopic techniques have expanded the scope and role of skull base surgery.[1] Resection of skull base pathology may result in exposed neurovascular structures, dura, or bone. Without appropriate tissue coverage and protection of these structures, the patient is at risk for potentially life-threatening complications, including osteomyelitis, meningitis, and vascular rupture. Local flaps such as the nasoseptal flap, middle turbinate flap, lateral nasal wall flaps, pericranial or temporoparietal fascia flap are typically first explored and successful in most cases.[2] However, with large defects, often in reoperative situations or in the setting of osteonecrosis, these local reconstruction options may be inadequate or unavailable, and reconstruction using a free flap may be considered.

Based on the reconstructive needs, the goals of free flap reconstruction of the central skull base could include providing support for multi-layered dural closure, coverage of large pharyngeal mucosal defects, protection of an exposed internal carotid artery or other major vessels, separation of the nasopharynx from a cervical operative wound, and providing vascularized tissue to support healing of chronically infected osteonecrosis of the bone. The anterolateral thigh (ALT) flap is a versatile option that can be harvested with large skin paddles and ample tissue bulk, making it an excellent alternative to address the many needs of the skull base reconstructive surgeon.[3] When a thinner flap is desired or when a patient's lower extremity anatomy precludes an ALT, a radial forearm free flap (RFFF), rectus abdominis myocutaneous flap, or latissimus dorsi flap are useful alternatives for skull base reconstruction.[4]

According to the Imola Classification, the central skull base is defined as the midline region between the anterior and middle skull base regions.[5] More specifically, it is the area confined by the lesser wing of the sphenoid anteriorly and the petrous ridge posteriorly.[6] The distance from the central skull base to suitable vessels for microvascular anastomosis is an inherent challenge of this approach. Current literature consists primarily of case reports and proof-of-concept publications regarding the repair of midline skull base defects with free-tissue flaps. We report free tissue transfer results for large central skull base defects, focusing on the vascular pedicle routing approaches applied to complete the reconstruction.

Methods

A retrospective database review was performed to identify patients with a central skull base defect that underwent free flap reconstruction. This study was evaluated and approved by the institutional review board. Free flap patients were identified from 2016-2020, and their electronic medical records were reviewed to characterize their postoperative course. Patients undergoing resection of the central skull base (defined as the region bounded laterally by the internal carotid arteries and including the clivus and nasopharynx) and free flap reconstruction were included in the study. Patients were excluded if the resection did not include the central skull base or a free flap was not utilized for repair.

Results

Seven patients were identified that met inclusion criteria: four patients with recurrent nasopharyngeal carcinoma, one with recurrent craniopharyngioma, one with clival-cervical chordoma, and one with meningioma of the middle cranial fossa [table 1]. All patients had prior radiation therapy to the skull base (range 13-60 Gy), with three receiving chemotherapy. Three

additionally had skull base osteoradionecrosis at the time of surgery. Two patients had ablations performed through an entirely endonasal approach, while the other five patients underwent a combined transcervical and endonasal procedure. Six defects were closed with an ALT flap and one with an RFFF. Various techniques for pedicle routing and flap inset and were utilized. The anastomosis from the pedicle occurred in four patients to the facial artery, two patients the external carotid artery, and in one patient the angular artery.

No flap failures were recorded, with an average follow-up time of 20.1 (range 3.2 - 47.1) months. With the backdrop of three patients having dural defects, all seven patients showed no evidence of cerebrospinal fluid (CSF) leak, meningitis, or tumor recurrence at the reconstruction site. One patient developed slurring of his speech and contralateral weakness on postoperative day three. Imaging revealed midline shift and compression of the cerebral hemisphere secondary to flap bulk and postoperative edema, which was treated with revision and debulking of the flap. Another patient required flap repositioning 13 days after surgery to decrease nasopharyngeal obstruction due to mass effect.

