Management of Central Skull Base Osteomyelitis

Kurren Gill, BA[1] ; Mindy Rabinowitz, MD[1] ; Jared Goldfarb, MD[1]; Christopher Farrell, MD[2] ; James Evans, MD[2] ; Marc Rosen, MD[1]; Gurston Nyquist, MD[1]

[1] Thomas Jefferson University, Dept. of Otolaryngology-Head and Neck Surgery, Philadelphia, PA

[2] Thomas Jefferson University, Dept. of Neurosurgery, Philadelphia, PA

ABSTRACT

Background: Skull base osteomyelitis (SBO) is an uncommon infectious condition usually affecting the temporal bone as a complication of malignant otitis externa (MOE) in elderly, immunocompromised, diabetic patients. Central SBO is a rare variant of this disease, localizing to the clivus, sphenoid, and occipital bone, and presents diagnostic and therapeutic challenges to physicians.

Methods: Retrospective chart review of patients with central SBO who underwent endoscopic, endonasal surgery for the debridement of SBO at a our academic institution and a Korean academic institution from 2008 to 2015.

Results: We identified 18 patients with central SBO: 12 from our institution and 6 from our Korean colleagues. Mean age was 63 years. Follow-up data was obtained for 10 of 18 patients and mean follow-up was 28.8 months. The were 14 males and 4 females. Eleven were diabetics. Four patients from our institution were immunocompromised (myelodysplastic syndrome, history of liver transplant, polymyalgia rheumatica, HIV). Nine patients were culture positive for *Pseudomonas aeruginosa*, 8 for *Staphylococcus,* and 4 for *Aspergillus*, with several patients positive for more than one species. All patients were treated with IV antibiotics except for one patient who received oral voriconazole and one who received no antibiotics. Six patients required repeat procedures (ten total), and these patients were culture positive for either aspergillus or pseudomonas.

Conclusion: Central SBO is an uncommon yet aggressive variant of SBO that requires prompt diagnosis and treatment to prevent neurologic sequelae and spread of disease. A high percentage may be due to *Staphylococcus spp.*, but other recognized pathogens include pseudomonas and aspergillus. IV antibiotics with serial MRIs should be employed after surgery with biopsies, and long-term follow-up is essential. Our findings indicate that staphylococcus-related SBO responds more to antibiotic treatment, while SBO due to pseudomonas or aspergillus is more refractory antibiotics, often requiring multiple repeat procedures to achieve eradication of disease.

CONTACT

Kurren Gill
Thomas Jefferson University Hospital Dept of Otolaryngology-Head and Neck Surgery
Email: kurrensingh@gmail.com

INTRODUCTION

Skull base osteomyelitis (SBO) is a rare infectious condition most commonly presenting in elderly, immunocompromised, diabetic patient populations.[1] SBO bone degradation is life-threatening, often initially presenting with chronic headaches then progressing to serious infection, associated cranial neuropathies, and possible seizures in later stages.[1] SBO usually affects the temporal bone as a complication of malignant otitis externa (MOE). Central SBO is a distinct variant of this disease process, being increasingly described in the skull base literature, and localizes to the clivus, sphenoid bone and occipital bone.

Even for the experienced clinician, central SBO is a challenging disease to recognize and manage. In general, initial presentation includes localizing headaches or otalgia. The hallmark of progressive disease is the involvement of cranial nerves. If untreated, it can quickly progress to involve the cavernous sinuses and brain, eventually leading to seizures and death in its advanced stages.

Lateral SBO is a common sequelae of advanced MOE, and typically the disease is culture positive for *Pseudomonas aeruginosa*.[2] However, fungal disease typically mediated by *Aspergillus* has been reported in close to 50% of patients in case series.[2] SBO of the central skull base is associated with chronic sinusitis in patients who are immunocompromised.[2] Ultimately, identification of the pathological source regularly involves surgical biopsy with subsequent treatment involving either antimicrobial and/or surgical interventions.

