Accepted Manuscript online: 2023-12-29 Article published online: 2024-01-29

Multidisciplinary Management of Total Anterior Skull Base Osteoradionecrosis

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J Neurol Surg Rep 2024;85:e11–e16.

Abstract

Cases of delayed osteoradionecrosis (ORN) of the anterior skull base have unique management considerations. A 59-year-old woman with a history of basaloid squamous cell carcinoma of the sinonasal cavity with intracranial extension through the anterior skull base developed delayed radiation sequelae of anterior skull base ORN. She underwent an initial endoscopic resection in 2011 with persistent disease that required an anterior craniofacial resection with left medial maxillectomy in 2012. She had a radiologic gross total resection with microscopic residual disease at the histologic margins prompting adjuvant chemoradiotherapy to target volume doses of 66 to 70 Gy with concurrent cisplatin chemotherapy. She subsequently developed an intracranial abscess in 2021 along the anterior skull base that required a craniotomy and endoscopic debridement. Despite aggressive surgical and medical therapy, she had persistent intracranial infections and evidence of skull base ORN. She ultimately underwent a combined open bifrontal craniotomy and endoscopic resection of the necrotic frontal bone and dura followed by an anterolateral thigh free flap reconstruction with titanium mesh cranioplasty. The patient recovered well from a microvascular free-tissue reconstruction without concern for cerebrospinal fluid leak. Anterior skull base reconstruction with free tissue transfer is a commonly utilized method for oncologic resections. Here, an anterolateral free flap was effectively used to treat an anterior skull base defect secondary to a rare indication of skull base ORN.

Keywords
- skull base
- osteoradionecrosis
- free flap

Introduction

The use of radiotherapy (RT) is common in the multimodal management of head and neck cancers.[1] While having oncologic efficacy, head and neck RT can carry long-term complications including osteoradionecrosis (ORN),[2] a potentially devastating complication that causes pain, diminished quality of life, as well as possible cerebrospinal fluid (CSF) leak, or carotid artery hemorrhage.[2–4]

received
October 24, 2023
accepted after revision
December 18, 2023
accepted manuscript online
December 29, 2023

DOI https://doi.org/10.1055/a-2236-6162.
ISSN 2193-6358.

Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

ORN of the skull base is rare with a reported incidence of 1.04% ORN development in the anterior skull base for nasopharyngeal cancer patients treated with RT.[5] The time of onset of ORN after RT varies with studies reporting latency times between 17 and 116 months.[5–7] The management of ORN requires aggressive multidisciplinary surgical and medical treatment, including debridement, intravenous antibiotics, and hyperbaric oxygen (HBO) therapy.[8,9]

Following debridement of necrotic tissue various reconstructive options can be utilized. While microvascular free flaps are effective in the primary reconstruction of oncologic defects, their use in the treatment of anterior skull base ORN is still less commonly implored.[7,10–15]

Here we describe the use of an anterolateral thigh (ALT) free flap to successfully treat delayed onset ORN following basaloid squamous cell carcinoma of the sinonasal cavity. With eight reported cases in the English medical literature of extensive anterior skull base reconstruction by a microvascular free flap for ORN, we present an important experience herein.[16]

Case Report

A 59-year-old woman with a remote history of treated breast cancer underwent an initial endoscopic resection of basaloid squamous cell carcinoma of the sinonasal cavity 12 years prior to presentation. One year after the initial oncologic resection, she underwent an anterior craniofacial resection with left maxillectomy and skull base reconstruction followed by adjuvant chemoradiotherapy for residual basaloid squamous cell carcinoma with intracranial extension through the anterior skull base. Reconstruction by the neurosurgical serve was performed with a pericranial galeal flap for the anterior skull base repair. She had a radiologic gross total resection with microscopic residual disease at the histologic margins prompting adjuvant chemoradiotherapy to target volume doses of 66 to 70Gy with concurrent cisplatin chemotherapy. She tolerated two out of four intended chemotherapeutic cycles and the full intended radiation treatment course. In the interim period, she had no signs of recurrence on close clinical and radiographic surveillance. At 9 years post-treatment, she developed a complicated sinusitis with a left frontal lobe abscess that required a combined open craniotomy with drainage and endoscopic debridement of the sinonasal cavity and anterior skull base. She was treated with intravenous antibiotics at that time.

