Candida Meningitis After Transsphenoidal Surgery: A Single-Institution Case Series and Literature Review

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Candida **meningitis after neurosurgical procedures is a rare but potentially devastating complication. The presentation of meningitis can be insidious in immunosuppressed patients and thus can be easily overlooked. Cerebrospinal fluid studies often resemble bacterial profiles, and cultures can be falsely negative.** ***Candida albicans*** **is the most common species identified in postsurgical** ***Candida*** **meningitis, and delay in diagnosis and treatment can be devastating. The standard induction therapy for** ***Candida*** **meningitis has been amphotericin B combined with flucytosine. A high index of suspicion is needed in any patient with risk factors such as abdominal surgery, bowel perforation, recent broad spectrum antibiotic therapy, intravenous drug use, extremes of age, indwelling catheters, and immunosuppression such as AIDS, malignancy, antineoplastic therapy, and steroid use. Here, we describe 3 case presentations of patients with giant skull base tumors who developed postsurgical** ***Candida*** **meningitis, each with vastly different clinical courses and outcomes, ranging from benign to catastrophic. We performed a literature review with special focus on common risk factors,** ***Candida*** **species, diagnostic criteria, and treatment.**

INTRODUCTION

Candida meningitis after neurosurgical procedures is a rare occurrence.[1-4] Typically, patients with postneurosurgical *Candida* meningitis have a recent history of bacterial meningitis, broad-spectrum antibiotic therapy, and multiple surgeries involving the central nervous system (CNS).[5] *Candida albicans* is the most common species identified in this patient population and is the culprit for most related mortalities.[1,4,5] Symptoms of *Candida* meningitis are often the same as those in patients with acute bacterial meningitis, such as fever, nuchal rigidity, altered mental status, and headache.[6] Furthermore, cerebrospinal fluid (CSF) laboratory studies may be unremarkable without identifiable yeast, making diagnosis difficult and often delayed.[4,7,8]

In a review of an institutional review board–approved pituitary repository of almost 400 patients who had a transnasal approach for resection of pituitary and anterior skull base tumors in the last 5 years at our institution, 3 were found to have developed postsurgical *Candida* meningitis.

Here, we present these 3 *Candida* cases in detail; each patient had multiple common risk factors for *Candida* meningitis but experienced widely different outcomes, ranging from benign to catastrophic. Two of the 3 patients had vascular involvement, which has rarely been reported. One case resulted in bilateral cerebral infarcts and severe neurologic injury, whereas the other resulted in a ruptured mycotic midbasilar aneurysm and death. The third patient's only symptom was transient headache. Three different species of *Candida* were involved in these cases. We also performed and summarized a review of the literature with focus on common risk factors, *Candida* species, diagnostic criteria, and approaches to treatment.

CASE DESCRIPTION 1: DIFFUSE VASOSPASM AND INFARCT

A 40-year-old man presented to clinic with complaint of 1-year of vision changes, including diplopia, worsening visual acuity, and visual obscurations of bouncing lights in the distance. His medical and social history consisted of methamphetamine abuse, alcohol

Key words
- *Candida*
- Meningioma
- Meningitis
- Pituitary adenoma
- Transnasal
- Transsphenoidal
- Skull base surgery
- Vasospasm

Abbreviations and Acronyms
CNS: Central nervous system
CSF: Cerebrospinal fluid
CT: Computed tomography
ICU: Intensive care unit
MRI: Magnetic resonance imaging

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Citation: World Neurosurg. (2017) 108:41-49.
http://dx.doi.org/10.1016/j.wneu.2017.08.115

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

1878-8750/$ - see front matter Published by Elsevier Inc.

abuse, frequent incarceration, multiple traumatic brain injuries, depression, anxiety, and poor dentition. On physical examination, visual fields were reduced in all quadrants. Brain magnetic resonance imaging (MRI) showed a 26 mm × 19 mm enhancing planum sphenoidale mass (Figure 1A and B). His hormonal workup showed central adrenal insufficiency and central hypothyroidism, and he was started preoperatively on hydrocortisone 20 mg daily. He subsequently underwent frameless stereotactic expanded endoscopic transnasal resection of a World Health Organization grade I planum sphenoidale meningioma. The meningioma was accessed via bilateral maxillary antrostomy, bilateral total ethmoidectomy, bilateral sphenoidotomy, left frontal sinusotomy, septoplasty, pedicled mucosal nasoseptal flap harvest, and bilateral middle turbinate resection, performed by the otolaryngologist. Ethmoidectomy is commonly performed at our institution to widen exposure when nasal passages are narrow. Maxillary antrostomy is often performed in conjunction with ethmoidectomy, because it provides an important anatomic landmark for the ethmoidectomy during the dissection, orienting the surgeon to the location of the orbit. Frontal sinusotomy is not commonly performed but was required here because of concern for frontal outflow stenosis to avoid postoperative obstruction. Closure products in this case included Duragen (Integra, Plainsboro, New Jersey, USA), a nasoseptal flap (Surgicel [Ethicon, Somerville, New Jersey, USA]), DuraSeal (Integra, Plainsboro, New Jersey, USA), Nasopore (Stryker, Kalamazoo, Michigan, USA), a piece of AlloDerm (LifeCell, Branchburg, New Jersey, USA), and a 30-mL Foley catheter balloon. Vancomycin was administered intraoperatively because a recent nasal swab was positive for methicillin-resistant *Staphylococcus aureus*, followed by an additional 24 hours of vancomycin for perioperative infection prophylaxis. There were no perioperative complications. Postoperative brain MRI showed no evidence of residual tumor (Figure 1C and D; Tables 1 and 2).