Due to subtle presenting symptoms, difficult diagnoses, and the risks of delayed intervention, early recognition and proper management of SBO is critical in preventing serious neuropathies and infection.[8] This study evaluated 18 central SBO cases with a focus on comorbid conditions, location of infection, pathological source and outcomes in order to inform future diagnoses and treatment.

METHODS AND MATERIALS

Retrospective chart review after IRB approval was performed on patients who underwent treatment for central SBO at our institution and a Korean institution from March 2008 to September 2015. Inclusion criteria included all patients who underwent endoscopic, endonasal surgery for the debridement of SBO. Exclusion criteria included patients with abnormal otologic exams, history or radiographic evidence of lateral SBO, history of malignant otitis externa, history of mastoidectomy, history of head and neck radiation treatment, and history of nasopharyngeal or temporal bone malignancy. Data reviewed included patient demographics, and clinical and surgical data. Clinical data reviewed included pathology, prior and subsequent treatment, length of stay (LOS), length of follow-up, and complications.

REFERENCES

1. Asimakopoulos, P., M. Supriya, S. Kealey, and G. A. Vernham. "A Case-based Discussion on a Patient with Non-otogenic Fungal Skull Base Osteomyelitis: Pitfalls in Diagnosis." *The Journal of Laryngology & Otology* 127.08 (2013): 817-21.
2. Blyth, C. C., L. Gomes, T. C. Sorrell, M. Da Cruz, A. Sud, and S. C.-A. Chen. "Skull-base Osteomyelitis: Fungal vs. Bacterial Infection." *Clinical Microbiology and Infection* 17.2 (2011): 306-11.
3. Cavel, Oren, Dan M. Fliss, Yoram Segev, Daniel Zik, Avi Khafif, and Roee Landsberg. "Rhe Role of the Otorhinolaryngologist in the Management of Central Skull Base Osteomyelitis." *American Journal of Rhinology* 3 (2007): 281-85.
4. Chang, Parick C., Nancy J. Fischbein, and Roy A. Holliday. "Central Skull Base Osteomyelitis in Patients without Otitis Externa: Imaging Findings." *American Journal of Neuroradiology* 24 (2003): 1310-316.
5. Clark, Matthew, Pieter Pretorius, Ivor Byren, and Chris Milford. "Central or Atypical Skull Base Osteomyelitis: Diagnosis and Treatment." *Skull Base* 19.04 (2009): 247-54.
6. Johnson, Andrew K., and Pete S. Batra. "Central Skull Base Osteomyelitis: An Emerging Clinical Entity." *The Laryngoscope* 00 (2013)
7. Rothholtz, Vanessa S., Alice D. Lee, Bahman Shamloo, Mohsen Bazargan, Deya Pan, and Hamid R. Djalilian. "Skull Base Osteomyelitis: The Effect of Comorbid Disease on Hospitalization." *The Laryngoscope* 118.11 (2008): 1917-924.
8. Sayhan, Mustafa Burak, Cemil Kavalci, Ozgur Sogüt, and Eylem Sezenler. "Skull Base Osteomyelitis in the Emergency Department: A Case Report." *Emergency Medicine International* 2011 (2011)
9. Spielmann, P. M., R. Yu, and M. Neeff. "Skull Base Osteomyelitis: Current Microbiology and Management." *The Journal of Laryngology & Otology* 127.S1 (2013): S8-S12.