Surgical Technique

Transmaxillary Approach

Two patients underwent an entirely endonasal resection of their nasopharyngeal carcinoma without neck dissection or cervical incision for ablation. A Caldwell-Luc antrostomy was performed, allowing an endoscopic transnasal and transmaxillary approach to complete a right-sided medial maxillectomy for access to the posterior nasopharyngeal and cranial base defect. The resulting nasopharyngeal mucosal defects extended inferiorly to the posterior fossa cranial base and clivus. Laterally, the mucosal defect included the area between the left and

right eustachian tubes. The deeper lateral resection was carried to the medial aspect of the distal petrous carotid artery, where in one case, the bony canal was found to be eroded. Given the exposure for the resection, a transmaxillary approach for inset was selected. The free flap with a skin paddle, tailored to the size and shape defect, was introduced endonasally, and the pedicle was passed through the medial maxillectomy and Caldwell-Luc antrostomy. Pedicle length was adequate to reach the facial artery and vein in the neck for anastomosis, which was completed through a small incision near the mandible. In the one case in which the angular artery was used for anastomosis, a separate 4 cm incision along the melolabial fold was performed for access. The flap was secured superiorly with endonasal sutures and sealed with fibrin glue.

Transoral and Parapharyngeal Approach

A combined endonasal and transcervical approach to the skull base was performed (two patients with nasopharyngeal carcinoma, one patient with chordoma). The transcervical component was deemed necessary in some cases given the lesion's size and lateral extent, desire to control and protect the carotid artery, the need for neck dissection, or exclusively for flap inset and anastomosis. A standard cervical approach to the nasopharynx was employed, entering the parapharyngeal space by dividing the digastric and stylohyoid muscles and protecting the facial vessels for microvascular anastomosis. The hypoglossal nerve was carefully guarded, and the pharynx was identified medial to the great vessels. Blunt dissection was used to follow the lateral pharyngeal wall up to the skull base. Any large branches of the glossopharyngeal nerve were protected, and access to the nasopharynx was achieved inferior to the eustachian tube. Endonasal dissection was carried inferiorly down to the level of the

clival recess and posterior fossa cranial base. When osteoradionecrosis was present, dissection of the nonviable bone was carried to the posterior fossa cranial base dura and inferiorly to the C1 and C2 odontoid process (Figure 1).

Posterior fossa cranial base debridement and resection were communicated with the lateral neck incision through a lateral pharyngotomy. A free flap with a skin paddle tailored to the size and shape of the defect was harvested. The flap could usually be mobilized towards the defect through the cervical incision, with the pedicle extending through the parapharyngeal tunnel towards the preserved facial vessels. However, in one case, due to a long and narrow tunnel that proved challenging to widen due to radiation fibrosis and proximity to the carotid artery, the flap was instead passed transorally and guided superiorly into the defect using endoscopic instrumentation. In this case, a Penrose drain was first passed through the tunnel and out of the patient's mouth. The flap pedicle was placed within the Penrose and passed first from the mouth to the neck so that the vessels could be oriented towards the neck and facial vessels after the flap inset (Figure 2).

In all cases, the flap was inset in an onlay fashion over the nasopharyngeal mucosa. The pedicle passed into the neck through the parapharyngeal tunnel. The flap was inset and secured to pharyngeal mucosa with endonasal sutures and DuraSeal® (Integra LifeSciences, Plainsboro, NJ, USA), and further reinforced with NasoPore® (Stryker, Plymouth, MN, USA). Nasal patency was maintained with a nasal trumpet. The microvascular anastomosis was subsequently performed, and the cervical incision closed in a standard fashion. The transorally placed flap prolapsed into the nasopharyngeal inlet, resulting in partial obstruction of the nasopharyngeal airway and requiring endoscopic repositioning on postoperative day three.

Retropharyngeal Tunnel Approach

In two patients (one with craniopharyngioma and one with meningioma), an endonasal approach to the skull base was utilized. Endoscopic dissection resulted in a nasopharyngeal defect spanning the anterior arch of C1 to the anterior and posterior fossa cranial base. Dissection resulted in the exposure of the internal carotid artery, planum sphenoidale, and tuberculum sella of the anterior cranial base.