Most recently at 11 years post-treatment she presented with headache and left visual disturbances with retroorbital pain, magnetic resonance imaging) was completed showing progressive edema with T2 enhancement involving the left frontal lobe with extension through the cribriform plate into the paranasal sinuses (►**Fig. 1**). Despite aggressive surgical and medical therapy, her symptoms persisted with objective evidence of chronic sinusitis, frontal cerebritis, and skull base ORN.

She then underwent a combined open bifrontal craniotomy with debridement of frontal lobe abscess and cerebritis,

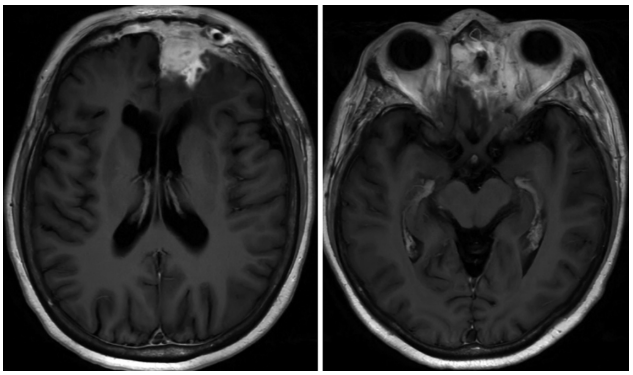

Fig. 1 Axial brain magnetic resonance imaging demonstrating edema with T2 enhancement in the left frontal lobe, and enhancement extension to the paranasal sinuses and through the cribriform plate.

along with endoscopic resection of the anterior skull base ORN with an ALT free flap reconstruction and titanium mesh cranioplasty, as shown in ►**Fig. 2**. An ALT flap appeared to be the best and least morbid option given the patient's status. Phlegmonous changes involving the epidural and dural tissues extending through the frontal sinus, anterior skull base, and left maxillary sinus were debrided until normal dura, sinonasal mucosa, and anterior skull base bone were encountered, as shown in ►**Fig. 3**. Remaining portions of supraorbital ethmoid air cells, the posterior table of the frontal sinus, and intersinus septum were removed with ablation of mucosal remnants to create a marsupialized

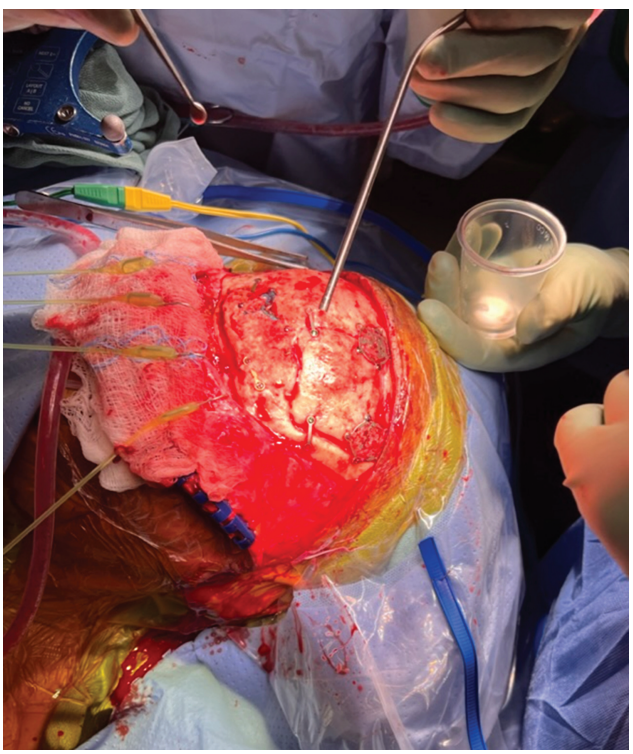

Fig. 2 A bicoronal approach was used to gain access to the frontal sinus and areas of cerebritis involving the frontal lobe. Shown here is the hardware from the previous craniotomy sites after the bicoronal approach was performed.