RESULTS

A total of 18 patients were identified according to our inclusion criteria that underwent transnasal endoscopic surgery for central SBO at our institution and a Korean institution (**Table 1**). There were 14 male and 4 female patients. Mean age of patients identified was 63 years of age. Mean follow-up was 28.8 months (range 6-90 months). Eight patients were lacking follow-up data and were not included in the mean follow-up calculation. Eleven patients had a history of diabetes mellitus and four patients had a medical history relevant for an immunocompromised state (myelodysplastic syndrome, history of liver transplant, polymyalgia rheumatica, HIV). The majority of patients presented with headache and 6 patients had cranial neuropathies (V, VI, VII, IX or X). Almost all patients had involvement of the clivus on imaging. Eight patients were culture positive for staphylococcus, nine for pseudomonas, and four for aspergillus. Most patients with a staphylococcus infection had eradication of disease: five patients were reported as improved on serial MRI and 2 were stable (1 unknown). All patients culture positive for pseudomonas demonstrated stable or improved disease on serial MRI except for one patient that had consistent worsening of disease. Three patients with aspergillus improved, and one remained stable. Overall, 11/18 patients improved, 5 were stable, 1 worsened, and 1 was lost to follow-up.

All patients were taken to the operating room for transnasal endoscopic biopsy and culture of the skull base and debridement as clinically indicated. Majority of staphylococcus positive patients required only 1 operative biopsy and debridement, and no repeat procedures. In contrast, 6 of the 13 patients with pseudomonas or aspergillus infections required 10 repeat procedures total. Long-term IV antimicrobial therapy was employed in all but one patient with a duration spanning from 2-25 weeks. Six patients had persistent disease despite antibiotic treatment and all six underwent repeat surgery; three of these patients were culture positive for aspergillus and three were positive for pseudomonas.

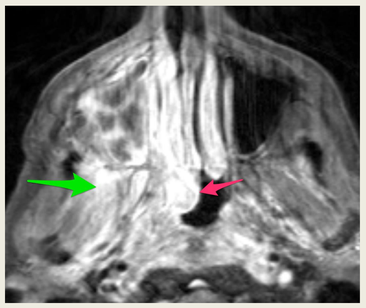

Figure A. T1 Post Contrast shows significant enhancement at nasopharynx (red arrow) with lateral extension (green) concerning for malignancy versus infection.

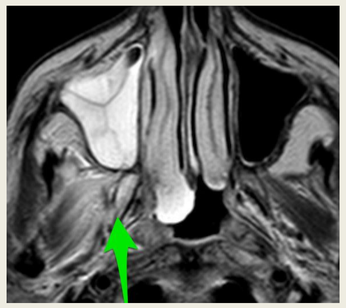

Figure B. T2 weighted MRI shows increased signal in nasopharynx (green) and infratemporal fossa indicating inflammation.