A free flap was harvested with a skin paddle size and shape appropriate for the resulting defect. As no cervical access was needed for the ablative portion of the procedure, a cervical incision was necessary. An entry into the retropharyngeal space was made by working medial to the carotid sheath and posterior to the esophagus. Blunt dissection of this space was performed until a Kelly clamp could be visualized in the central skull base defect with the endonasal instrumentation. The flap was then passed within a Penrose drain up through the retropharyngeal tunnel and then secured through the nose. This allowed the flap to sit deep to the remnant mucosa of the nasopharynx in an underlay fashion. The graft was positioned against the central skull base defect and secured using interrupted 2-0 vicryl sutures, NasoPore® packing, and TISSEEL® (Baxter Healthcare Corporation, Westlake Village, CA, USA). Nasopharyngeal patency was maintained with nasal trumpets. The pedicle extended through the retropharyngeal space down the neck and was anastomosed to the facial vessels (Figure 3). While the use of nasal trumpets precluded direct visualization of the flap paddle for monitoring in the immediate postoperative period, the pedicle was monitored with a handheld Doppler at the site of anastomosis.

Discussion

Skull base reconstruction provides a critical barrier between the central nervous system and nasal cavity to prevent life-threatening conditions such as CSF leak, pneumocephalus, and meningitis. In some cases, free tissue transfer is required, and several approaches may be used. Several case reports have shown the use of free tissue transfers for clival defects.[7-10] Larger, more comprehensive studies have studied skull base reconstruction outcomes following tumor resection with free tissue flap usage.[11-15] One retrospective study utilized free vastus lateralis flaps in most surgical treatments of osteoradionecrosis for nasopharyngeal carcinoma.[16] Here, we present four flap inset approaches specifically to the midline skull base: the transmaxillary, transoral, parapharyngeal, and retropharyngeal approaches. Each was employed with success, and each has different advantages and risks.

The Caldwell-Luc approach has been described in the literature as providing greater surgical mobility and access in otherwise challenging sites in the skull base.[17] The transmaxillary method through a Caldwell-Luc is an excellent option for pedicle routing when no cervical incision is required during the ablative procedure or when Caldwell-Luc is already being utilized for endonasal tumor resection.[18] This approach entails a sublabial incision and anterior maxillary antrostomy.[19] A medial maxillectomy usually must be performed, and the bony surfaces that the pedicle will rest on, including the crista ethmoidalis, should be smoothed with a drill. Pedicles routed from the skull base through a Caldwell-Luc can often reach the robust facial vessels but can also be used to target the smaller angular vessels, which are often suitable for anastomosis, provided the size mismatch is not significant.[13] In one study, this approach in sinus procedures reported chronic facial pain and tooth numbness in 46% and 31% of patients, respectively.[20]

The parapharyngeal approach can be considered when a lateral route to the skull base is employed for carotid protection or when a neck dissection is performed. [21] With this approach, the flap is placed onto the skull base defect in an overlay fashion, and the pedicle is routed through a lateral pharyngotomy (which may be part of the ablation) into the parapharyngeal space. The combined approach is ideal in these circumstances as no extra dissection is required other than the lateral pharyngotomy, if not already performed. This approach conserves pedicle length compared to the transmaxillary method, as it provides a direct route to the cervical vessels without having to course through the nasal cavity. It is also a good option when the flap pedicle is short or shorter than expected. This approach's risks are the same as those for neck dissection, including injury to adjacent vascular and neural structures. Particular attention is paid to protecting the hypoglossal nerve and preserving any visible branches of the glossopharyngeal nerve to minimize dysphagia.[22,23]

Delivery of a pedicled flap into the nasopharynx through a prevertebral space corridor with retropharyngeal exposure has been shown in cadavers.[24] The retropharyngeal inlay inset technique requires cervical incision and subsequent dissection, which provides the advantage of allowing the flap to be inset deep to the nasopharyngeal mucosa in an underlay fashion to prevent dehiscence into the nasal cavity.[25] This method avoids a medial maxillectomy and passing of the pedicle through the nasal cavity and the Caldwell-Luc's morbidity risks.[2] Dissection in the retropharyngeal area often does not require additional tissue removal since it is a potential empty space.[26] One potential drawback of this approach is that swelling or obstruction of the flap tunneled through the retropharyngeal space may impact breathing or swallowing. However, neither patient in our series experienced either.

