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Nasoseptal Flap Necrosis After Endoscopic Skull Base Surgery in the Setting of COVID-19 Pandemic

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Key words

- Cerebrospinal fluid leak
- COVID-19
- Endoscopic skull base surgery
- Nasoseptal flap necrosis
- Pituitary adenoma
- SARS-CoV-2
- Transsphenoidal

Abbreviations and Acronyms

ACE2: Angiotensin-converting enzyme 2

COVID-19: Coronavirus 2019

CSF: Cerebrospinal fluid

NSF: Nasoseptal flap

SARS-CoV-1: Severe acute respiratory syndrome 1

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2

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INTRODUCTION

Beginning in December 2019, severe cases of pneumonia were reported in Wuhan, China. These cases were linked to a novel coronavirus strain related to severe acute respiratory syndrome and Middle East respiratory syndrome. This novel strain, now known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has since spread globally, resulting in the coronavirus 2019 (COVID-19) pandemic. A declaration of a public health emergency of international concern was further issued by the World Health Organization in March 2020.¹ Over 4 million cases of COVID-19 have been reported worldwide to date.² Clinical observations of COVID-19 indicate a viral syndrome which

■ **BACKGROUND:** A novel viral strain known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has created a worldwide pandemic known as coronavirus 2019 (COVID-19). Early reports from China have highlighted the risks associated with performing endoscopic endonasal skull base surgery in patients with SARS-CoV-2. We present a rare complication of nasoseptal flap (NSF) necrosis associated with COVID-19, further emphasizing the challenges of performing these procedures in this era.

■ **CASE DESCRIPTION:** A 78-year-old man underwent an extended endoscopic endonasal transplanum resection of a pituitary macroadenoma for decompression of the optic chiasm. The resulting skull base defect was repaired using a pedicled NSF. The patient developed meningitis and cerebrospinal fluid (CSF) leak on postoperative day 13, requiring revision repair of the defect. Twelve days later, he developed persistent fever and rhinorrhea. The patient was reexplored endoscopically, and the NSF was noted to be necrotic and devitalized with evident CSF leakage. At that time, the patient tested positive for SARS-CoV-2. Postoperatively, he developed acute respiratory distress syndrome complicated by hypoxic respiratory failure and death.

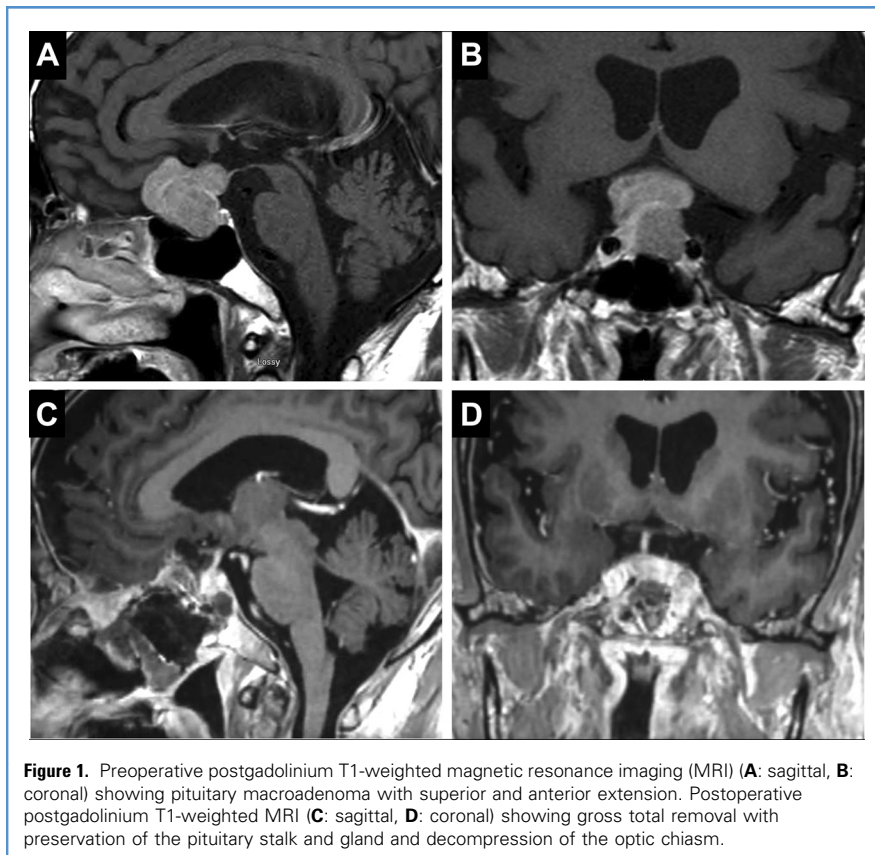
■ **CONCLUSIONS:** To our knowledge, this is the first reported case of NSF necrosis in a patient with COVID-19. We postulate that the thrombotic complications of COVID-19 may have contributed to vascular pedicle thrombosis and NSF necrosis. Although the pathophysiology of SARS-CoV-2 and its effect on the nasal tissues is still being elucidated, this case highlights some challenges of performing endoscopic skull base surgery in the era of COVID-19.