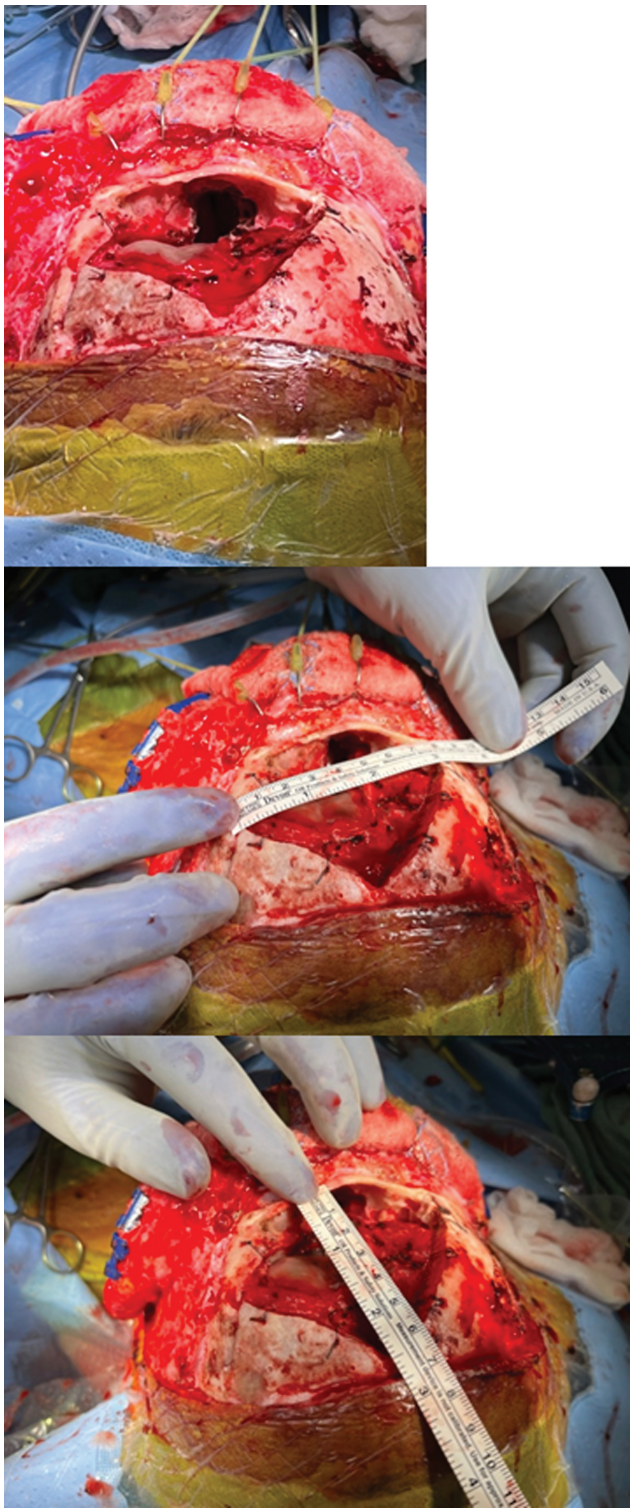

Fig. 3 After the 8 × 6.5 cm frontal and temporal craniotomy, a view of the frontal lobe and cranialization of the frontal sinus is visible with the left frontal area of DuraGen dural repair.

and cranialized frontal sinus. The 5 × 5 cm dural defect was reconstructed with DuraGen inlay (Integra Life Sciences, Plainsboro, New Jersey, United States), and the 5 × 4cm bony anterior skull base defect was repaired by a fasciocutaneous ALT extradural free flap reconstruction (►**Figs. 4** and **5**). A parachute inset was performed between the tensor fascia of the free flap and the dural margin at the posterior cribriform with tacking sutures placed around the margins of the craniotomy to create broad cranial and dural coverage for the vascularized anterior skull base repair. The free flap pedicle was then anastomosed to the recipient left superficial temporal artery and vein (►**Fig. 5**).