The transorally passed flap required repositioning to improve the nasopharyngeal airway secondary to prolapse. This was likely because the flap was not underlaid deep to the mucosa, which could potentially be avoided by selecting a retropharyngeal or parapharyngeal approach to lay the flap under the mucosa.

Postoperative edema and flap swelling after inset at the skull base are potential, resulting in compression and midline shift. In our case, the tissue may have begun to swell after anastomosis was completed. Being aware of this potential can allow the surgeon to consider and plan accordingly, ensuring that the flap is not excessively thick or redundant. Particular attention should be given to creating the retropharyngeal tunnel and dissection of the superior thyroid artery to avoid superior laryngeal nerve injury.[27]

In all central skull base reconstruction cases, the effects of gravity will pull the flap inferiorly and risk dehiscence from the clival bone. Endonasal suturing provides some support; however, this is often cumbersome, and in the setting of prior radiation, the tissue may be suboptimal to hold stitches to support a large flap. Fibrin glue can help secure the flap, which in our series did not result in any flap compromise or failures. Additionally, placing nasal trumpets or Merocel sponges into the nasal cavity is another option to support the flap. The retropharyngeal approach, in which the flap is secured within the narrow space behind the nasopharyngeal mucosa, prevents inferior flap displacement if a flap larger than the mucosal defect is harvested.

In our case series, the pedicle's anastomosis occurred to the facial artery in four patients, the external carotid artery in two patients, and the angular artery in one patient. In most cases, the pedicle can reach the facial vessels, even with the ALT, which may have a

shorter pedicle. As such, a reconstructive surgeon benefits from being familiar with these different techniques, adapting to various defects and target vessels, and harvesting sites based on a patient's anatomy.[28]

Our findings demonstrate that these transcervical approaches can be completed safely with low risk to anatomic structures and can benefit an inlay graft. The transmaxillary method is useful when the Caldwell-Luc is already competed for the resection and has the advantage of less dissection in the neck and thus a lower potential for dysphagia, first bite syndrome, abscess formation, and other neck sequelae.

Conclusion

Free flap reconstruction of central skull base defects can be achieved through transmaxillary, transoral, parapharyngeal, and retropharyngeal approaches. Each approach can achieve the objectives of skull base reconstruction with excellent long-term outcomes. Familiarity with these different approaches' nuances and selection criteria can help the reconstructive surgeon optimize outcomes for these complex patients.

Figure 1: Intra-operative imaging in patient #7 reveals osteonecrosis of the clivus (white arrow denotes clivus)