Approximately 4 days postoperatively, the patient began acting impulsively; drinking water from a faucet, picking his nose, removing his peripheral intravenous lines, and refusing interventions. Eight days postoperatively, he developed fever, increasing white blood cell count, and somnolence warranting transfer to our institution's neuroscience intensive care unit (ICU). A lumbar puncture was performed, and the profile was consistent with meningitis, with a significant hypoglycorrhachia. CSF cultures were negative; however, blood cultures were positive for *Fusobacterium necrophorum*. Before this result, the patient was treated empirically with intravenous vancomycin, cefepime, and metronidazole. The infectious disease team determined that *Fusobacterium necrophorum* was the likely cause of meningitis, noting that the pathogen is a strict anaerobe, unlikely to grow on routine CSF cultures. Vancomycin was discontinued, and the patient was

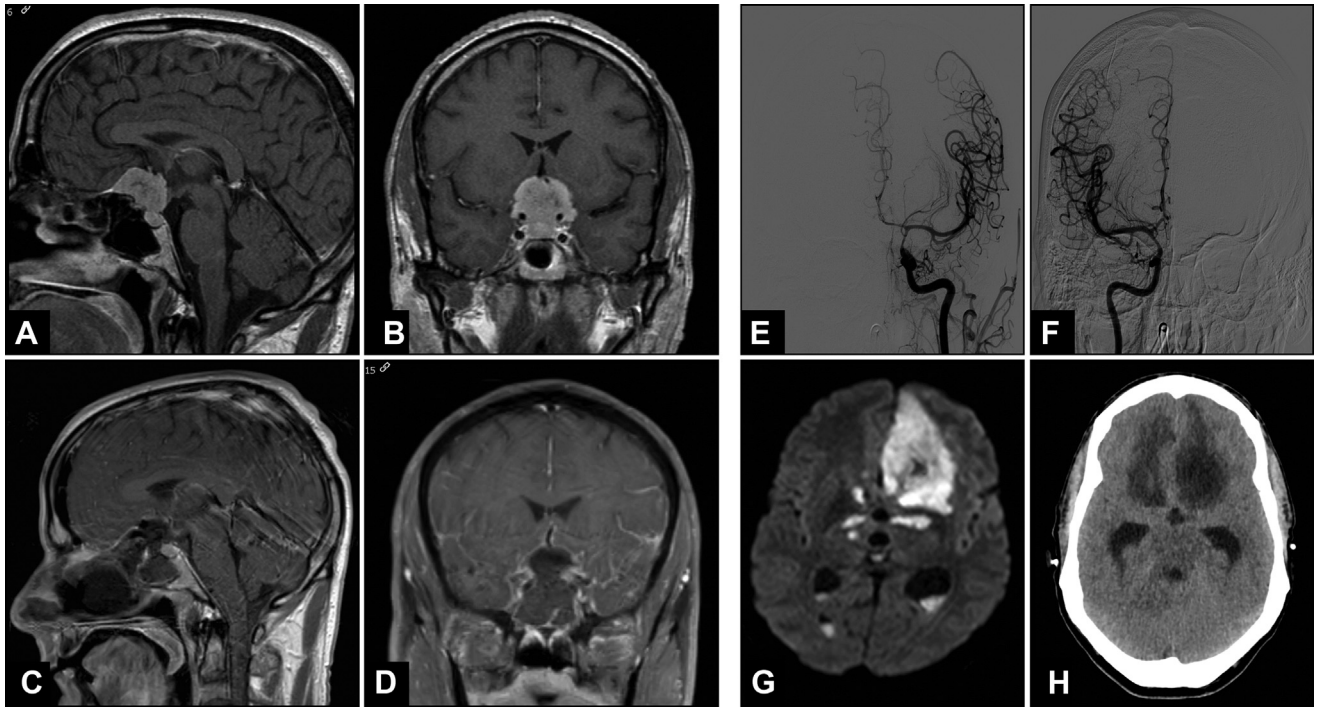

Figure 1. (**A**, **B**) Preoperative magnetic resonance imaging (MRI) with and without gadolinium shows a 26 mm × 19 mm enhancing planum sphenoidale mass. (**C**, **D**) Postoperative MRI with and without gadolinium shows no evidence of residual tumor. (**E**) Cerebral angiogram shows moderate to severe vasospasm involving the left internal carotid artery and A1 segment of the anterior cerebral artery, and occlusion of the left A2 segment. (**F**) Moderate vasospasm is also seen in the right supraclinoid internal carotid artery. (**G**) Thirteen days after surgery, MRI diffusion-weighted imaging shows acute ischemic infarct of bilateral basal ganglia and the left anterior cerebral artery distribution. (**H**) Approximately 1 month after surgery, head CT shows bifrontal infarcts and hydrocephalus.