The cranioplasty was performed for the coverage of the bifrontal craniectomy defect utilizing a Synthes preformed MatrixNeuro 8 to 10 CM frontal titanium mesh implant (Johnson and Johnson, West Chester, Pennsylvania, United States). The free flap pedicle exited the left side where it was anastomosed to the left superficial temporal artery and vein, as shown in ►**Fig. 6**. The bicoronal incision was then closed with a combination of deep dermal sutures and staples for skin closure. After the bicoronal incision was closed, the anterior skull base reconstruction was examined endoscopically (►**Fig. 7**), revealing a low-flow CSF leak along the cribriform plate that was plugged with Gelfoam (Pfizer, New York, NY, United States) and Adherus dural sealant (Stryker, Chicago, Illinois, United States).

Postoperatively, the patient was monitored in the intensive care unit with a lumbar drain in place and she had an uncomplicated postoperative course. The lumbar drain remained in place for 6 days postoperatively, following a 48-hour clamping trial without signs of CSF leak. Final pathology revealed fibrous tissue with extensive inflammation and necrosis, numerous fungal elements, and osteonecrosis. She received inpatient antimicrobials and had an uncomplicated hospital course without concern for CSF leak or viability of the free flap, as assessed by doppler flow monitoring. She was discharged to home on a long-term course of voriconazole and nafcillin, for positive intraoperative cultures of *Aspergillus fumigatus* and *Staphylococcus hominis*. At 3 months follow-up, she had healed appropriately with no evidence of recurrence or complications (►**Fig. 8**). She remains on long-term antifungal therapy with involvement by infectious disease colleagues for chronic fungal frontal cerebritis.

Discussion

Skull base ORN is associated with significant morbidity, and treatment can be challenging, with patients often failing conservative measures. Here, we expound upon limited previous reports of free tissue transfer as an effective option for delayed ORN in the setting of concurrent active infection.

In our patient, ORN was complicated by a chronic fungal infection, for which she received antifungals and antibiotics. For patients presenting with ORN in its early stages, a trial of medical management can be prudent. When therapies such as antimicrobials or HBO fail, early and aggressive surgical management is essential to mitigate the development of more serious neurological and intracranial complications. In our case, the latency from radiation to ORN was approximately 9 years, which is delayed compared with the average 2 to 4 years length reported in the literature for most head and neck cancers.[17] Our patient's initial complications 9 years post-treatment had been identified and managed as