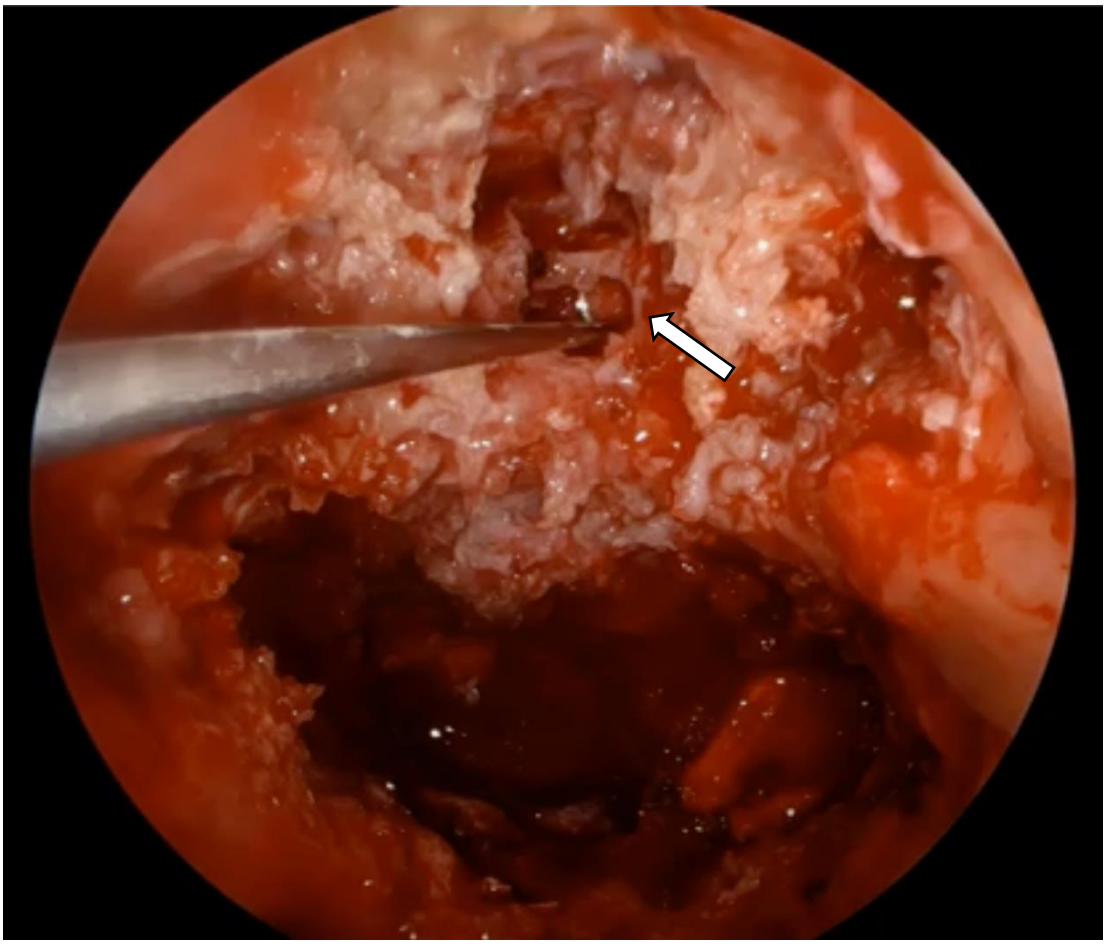

Figure 2: Nasal endoscopy of patient #3 reveals a well-healed ALT flap along the left aspect of the skull base (black arrows denote flap to nasal mucosa junction; white arrow indicates healthy flap)