Table 1. Review of Patient Demographics, Surgical Pathology, Risk Factors, Organisms, Treatment, and Outcomes of *Candida* Meningitis

Age (years)	Medical/Social Comorbidities	Initial Pathology	Postoperative CSF Rhinorrhea	Autologous and Synthetic Materials and Implants Used During Surgical Course	Postresection Glucocorticoids Regimen	Antecedent Bacterial Infection (and Source)	Antibiotic Regimen for Bacterial Infection/Prophylaxis and Yeast
40	Methamphetamine abuse, alcohol abuse, poor dentition, + methicillin-resistant *Staphylococcus aureus* nasal swab preoperatively	Planum sphenoidale World Health Organization I meningioma	No	Nasoseptal flap, Duragen, Surgicel, DuraSeal, Nasopore, AlloDerm, Foley catheter, VPS	Hydrocortisone 20 mg daily	*Fusobacterium necrophorum* (blood)	Vancomycin perioperatively, later cefepime and metronidazole for *F necrophorum*
75	30 pack year tobacco use, chronic obstructive pulmonary disease	Gonadotroph pituitary adenoma	Yes; recurrent	Nasoseptal flap, Duragen, DuraSeal, Avitene, Surgicel, Merocel, fascia lata graft, abdominal fat graft, lumbar drain, pericranial flap, VPS	Hydrocortisone 20 mg twice a daytapered to 20 mg daily	Coagulase-negative *Staphylococcus* (CSF)	Vancomycin, cefepime, metronidazole empirically, then ceftriaxone
55	Cushing disease, history of hepatic pyogenic abscess, acute diverticulitis, portal vein thrombosis, sepsis, poor wound healing	Corticotroph adenoma	Yes; recurrent	Nasoseptal flap, Duragen, DuraSeal, Nasopore, abdominal fat graft, lumbar drain ×2, pericranial flap, VPS	Hydrocortisone 50 mg 4 times a day, slowly weaned to 2 times a day	*Serratia* species (CSF)	Prophylactic cefuroxime and metronidazole perioperatively × 1 month; meropenem then ciprofloxacin for *Serratia*

CSF, cerebrospinal fluid; VPS, ventriculoperitoneal shunt.

treated with cefepime and metronidazole. His neurologic examination continued to decline, and head computed tomography (CT) 10 days after surgery showed new hydrocephalus, requiring placement of a right frontal external ventricular drain (Tables 1 and 2). Thirteen days postoperatively, he developed a focal neurologic decline, no longer moving his right upper extremity and withdrawing only his right lower extremity. An MRI/magnetic resonance venography showed evidence of infection within the surgical cavity, as well as acute ischemic infarct of the left anterior cerebral artery distribution and bilateral basal ganglia (Figure 1G). A cerebral angiogram showed moderate to severe vasospasm involving the left internal carotid artery and A1 segments, and occlusion of the left A2 segment. Moderate vasospasm was also observed in the right supraclinoid

Table 2. Review of Patient Age, Organisms, Treatment, and Outcomes of *Candida* Meningitis

Age (years)	*Candida* Identified in CSF	Systemic *Candida* Identified	Antifungal Treatment	Timing of *Candida* Diagnosis	Sequelae
40	*Candida glabrata*	No	Ambisome, flucytosine	13 days after tumor resection; 5 days after symptoms (when cultures positive for bacteremia); 3 days after external ventricular drain	Vasospasm bilateral internal carotid arteries and left A1 and A2; tracheostomy, percutaneous endoscopic gastrostomy, diplegic in lower extremities
75	*Candida albicans*	No	?	61 days after tumor resection; 53 days after initial CSF leak (when cultures positive for *Staphylococcus meningitis*); 0d from lumbar drain placement, 9 days before VPS	Headache (resolved)
55	*Candida tropicalis*	No	Fluconazole	86 days after tumor debulking; 79 days after initial occult CSF leak; 55 days after *Serratia* meningitis diagnosed; 38 days after VPS	Midbasilar mycotic aneurysm with repeated rupture, brainstem infarct, death

CSF, cerebrospinal fluid; VPS, ventriculoperitoneal shunt.

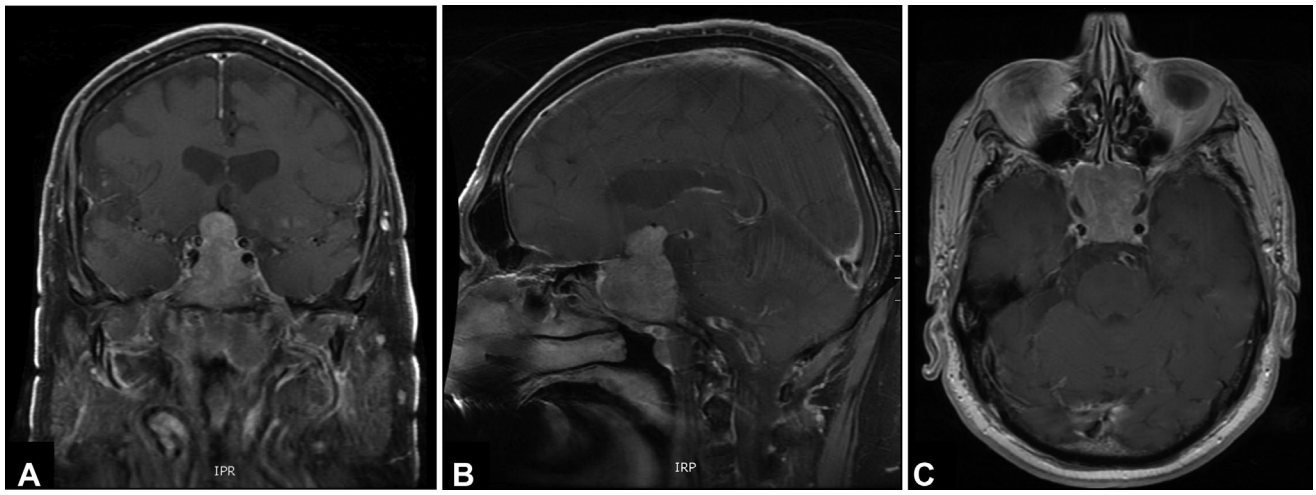

Figure 2. Brain magnetic resonance imaging with and without gadolinium shows a 4-cm homogenously enhancing sellar mass with suprasellar extension compressing the optic apparatus and extending into the cavernous sinus bilaterally.