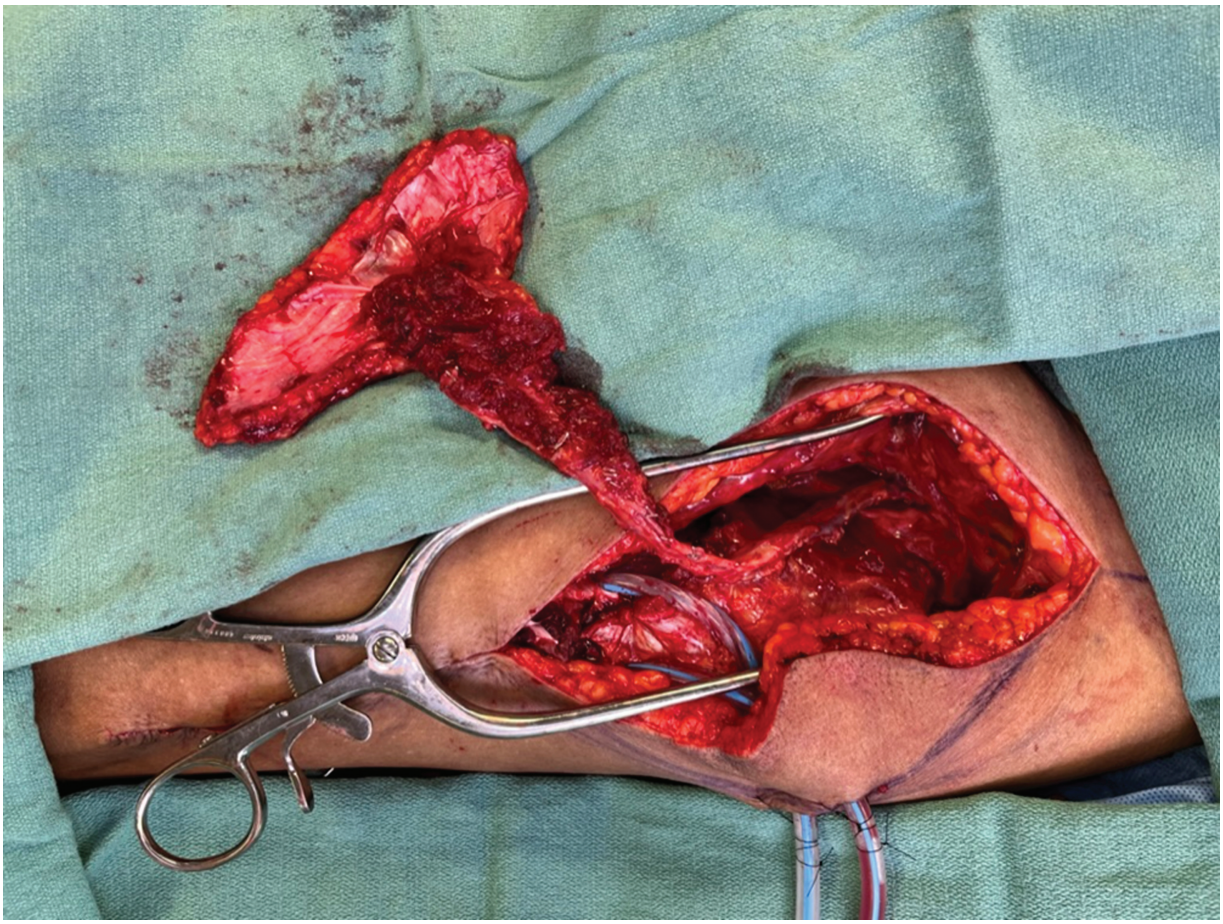

Fig. 4 The anterolateral thigh musculofascial free flap with the lateral circumflex vessels in situ.

sinusitis; however, they were most likely the early stages of developing ORN. At the time of the initial anterior craniofacial resection, there was notably a near-total cranialization of the frontal sinus. However, residual cells in the supraorbital areas may have served as a potential nidus for this delayed infectious presentation. For this reason, a thorough debridement and revision cranialization were undertaken at the time of the debridement and microvascular reconstruction for source control. Imaging findings as shown in ►**Fig. 1**, including enhancement in the frontal lobes and paranasal sinuses, can aid in the recognition of ORN, although clinical worsening and symptoms prompted further evaluation. Early identification and treatment with free flap can avoid prolonged "stop-gap" solutions and address the source pathology by facilitating more complete surgical debridement with this advanced reconstructive option.

Initial surgical treatment strategies for skull base ORN include serial debridement with healing by secondary intention where feasible.[10] Our decision to pursue aggressive debridement and free flap reconstruction was based on the disease extent and the anticipated large-area skull base defect necessary to gain adequate surgical debridement of the extracranial and intracranial extent of necrosis.

The traditional mainstay of surgical therapy for ORN consists of complete debridement, optimally with resection to viable unaffected tissues.[18] Following debridement of necrotic tissue, vascularized reconstructions can aid in healing and preventing additional complications. In reconstructive surgery, the principle of a reconstructive ladder regards microvascular free tissue transfer as the near-final step after other options have been exhausted.[19] In our case, the extent of ORN of the skull base dictated a need for free tissue reconstruction.

For head and neck oncologic reconstructions, free tissue transfer has been associated with improved functional and aesthetic outcomes across various pathologic process and anatomic subsites.[20] Moreover, microvascular free flaps can be particularly suited to ORN given the underlying pathology of compromised blood supply to the region.[21] In cases of ORN for the mandible, free flap reconstruction is considered part of the gold standard after adequate surgical debridment.[17] A gold standard for the management of skull base ORN has not similarly been established, although other groups have also reported successful outcomes for skull base ORN definitively treated with microvascular free flaps.[7,21] Notably, in these reports ample time was provided for the failure of conservative treatment options. However, in a systematic review of central skull base ORN, the success rate following primary medical therapy was approximately 41%, whereas for patients who were treated with primary surgical therapy, treatment success rates were approximately 88%.[22] In light of a successful outcome with our patient, we advocate