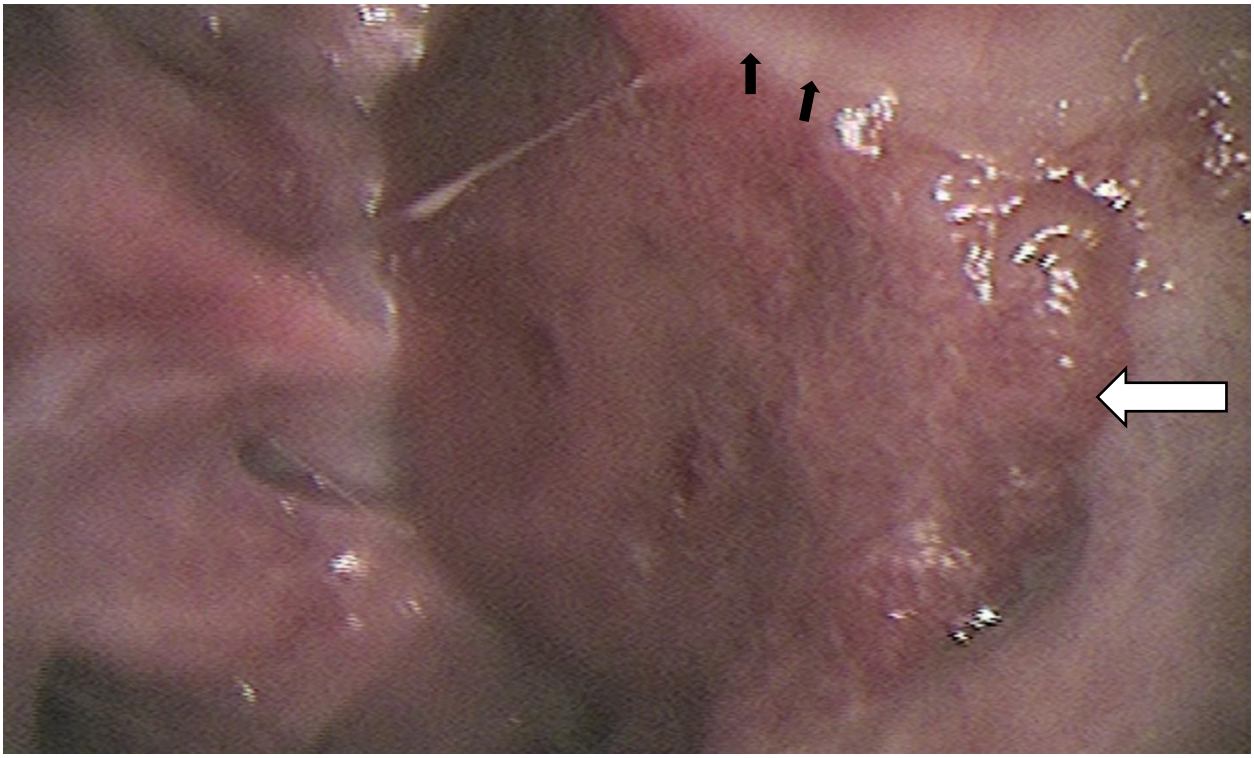

Figure 3: Postoperative MRI with contrast revealing ALT flap secured to the midline skull base in patient #7

Table 1. Case Description

Patient	Case Description
1	A 35-year-old female with a history of nasopharyngeal carcinoma, status-post proton beam, and chemoradiotherapy 15 years prior presented with diffuse skull base osteoradionecrosis and velopharyngeal incompetence (VPI). She received endonasal resection of osteoradionecrosis and infection along the posterior fossa cranial base and posterior nasopharynx. An anterolateral thigh (ALT) free flap was selected for reconstruction. An ipsilateral Caldwell-Luc approach was performed to route the pedicle through the maxillary sinus anteriorly towards the facial vessels. Two years after surgery, she underwent an incision and drainage for a parapharyngeal abscess. At 2.5 years post-surgery, the patient remains free of disease with resolution of her VPI, but with dysphagia complaints.
2	A 61-year-old female with a history of nasopharyngeal carcinoma, treated initially with chemotherapy, suffered from recurrence two years later, and was treated with salvage nasopharyngectomy. After two years, she developed osteonecrosis and osteomyelitis of the skull base with an exposed carotid artery. Her episodes of osteonecrosis were treated with multiple cranial base debridements. Multiple local reconstructions were attempted to prevent carotid blowout, including a temporoparietal fascial flap, which partially dehisced. She then received a radial forearm free flap reconstruction. An ipsilateral Caldwell-Luc approach was performed to allow access to inset the free flap through the maxillary sinus' antrum and route the pedicle anteriorly towards the facial vessels, including the angular