internal carotid artery (Figure 1E and F). Intra-arterial verapamil infusion resulted in significant improvement.

Endoscopic transnasal exploration and washout were performed emergently, and purulent material was encountered within the sellar surgical site; culture swabs were positive for *Candida glabrata*. Mean arterial pressures were increased to the 100s of mm Hg. The following day, the patient was noted to have left gaze deviation and worsening neurologic examination results, no longer moving his left extremities. Head CT showed a trapped left ventricle, and a left-sided external ventricular drain was placed. Electroencephalography showed focal neuronal dysfunction localized to the left temporal lobe but no epileptiform abnormalities. Subsequent imaging showed a new right inferior frontal infarct (Figure 1H). At this point, the patient was intubated, not opening his eyes, flexing his upper extremities to noxious stimuli, and triple flexing his lower extremities. Placement of an open tracheotomy tube and percutaneous endoscopic gastrostomy were performed. The patient continued to be treated for his infection with metronidazole, cefepime, amphotericin B, and flucytosine (with a prior 8-day course of vancomycin). A permanent CSF diversion and placement of a right frontal ventriculoperitoneal shunt, in addition to an endoscopic-assisted septostomy, were performed 34 days after the initial surgical resection. By 6 weeks postoperatively, the patient slightly improved neurologically and was discharged to long-term acute care. He remained nonverbal and would withdraw his right upper extremity while spontaneously moving his left upper extremity and triple flexing bilateral lower extremities. Five months after surgery, he was alert, saying some simple sentences, and following simple commands using his upper extremities, and contractured and diplegic in his lower extremities.

CASE DESCRIPTION 2: RECURRENT CSF RHINORRHEA

A 75-year-old man presented to clinic with bitemporal hemianopsia noted by his ophthalmologist, who was following him for cataracts. His social history consisted of a 30-pack/year history of smoking (Tables 1 and 2). Brain MRI showed a giant, 4-cm homogenously enhancing sellar mass with suprasellar extension compressing the optic apparatus and extending into the cavernous sinus bilaterally (Figure 2). The patient subsequently underwent a transnasal transsphenoidal resection of a nonsecreting pituitary adenoma. CSF was encountered, and the defect was repaired with a left pedicled nasoseptal flap, Duragen, DuraSeal, Avitene (Bard Davol, Warwick, Rhode Island, USA) wrapped in Surgicel, and Merocel packs (Medtronic, Minneapolis, Minnesota, USA). One week later, the patient presented with CSF rhinorrhea, altered mental status, and fevers, at which time he underwent surgical repair with a right nasal floor free mucosal graft, Duraseal, and Avitene wrapped in Surgicel. CSF cultures were positive for coagulase-negative *Staphylococcus* meningitis, which was treated initially with vancomycin and cefepime, and later with ceftriaxone. Six weeks later, the patient presented with recurrent CSF rhinorrhea and headache, and head CT showed pneumocephalus. He returned to the operating room for endoscopic exploration and repair with a modified gasket seal technique, Duragen, fascia lata graft harvest, fat graft harvest, and attempted lumbar drain. He remained intubated to avoid worsening pneumocephalus, and a lumbar drain was placed 3 days later for persistent CSF rhinorrhea. At this time, CSF cultures were positive for *Candida albicans*, and fluconazole was added to the patient's previous regimen of vancomycin, cefepime, and metronidazole. Ten days later, because of persistent CSF rhinorrhea, the patient underwent a transnasal endoscopic regional middle turbinate rotational flap and placement of a right frontal ventriculoperitoneal shunt. One month later, he presented with pneumocephalus and underwent a bicoronal incision with pericranial flap and an additional middle turbinate flap, with abdominal fat graft. The leak persisted, and 10 days later, the patient underwent another endoscopic repair with more abdominal fat graft as well as a free mucosal graft from the nasal septum. This graft was topped