ranges in severity from asymptomatic infection to acute respiratory failure and death. Common clinical manifestations include fever, cough, rhinorrhea, dyspnea, and hypoxia.³

Previous research during the initial severe acute respiratory syndrome epidemic in 2004 identified the functional receptor for severe acute respiratory syndrome 1 (SARS-CoV-1) to be angiotensin-converting enzyme 2 (ACE2) receptor. This receptor is present on pneumocytes and was thought to be the initial site of entry for SARS-CoV-1.^{4,5} SARS-CoV-2 similarly binds ACE2 receptors. However, this binding occurs at a higher affinity than SARS-CoV-1.⁶ A recent study found that ACE2 messenger RNA is expressed in nasal epithelial cells at a level similar to that of type 2 pneumocytes, with high concentrations of SARS-CoV-2 DNA

found on nasal swabs.⁷ This suggests a high level of viral uptake by nasal epithelial cells. As such, nasopharyngeal swab is currently the accepted sampling method for nucleic acid amplification testing to diagnose COVID-19 infection.⁸ The clinical significance of the ACE2 receptor presence in nasal epithelium remains poorly understood, but may have ramifications regarding endonasal surgery.

Early in the COVID-19 pandemic, endoscopic endonasal procedures were identified as significantly high risk. According to an unpublished report of endoscopic endonasal skull base surgery performed in Wuhan, 14 care team members developed symptoms of COVID-19 after endoscopic endonasal transsphenoidal resection in an affected patient.⁹ Moreover, anosmia has been recognized as a significant symptom



of COVID-19 infection.¹⁰ Preliminary reports suggest that ACE2 receptors are present in olfactory support and stem cells. Therefore, the presence of anosmia may be secondary to direct viral involvement of nasal olfactory epithelium.¹¹ At this time, there are no reports in the literature regarding outcomes or complications of patients with COVID-19 undergoing endoscopic endonasal skull base surgery. We present a case of a patient who underwent endoscopic endonasal transsphenoidal resection of a pituitary macroadenoma with postoperative COVID-19 infection and subsequent cerebrospinal fluid (CSF) leak and nasoseptal flap (NSF) necrosis.

CASE REPORT

The patient is a 78-year-old man with a prior history of gastric cancer who initially presented with progressive bitemporal hemianopsia. Magnetic resonance imaging of the pituitary was notable for a sellar/suprasellar mass consistent with a

pituitary macroadenoma with anterior extension over the planum sphenoidale, measuring $3.4 \times 2.9 \times 3.0$ cm. The lesion extended to the suprasellar region, compressing the optic chiasm. The patient underwent endoscopic endonasal resection via an extended transplanum trans-tuberculum approach. A gross total resection was achieved and the skull base defect was repaired with a multilayer closure, using 2 layers of autologous fascia lata graft and a right-sided pedicled NSF. SURGICEL (Ethicon Inc, Somerville, New Jersey, USA) and Gelfoam (Pfizer Inc., New York, New York, USA) were used to further bolster the repair followed by a Meroceal pack, with no residual CSF leak noted. The patient's immediate postoperative course was uncomplicated and lumbar drainage was used for 5 days after surgery. Postoperative magnetic resonance imaging confirmed gross total resection. No CSF leak was clinically observed, and the patient was discharged home on postoperative day 7.

Six days after discharge (postoperative day 13), the patient presented to the emergency room with fever and persistent rhinorrhea. Computed tomography scan was notable for worsening pneumocephalus. Lumbar puncture and CSF studies revealed rare gram-negative coccobacilli and over 1000 white blood cells. The patient was admitted and treated empirically for bacterial meningitis with vancomycin and ceftazidime. The patient was taken immediately to the operating room to inspect and revise the repair. Intraoperatively, CSF leakage was noted underneath a viable NSF along the left lateral aspect of the skull base defect. The defect was reconstructed with fascia lata and adipose tissue, and the original viable NSF was repositioned and replaced over the skull base defect. Postoperative lumbar drainage was used for about 7 days. The patient was persistently febrile for 3 days after the operation, requiring continued treatment with intravenous antibiotics. Repeat CSF cultures were negative and no further CSF leakage was noted. The patient improved clinically and remained afebrile.