	artery. At four years post-surgery, the patient has no recurrence of symptoms other than some postnasal drainage.
3	A 71-year-old male with a history of nasopharyngeal carcinoma, status post nasopharyngectomy and placement of cesium beads (2.75 years ago), presented with recurrent nasopharyngeal carcinoma. The patient received combined endoscopic and open nasopharyngectomy via a transoral approach. The ablative defect extended from the midline nasopharynx to the lateral aspect of the left infratemporal fossa and from the clivus posteriorly to the foramen lacerum superiorly. An ALT was selected for reconstruction, which was passed transorally up to the nasopharynx, and the pedicle was routed through the lateral exposure towards the facial vessels in the neck. Thirteen days after surgery, he required flap repositioning, tracheostomy, and PEG due to nasopharyngeal obstruction. He developed no further postoperative complications three months after surgery.
4	A 41-year-old female with a history of clival-cervical chordoma status post resection and proton beam radiation ten years ago, followed by episodes of cranial base dehiscence and infection, and chronic cocaine abuse, presented to the emergency room in status epilepticus. Further workup revealed pneumocephalus and cranial base dehiscence. She required removal of her ventriculoperitoneal shunt and debridement in the operating room, which showed an area of necrosis inferior to her previous left-sided temporoparietal fascia flap repair of the clivus and a CSF leak. The defect extended from the sphenoid to the clivus towards the right eustachian tube orifice. She underwent skull base reconstruction with an ALT flap through the parapharyngeal approach. The graft was seated into the cranial base defect, covering the posterior fossa cranial base dura. On her three month follow-up, she

	developed dysphagia, which was treated with a PEG tube but was otherwise free of surgical complications.
5	A 75-year-old male underwent a combined endoscopic endonasal and open resection of nasopharyngeal squamous cell carcinoma with nasal septal flap reconstruction and chemotherapy one year prior. He then developed recurrent tumor in the nasopharynx, extending inferiorly along the internal carotid artery with a positive lymph node in the neck. He underwent a combined open and endoscopic transnasal nasopharyngectomy and neck dissection, with the placement of cesium radiation seeds. Preoperatively a balloon occlusion test was performed, which he passed. An ALT flap was utilized, and the flap was positioned behind the soft palate and guided into the nasopharynx. The pedicle was routed into the neck through a tunneled parapharyngeal approach. At 15 months following surgery, the patient showed no evidence of flap dehiscence, infection, or cancer recurrence.
6	A 40-year-old male with a history of recurrent left medial sphenoid wing meningioma was treated with multiple craniotomies (most recently two years prior), fractionated external beam, and gamma knife. On serial MRI imaging, the residual meningioma of the superior orbit has grown through the cavernous sinus and into the sphenoid sinus and posterior aspect of the nasopharynx. The patient opted for open and endoscopic resection of the lesion of the clivus, inferotemporal fossa, and cavernous sinus, with subsequent skull base reconstruction of the defect. The tumor dissection occurred from the maxillary sinus, intertemporal fossa, and clivus through an endoscopic approach. The initial plan was for anastomosis to the superficial temporal vessels; however, they were inadequate and presented a large size-mismatch. As such, a parotidectomy was performed to secure a larger

	caliber retromandibular vein and external carotid artery for microvascular anastomosis. The flap was inserted over the defect with threading of the pedicle into the neck through a retropharyngeal approach. The patient required fascial flap debulking three days after surgery due to a midline shift seen on imaging. The patient also developed a seroma two months postoperatively, which resolves after drainage. Following a 4-day ICU admission, the patient was terminally extubated 44 months postoperatively due to brain stem compression secondary to meningioma.
7	A 37-year-old male with a longstanding history of craniopharyngioma status post multiple oncological resections and radiation resulting in vision loss. The patient developed an extensive recurrence along the anterior and posterior fossa cranial base down to the level of the C1-C2 and clivus, extending anteriorly in the tuberculum sellae, with encasement of the bilateral internal carotid arteries and anterior cerebral arteries. He received an intradural and extradural resection of recurrent invasive craniopharyngioma through an endoscopic transnasal approach, and skull base reconstruction with an ALT free flap, with pedicle routing to the neck via a retropharyngeal tunneled approach. He had no reported postoperative complications or evidence of disease five months after surgery.

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