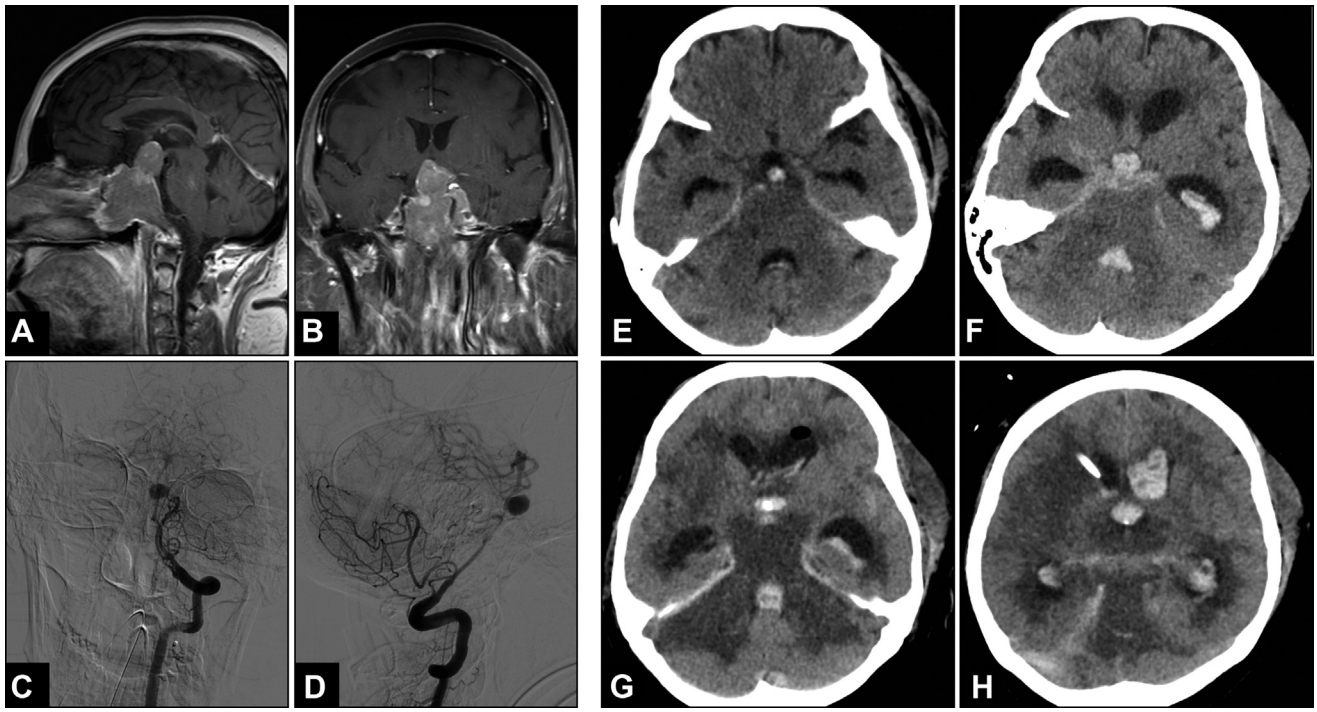

Figure 3. (**A**, **B**) Preoperative magnetic resonance imaging of the brain with and without gadolinium shows a 3.8 cm × 4.6 cm sellar mass extending into the suprasellar cistern with invasion of the cavernous sinus bilaterally and mass effect on the optic chiasm. The mass in addition invades the clivus as well as the sphenoid and left maxillary sinuses. (**C**, **D**) Diagnostic cerebral angiogram shows a wide-necked 7 mm × 8 mm × 9 mm midbasilar artery aneurysm with proximal and distal stenosis. (**E**, **F**) Progressively worsening intraventricular hemorrhage and hydrocephalus. (**G**, **H**) New infarct involving the brainstem and bilateral superior cerebellar hemispheres as well as areas of the bilateral cerebral hemispheres and thalami.

with Tisseel (Baxter International, Deerfield, Illinois, USA), DuraSeal, FloSeal (Baxter International), and a 30-mL Foley catheter, and Surgicel and Avitene were placed around the catheter. The patient had no further rhinorrhea and was doing well at his follow-up 10 months later (Tables 1 and 2).

CASE DESCRIPTION 3: MYCOTIC MIDBASILAR ANEURYSM

A 55-year-old woman presented to clinic with an incidental finding of a giant sellar mass, measuring 3.8 × 4.6 cm, extending into the suprasellar cistern with invasion of the cavernous sinus bilaterally and mass effect on the optic chiasm (Figure 3A and B). The tumor was diagnosed during workup for meningitis in the setting of *Streptococcus anginosus* bacteremia, hepatic pyogenic abscess, hepatic vein thrombosis, and acute diverticulitis requiring partial colectomy. The patient had a history of 2 years of blurred vision, central weight gain of up to 22.6 kg (50 lb), intermittent headaches, and poor wound healing. Hormonal workup confirmed Cushing disease with increased levels of urine free cortisol (up to 10× upper limit of normal). The patient had a history of diabetes mellitus, which progressively worsened before the diagnosis of Cushing disease. Once fully recovered from her gastrointestinal and infectious diseases, she was started preoperatively on etomidate with subsequent decrease in cortisol. She then underwent an expanded endoscopic endonasal transsphenoidal resection with debulking of a corticotroph adenoma. The approach again included left middle turbinate resection, left total ethmoidectomy, bilateral sphenoidotomy, and bilateral pedicled nasoseptal flaps. DuraSeal and Nasopore were applied upon closure. Pathology confirmed corticotroph adenoma with Crooke changes. Perioperatively, the patient was also treated with cefuroxime and metronidazole because of her previous infections. One week postoperatively, there was concern for CSF rhinorrhea, and the patient returned to the operating room for lumbar drain placement, intrathecal injection of fluorescein, and endoscopic endonasal exploration, at which time no active leaking was identified. Cortisol postoperatively was normal (however, with no adrenal insufficiency postoperatively) and was treated with stress-dose glucocorticoids with subsequent taper to physiologic doses, as well as a 1-month course of prophylactic cefuroxime and metronidazole. While still on physiologic replacement of glucocorticoids 1 month after surgery, the patient was readmitted with altered mental status and found to have *Serratia* meningitis, for which she was treated with 3 weeks of meropenem, followed by ciprofloxacin. A CSF leak was apparent on nasal endoscopy and clinically, and she underwent endoscopic repair of a