On postoperative day 25, the patient developed recurrent fever with hypoxia and rhinorrhea. The patient was once again taken to the operating room to endoscopically explore the skull base for recurrent CSF leak. Prior to surgery, the patient was tested for COVID-19, which was determined to be positive the following day. Intraoperatively, the right-sided NSF was now noted to be necrotic and devitalized. This was excised and a new contralateral left-sided NSF was elevated and placed over the repair site until no further leak was observed. The initial devitalized flap and contralateral NSF are shown in **Figures 1** and **2**. No empyema was found at the surgical site and repeated CSF cultures remained negative. Postoperatively, he was started on azithromycin and hydroxychloroquine for COVID-19. The patient remained febrile with increasing oxygen demand. The patient was persistently agitated and hypotensive. Chest radiography and serial arterial blood gas tests indicated progression of acute respiratory distress syndrome. The patient subsequently died on postoperative day 28 because of acute hypoxic respiratory failure in the setting of COVID-19.

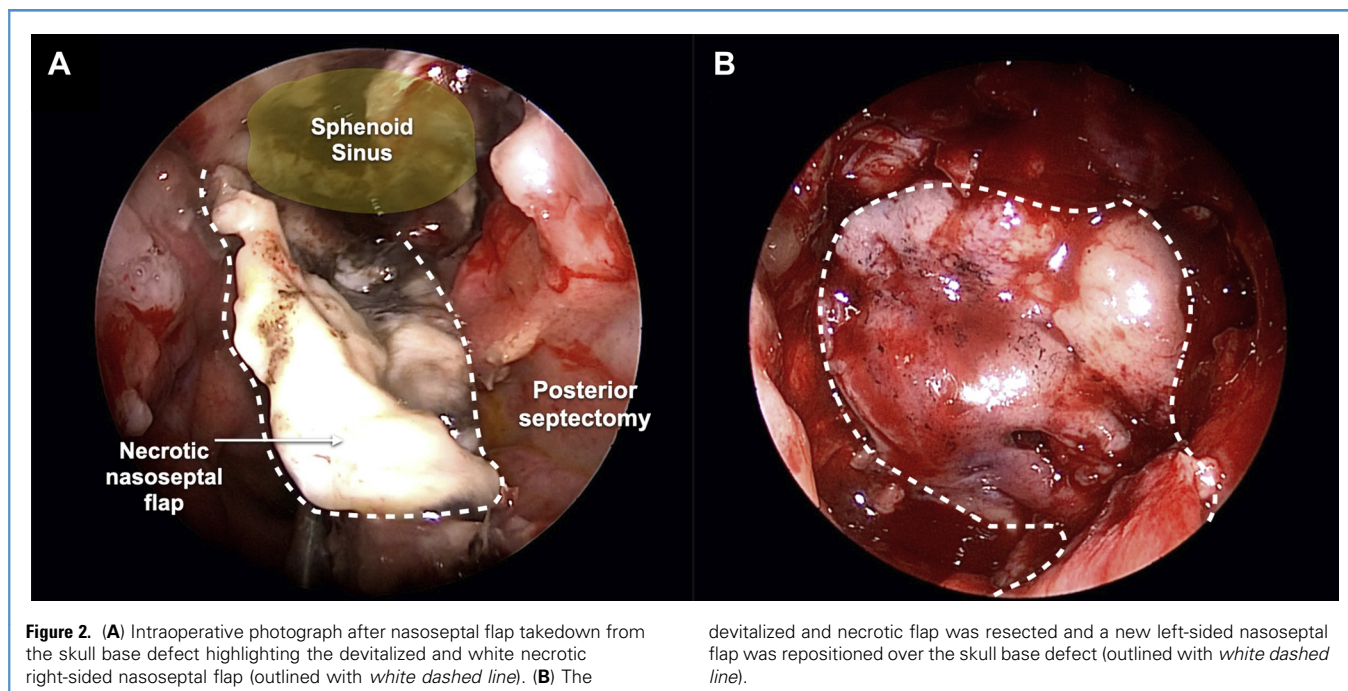


Figure 2. (A) Intraoperative photograph after nasoseptal flap takedown from the skull base defect highlighting the devitalized and white necrotic right-sided nasoseptal flap (outlined with white dashed line). (B) The

devitalized and necrotic flap was resected and a new left-sided nasoseptal flap was repositioned over the skull base defect (outlined with white dashed line).