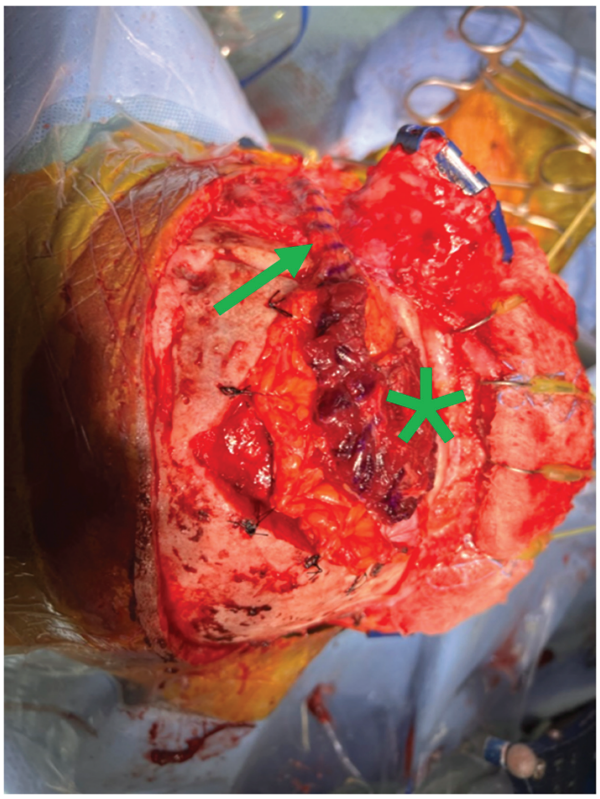

Fig. 5 The anterolateral thigh free flap extradural onlay reconstruction (star), flap pedicle (arrow) by superior external view.

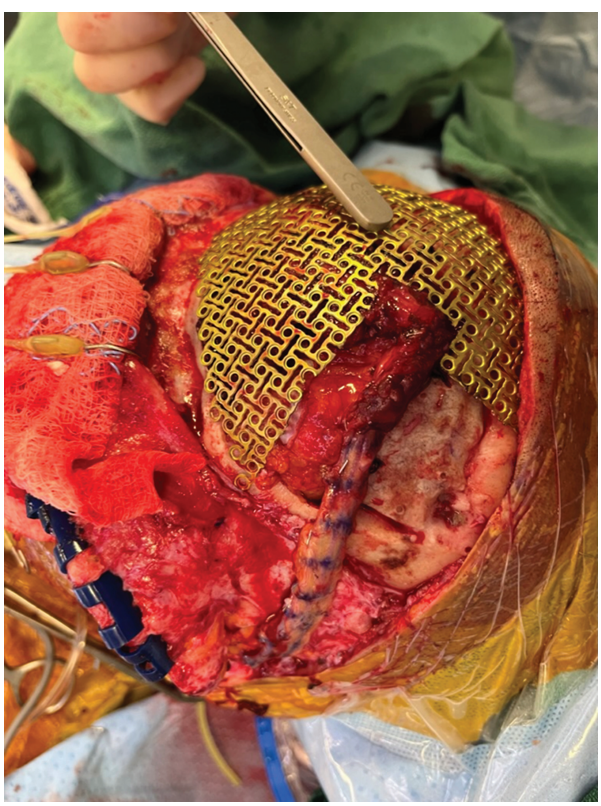

Fig. 6 After placement of the free flap, a titanium mesh cranioplasty was placed over the cranial defect with the free flap pedicle exiting the left side where it was anastomosed to the left superficial temporal artery.