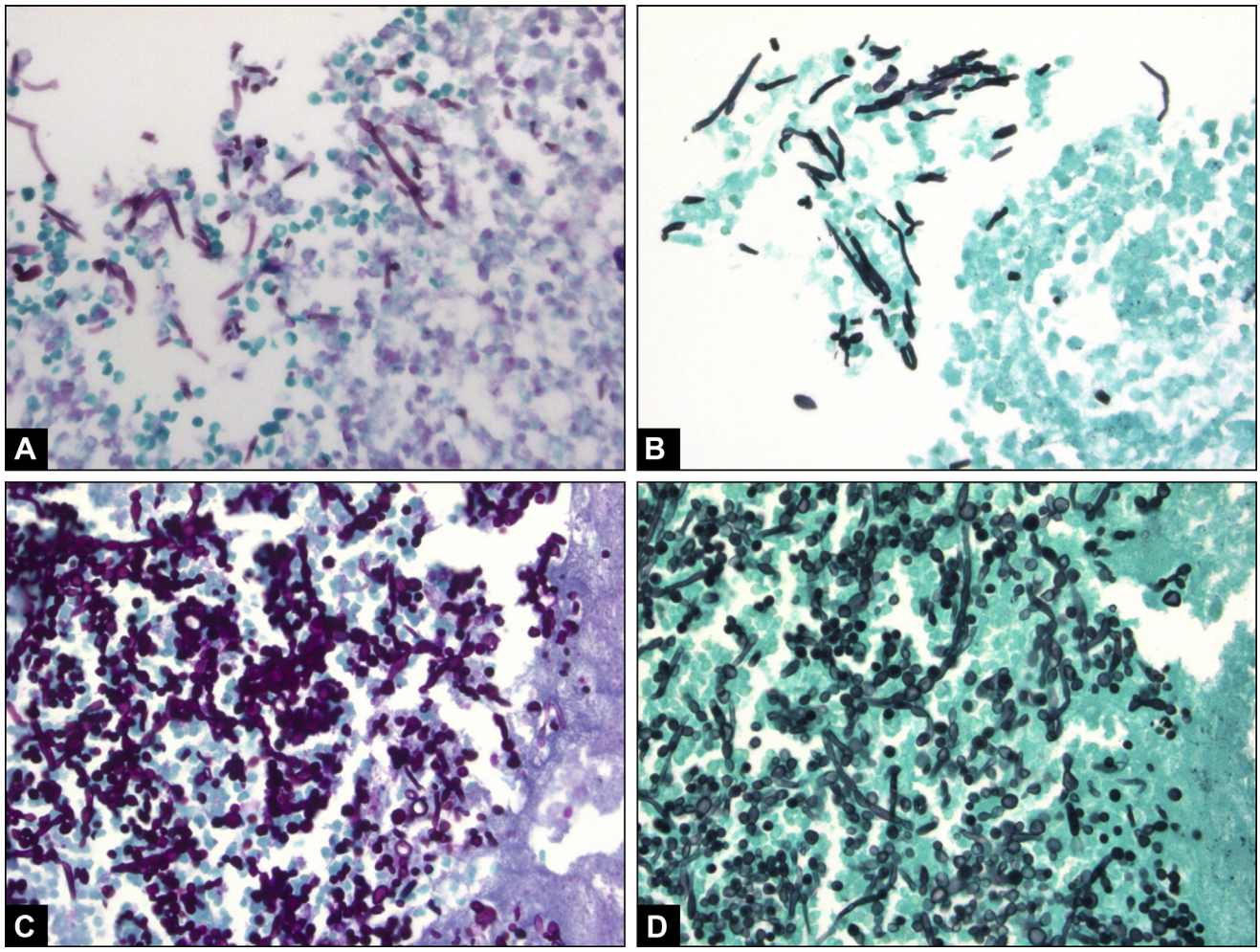

Figure 4. Pathology slides from autopsy showing *Candida* within the basilar artery and the sella. Sections with the fungus were highly necrotic, inflamed, and fragmented, making it difficult to visualize a clear vessel wall. (**A**) Periodic acid-Schiff stain at 400× magnification shows fungal forms consistent with *Candida* involving necrotic tissue and hemorrhage from basilar artery section. (**B**) Gomori methenamine silver stain at 400× magnification shows fungal forms consistent with *Candida* involving fragmented, necrotic tissue from basilar artery section. (**C**) Periodic acid-Schiff stain at 400× magnification exposes fungal forms involving the sellar tissue. (**D**) Gomori methenamine silver stain at 400× magnification shows fungal forms involving the sellar tissue.