DISCUSSION

The NSF is considered the workhorse flap for reconstruction of skull base defects after endoscopic endonasal surgery.¹² Because the NSF has become more commonly used, the reported rate of postoperative CSF leaks in large skull base defects has declined from 50% to less than 5%.¹³⁻¹⁷ Complication rates of the NSF are low and include mucocele formation, septal perforation, olfactory loss, and nasal dorsum collapse.¹⁷ Flap necrosis is a particularly rare complication. A single-institution review of 601 NSFs found a necrosis rate of 1.3% on re-exploration.¹² Similar studies found a 0% incidence of NSF necrosis among their patient populations.¹⁸⁻²⁰ The reported cases of NSF necrosis described in the literature have found that patients usually presented with signs of meningitis at least 1 week after endoscopic skull base surgery, and that 50% developed empyema at the surgical site.¹⁷

The patient in this report developed signs and symptoms of meningitis later in his postoperative course, with initial fever onset occurring on postoperative day 11. Re-exploration and CSF leak repair initially took place on postoperative day 13

with the NSF found to be intact and viable at the time. Lumbar puncture was positive for bacterial meningitis, and the patient responded well to antibiotic therapy. He was afebrile with no clinical evidence of a CSF leak for several days before his symptoms recurred on postoperative day 25. It was only on subsequent re-exploration that the NSF was found to be necrotic with persistent CSF leakage. Pertinently, SARS-CoV-2 testing performed on that day was positive. No empyema was found at the surgical site and repeat CSF cultures were negative at that time. Interestingly, the diagnosis of NSF necrosis coincided with the onset of clinical manifestations of COVID-19.

Research efforts to characterize the pathogenesis of SARS-CoV-2 and viral entry into nasal epithelium are ongoing. Preliminary reports indicate the presence of ACE2 in the nasal epithelium, which is the functional receptor for SARS-CoV-2. The clinical significance of this finding remains unclear; however, it has been hypothesized that the presence of ACE2 receptors in nasal epithelium is the underlying reason for the high incidence of anosmia reported in COVID-19 infection.¹¹ Additionally, it has also been previously noted that there are derangements in coagulation profiles of patients with

COVID-19, resulting in hypercoagulation, venous and arterial thrombosis, and thromboembolic disease.²¹⁻²³ Recent studies have reported cases of myocardial infarction, ischemic stroke, and cerebral venous thrombosis.²³⁻²⁵ Giacomelli et al.²⁶ recently described a case of acute thrombosis of an aortic prosthetic graft in a patient with severe COVID-19-related pneumonia resulting in bilateral acute limb ischemia. This may suggest that the NSF necrosis presented here may possibly be caused by a thrombotic event in the vascular pedicle of the NSF; however, the significance and pathophysiology of thrombotic angiopathies are still being elucidated. Until a direct mechanism of damage at the cellular level is uncovered, it is unclear what role SARS-CoV-2 infection played in this patient's NSF necrosis. Nonetheless, the present case highlights that the COVID-19 pandemic may increase the complication rates observed in endonasal endoscopic skull base surgery. This is supported by a recent retrospective review from Wuhan, which examined 34 asymptomatic patients with COVID-19 who underwent surgery during the incubation period. Of these patients, 44% subsequently required intensive care unit admission for respiratory deterioration

with a noted mortality rate of 20.5%.²⁷ For these reasons, along with the increased risk of transmission to providers performing endonasal skull base surgery, we recommend deferring nonessential endoscopic endonasal skull base procedures at this time, especially those that require removal of bone with a high-speed drill. In emergent cases, preoperative SARS-CoV-2 testing is indicated to further stratify patients for surgery and anticipate complications postoperatively.

CONCLUSIONS

To our knowledge, this is the first reported case of pedicled NSF necrosis in a patient who had undergone endoscopic endonasal skull base surgery with concomitant SARS-CoV-2 infection. We postulate that the thrombotic complications of COVID-19 may have contributed to NSF necrosis. However, further research is needed to further elucidate the complex pathophysiology of SARS-CoV-2 and its effect on the nasal epithelium in patients with COVID-19 infection. It is possible that the ongoing COVID-19 pandemic may result in an increased rate of complications in endoscopic endonasal skull base surgery.

CRedit AUTHORSHIP CONTRIBUTION STATEMENT

Guy Talmor: Writing - original draft, Writing - review & editing. **Jordon G. Grube:** Writing - original draft, Writing - review & editing. **Jean Anderson Eloy:** Writing - original draft, Writing - review & editing. **James K. Liu:** Conceptualization, Supervision, Writing - original draft, Writing - review & editing. **Wayne D. Hsueh:** Conceptualization, Supervision, Writing - original draft, Writing - review & editing.

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