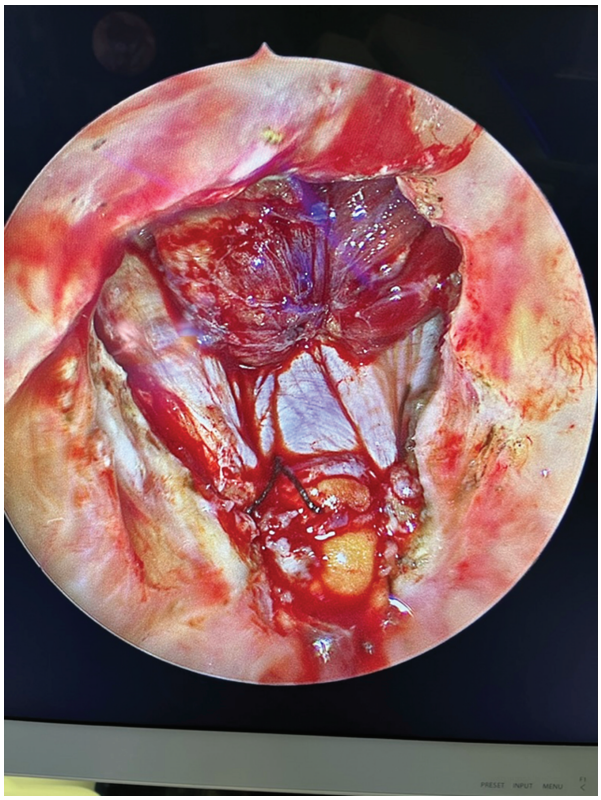

Fig. 7 An endoscopic view of the anterolateral thigh free flap reconstruction along the anterior skull base extending from the anterior table of the frontal sinuses, posteriorly to the cribriform fossa, and laterally to the lamina papyracea bilaterally.

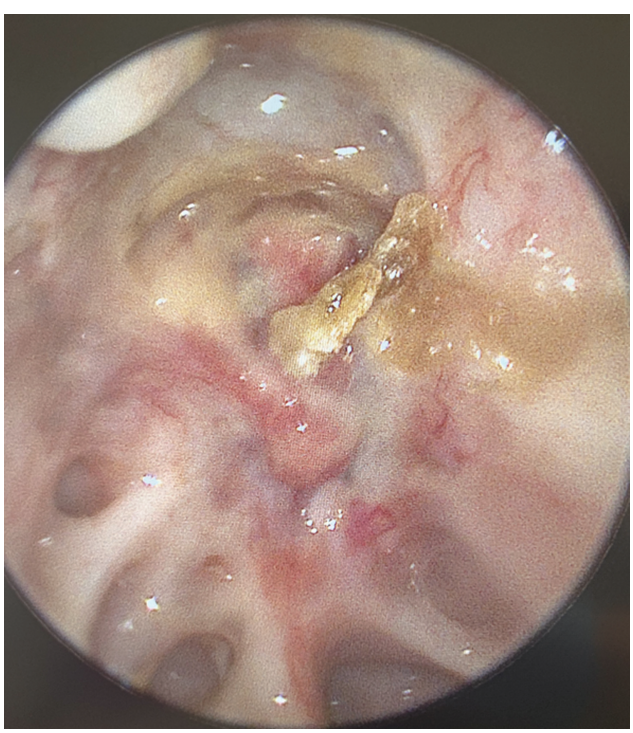

Fig. 8 Three-month postoperation. Well-healing external excision and endoscopic view of well-healing anterolateral thigh free flap repair of skull base defect.

considering vascularized free tissue transfer early in the treatment paradigm for skull base ORN with careful patient selection. The multidisciplinary approach of endoscopic and open skull base surgery alongside free tissue transfer techniques can be taken to manage complex skull base and intracranial cases of ORN as shown herein. At 3 months follow-up, our patient has shown baseline neurologic and functional outcomes while remaining on prolonged medical therapy with antifungal therapy for cerebritis not amenable to further resection.

In conclusion, we affirm this unique treatment modality as a viable option in the reconstruction of skull base defects following ORN, even in cases with numerous complicating factors. As advancements in the primary treatment of head and neck cancers continue resulting in improved patient survival, so too should the management of late-treatment complications. In areas where access can be limited such as the skull base, a multiteam approach such as endoscopic-assisted skull base resection with free tissue transfer reconstruction may offer definitive solutions for ORN in select patients.

Conflict of Interest
None declared.

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