CSF leak with Duragen, abdominal fat graft, and a lumbar drain. The nasoseptal flaps remained viable and were repositioned. Twelve days later, a CSF leak became clinically apparent again, and further surgical repair included abdominal fat grafting and fascia lata for both underlay and overlay coverage, followed by repositioning of the 2 nasoseptal flaps. Because of persistent leakage, approximately 2 months after initial surgery, the patient underwent placement of a ventriculoperitoneal shunt for permanent CSF diversion. This treatment proved insufficient to cease her rhinorrhea, and she subsequently underwent harvest of a pedicled pericranial flap via a bicoronal approach, tunneled through a transnasal osteotomy, and endoscopically positioned. The abdominal fat graft harvest sites required debridement for poor healing, and the ventriculoperitoneal shunt failed, requiring revision. Three months after her initial surgery, and 1 month after her pericranial flap, CSF obtained in the setting of fever was positive for *Candida tropicalis*, for which the patient was started on fluconazole; neurologic examination was normal. Two days later, she developed sudden onset severe headache and was found to have intraventricular hemorrhage (Tables 1 and 2). A cerebral angiogram was performed showing a wide-necked 7 mm × 8 mm × 9 mm midbasilar artery aneurysm with proximal and distal stenosis as well as fusiform enlargement of the proximal right anterior inferior cerebellar artery and narrowing of the M1 segments, consistent with infectious vasculitis and mycotic aneurysm (Figure 3C and D).

The interventional neuroradiology team determined that the aneurysm was not amenable to endovascular treatment. The patient continued to decline neurologically, and repeat brain CT

Table 3. Summary Characteristics of *Candida* Meningitis as Previously Published in Other Series

Risk Factors	Clinical Presentation	Mortality (%)	Cerebrospinal Fluid Findings	Rate of Culture Positivity (%)	Induction Therapy
Abdominal surgery Bowel perforation Broad-spectrum antibiotic therapy Intravenous drug use Extremes of age Indwelling catheters Immunosuppression*	Fever Nuchal rigidity Headache Altered mental status	10–33	Pleocytosis, increased protein levels	80†	Amphotericin B and flucytosine

*Includes AIDS, malignancy, antineoplastic therapy, and steroid use.
†A positive cerebrospinal culture should not be considered a contaminant.

showed progressively worsening hemorrhage and hydrocephalus, despite placement of bilateral external ventricular drains (Figure 3E and F). The patient lost brainstem reflexes, and imaging was consistent with infarction involving the brainstem and bilateral superior cerebellar hemispheres as well as areas of the bilateral cerebral hemispheres and thalami (Figure 3G and H). Four months after her initial surgery, and 1 month from her *Candida* diagnosis, she died. An autopsy was performed, during which fungal organisms in the form of yeasts and pseudohyphae were identified within the suprasellar cavity and the basilar artery aneurysm wall (Figure 4). There was no report of bacteria.

DISCUSSION

Candida meningitis after neurosurgical procedures is a rare occurrence. O'Brien et al.[1] reviewed their institutional records for 12 years from 1998 to 2009 and found 11 postsurgical cases in which CSF was positive for *Candida*. Nguyen et al.[2] identified 3 cases in 4 years at their institution, from 1989 to 1993. McClelland et al.[3] reported no cases of *Candida* meningitis in their review of neurosurgical cases over 14 years, from 1991 to 2005; however, only 2111 cases were reviewed. Geers et al.[4] identified 28 patients with CSF meningitis at their institution over 8 years, from 1990 to 1998.

Risk factors for *Candida* meningitis include abdominal surgery, bowel perforation, broad-spectrum antibiotic therapy, intravenous drug use, extremes of age, indwelling catheters, and immunosuppression such as AIDS, malignancy, antineoplastic therapy, and steroid use (Table 3).[2,5,7,9] Typically, patients with postneurosurgical *Candida* meningitis have a recent history of bacterial meningitis, antibiotic therapy, and multiple surgeries involving the CNS.[5] Drainage device infection usually occurs within several months of the surgical procedure and is believed to result from contamination during the procedure rather than postprocedural hematogenous seeding of the device.[2,7,10-12] In O'Brien et al.'s 12-year retrospective study,[1] all infections were associated with foreign intracranial material. All patients had received broad-spectrum antibiotics before the development of *Candida* CSF infection, and 9 were on treatment for antecedent bacterial CSF device-related meningitis. Three patients died (mortality of 27%). The implicated species of *Candida* can vary; however, *C albicans* is the most common species identified in postsurgical *Candida* meningitis (Table 4).[1,4,5] Each of the 3 patients we present here was culture positive for different *Candida* species; *C albicans*, *C glabrata*, and *C tropicalis*. Furthermore, *C albicans* has been the most commonly implicated species in deaths related to *Candida* meningitis,[4] although the 1 death in our series was in a patient infected with *C tropicalis*.

The symptoms of *Candida* meningitis are often the same as in patients with acute bacterial meningitis, such as fever, nuchal rigidity, altered mental status, and headache.[6] Mortality from *Candida* meningitis ranges from 10% to 33%,[2,4,7,13-17] whereas mortality from bacterial meningitis has been reported at 14.8% (Table 3).[17] Rarely does CNS *Candida* present with vascular involvement. In our literature review, which spanned more than 30 years, only 4 cases of *Candida*-related mycotic aneurysms were reported,[18-21] and 4 other cases of proven *Candida*-related vasculitis and ischemia have been reported.[5,22] In our case series of 3 patients, 2 had vascular involvement with *Candida* species, both of whom were immunocompromised.

The presence of CNS *Candida* infection should be suspected in patients with neurologic symptoms who have isolation of *Candida* from the CSF or have pleocytosis on CSF analysis and *Candida* isolated from another naturally sterile site.[8] Lack of adequate

Table 4. Review of the Most Common Species Identified in Postsurgical *Candida* Meningitis

Reference	Review Type	Time Span (years)	*Candida* Species Reported	Isolate (%)
Geers et al.[4]	Retrospective	8	*C albicans*	48
			C parapsilosis	24
			C glabrata	19
			C tropicalis	9
O'Brien et al.[1]	Retrospective	12	*C albicans*	73
			C parapsilosis	18
			C glabrata	Not reported
			C tropicalis	9

response of presumed bacterial or mycobacterial meningitis to appropriate therapy should also raise suspicion for *Candida* involvement.[8] The overall rate of culture positivity is approximately 80%.[8] Furthermore, a positive CSF culture should not be considered a contaminant, particularly in immunocompromised patients, even if other pathogens are identified.[8] Repeated CSF cultures are recommended before *Candida* isolates are considered to be colonizers or contaminants.[4] Laboratory values are not consistently helpful in the diagnosis of *Candida* meningitis. Although increased CSF protein level and pleocytosis are usually present, significant hypoglycorrhachia may not be observed.[4] Some investigators have suggested that 10–15 mL of CSF be tested if suspicious for *Candida*, given the high possibility of a false-negative result.[7]

The standard induction therapy for *Candida* meningitis has been amphotericin B combined with flucytosine.[1,23] Amphotericin B is used because of its fungicidal activity against almost all *Candida* species.[24,25] Flucytosine is added because of its anti-*Candida* activity and excellent penetration into CSF and brain tissue.[25] Fluconazole has excellent CNS penetration and is active against most *Candida* isolates causing CNS infections.[26] However, treatment outcomes have varied with use.[10,11,15,27] Infected ventricular devices should be removed immediately, because *Candida* species are capable of forming biofilms on synthetic materials, rendering them relatively refractory to medical therapy.[1,12,23,28]

In the last 5 years at our institution, almost 400 patients have undergone a transnasal approach for resection of pituitary and anterior skull base tumors. Three of these patients developed postsurgical *Candida* meningitis, each with vastly different outcomes. These 3 patients had risk factors similar to those previously reported in the literature. All had implantable devices, specifically ventriculostomy catheters, as well as antecedent bacterial infections treated with broad-spectrum antibiotics; none had candidemia. Furthermore, these 3 patients had risk factors for immunocompromise including intravenous drug abuse, Cushing disease, and high-dose steroid use. The patient who died also had a history of abdominal surgery for acute diverticulitis and subsequent infection, increasing her risk of *Candida* meningitis. The vasculitis associated with *Candida* meningitis in this case review is a unique feature. In one patient, this vasculitis resulted in bilateral infarcts, whereas in the other patient, it resulted in rupture of a mycotic basilar artery aneurysm and death. In each case, a different species of *Candida* was involved.

At our institution, we have been aggressive about early CSF diversion in the setting of CSF leak, although we acknowledge the risk of shunt infection in this setting. In our experience, shunting patients to expedite resolution of CSF rhinorrhea has had low morbidity and high success rates. Moreover, most of our patients with CSF leaks are found to have derangements in CSF flow dynamics, requiring diversion. However, the implantation of hardware in the setting of CSF rhinorrhea increases risk of infectious seeding, and this must be considered more closely in the future.

At our institution, pediatric neurosurgeons use nystatin swish-and-swallow for *Candida* prophylaxis in children with indwelling catheters who are receiving broad-spectrum antibiotics. This practice has not been used in adult patients, which may suggest a reason for the presence of postsurgical *Candida* meningitis (the incidence has been nil in the pediatric population). Giglio et al.[29] reported that nystatin prophylaxis significantly reduced fungal colonization in surgical/trauma ICU patients. Giuliano et al.[30] reported effectiveness in preventing invasive candidiasis in neuroscience ICU patients with central venous catheters. In the population with burn injury, an 11-year study[31] showed a significant reduction in *Candida* wound infection after implementing nystatin swish-and-swallow. It is possible that a change in practice may decrease the incidence of *Candida* meningitis in the adult neurosurgical population, and further investigation is warranted.

CONCLUSIONS

We report 3 cases with varied presentations and outcomes of *Candida* meningitis after an endoscopic transnasal approach for resection of pituitary and anterior skull base tumors. Two of the 3 patients had vascular involvement, which is relatively rare, resulting in significant neurologic decline, with 1 patient dying. A high index of suspicion is needed in any patient with recent abdominal surgery, broad-spectrum antibiotic therapy, indwelling catheters, or reasons for immunocompromise, including steroid use and malignancy. Laboratory values are not consistently helpful, and empiric treatment should be considered in patients without other identified infectious causes and in patients who lack adequate response to treatment of presumed bacterial meningitis. Nystatin swish-and-swallow may provide successful prophylaxis against *Candida* meningitis in our at-risk population.

ACKNOWLEDGMENTS

The authors thank Shirley McCartney, Ph.D., and Andy Rekito, M.S., for editorial and illustrative assistance, respectively. The authors additionally thank Aaron Halfpenny, D.O., for providing pathology figures.

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Conflict of interest statement: The authors declare that the article content was composed in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Received 11 April 2017; accepted 17 August 2017

Citation: World Neurosurg. (2017) 108:41-49.
http://dx.doi.org/10.1016/j.wneu.2017.08.115

Journal homepage: ***www.WORLDNEUROSURGERY.org***

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1878-8750/$ - see front matter Published by Elsevier Inc.