Patient #	Age	Sex	DiabetesMellitus	Immunocomp. State	Medical Comorbidities	Presenting Symptoms	Cranial Neuropathies	Location	Surgery	Culture Results	Treatment	Length of Tx (wks)	Last MRI	Repeat Procedures	Length of follow-up (mos)
1	67	M	Yes	Yes	Liver Transplant	Right posterior headache	None	clivus, ITF, PPS	Yes	pseudomonas; staphylococcus (Coag neg)	Ceftazidime, Ciprofloxacillin, Daptomycin	8	Improved	0	17
2	64	M	No	No	none	Severe headache and neck pain	None	petroclival	Yes	staphylococcus (clival bone)	Vancomycin, Ertapenem	6	Improved	0	17
3	73	F	No	Yes	polymyalgia rheumatica on chronic steroids	Left ear pain	None	petroclival/ petrous apex; PPS	Yes	Aspergillus	Zosyn, Metronidazole	4	Improved	1	34
4	76	M	Yes	Yes	myelodysplastic syndrome	facial pain, headache	None	PPF/MCF/ paraclival	Yes	Pseudomonas	Ciprofloxacillin	Unknown	Worse	2	N/A
5	68	M	Yes	No	Cardiac Stent	right facial pain head ache	None	Right temporal bone, clivus	Yes	Staphylococcus aureus (MRSA)	Vancomycin, Zosyn	6	Improved	0	90
6	78	M	Yes	No	arthritis, sinusitis, chronic otitis media	facial pain	VII	Skullbase, clivus	Yes	Aspergillus, staph (coag neg)	Voriconazole, Ertapenem, Ambisome	8	Improved	3	35
7	60	M	Yes	No	Chronic otitis media	otalgia	None	clival, ITF, PPS	Yes	Pseudomonas, staph aureus	Ceftazidime, Daptomycin	8	Stable	2	37
8	53	M	Yes	No	ESRD on hemodialysis, prior temporal osteo (x3 surgeries)	chronic temporal osteomyelitis	None	Clivus	Yes	Pseudomonas, MRSA	Vancomycin, Ceftazidime	6	Unknown	0	N/A
9	48	F	No	No	Stroke, DVT, PE	sinus headache	None	Clivus, PPS, PPF	Yes	Aspergillus	Oral Voriconazole	25 (current long-term maintenance)	Improved	1	6
10	72	M	Yes	Yes	HIV	migraine	None	Right temporal bone, clivus	Yes	Pseudmonas	Cefepime, Ciprofloxacillin	6	Stable	0	8
11	56	F	No	No	Recurrent nasopharyngeal carcinoma	facial pain, decreased hearing	Diplopia	Clivus	Yes	Pseudmonas	Vancomycin, Doripenem	8	Stable	1	12
12	69	M	No	No	PE, sinusitis	epistaxis, headache	None	Clivus, sphenoid	Yes	Pseudmonas, Staph aureus	No Antibiotics	N/A	Stable	0	32
13	77	M	Yes	Unknown	None	Headache, Voice change	IX/X	sphenoid	Yes	Pseudomonas	IV abx	5wks(IV) and 4wks(oral)	Improved	0	Unknown
14	51	M	No	Unknown	None	Headache, neck pain,	None	Unknown	Yes	none	IV abx	6wks(IV) and 4wks(oral)	Improved	0	Unknown
15	45	M	Yes	Unknown	None	Headache, dysarthria	V,XII	sphenoid	Yes	Pseudomonas	IV abx	4wks(IV) and 4wks(oral)	Improved	0	Unknown
16	53	M	No	Unknown	None	Headache, diplopia, eye pain	V,VI	hematogeneous	No	Parvimonas micra	IV abx	2wks(IV) and 4wks(oral)	Improved	0	Unknown
17	67	M	Yes	Unknown	HTN, stroke	Headache, hoarseness	VI,X	sphenoid	Yes	Fungus (aspergillus)	Antifungal	2wks(IV) and oral 6month	Stable	0	Unknown
18	58	F	Yes	Unknown	None	Headache	None	Unknown	No	Staphylococcus species	IV abx	3wks(IV) and 4wks(oral)	Improved	0	Unknown

Table 1. Demographics and clinical results of Central SBO patients

ITF: infratemporal fossa; PPF: pterygopalatine fossa; MCF: middle cranial fossa; abx: antibiotics

DISCUSSION

Central SBO is a challenging disease process that requires a multi-disciplinary approach for optimal treatment. Our experience suggests that central SBO is a distinct disease process compared to lateral SBO. Nearly every patient in our study had imaging concerning for a nasopharyngeal or skull base tumor which represented a significant delay in diagnosis.

MRI imaging is the accepted standard for both diagnosis and management of SBO. Typical findings include T1 contrast enhancement in the surrounding soft tissues **(Figure A)** with loss of marrow signal in T1 sequences indicating marrow involvement. In addition, T2 hyperintensity is often noted indicating an inflammatory process **(Figure B)**. In the majority of cases, an erosive and infiltrative process was identified with enhancement of the soft tissue, clivus, sphenoid bone, or occiput.

Typical operative management for these patients at our institution involve directed biopsies augmented by intraoperative navigation with anaerobic, aerobic and fungal microbiological studies. It is imperative to rule out malignancy or invasive fungal sinusitis with frozen section analysis and rapid pathologic analysis. It can be difficult to identify the pathogen of the infection so multiple tissue samples and culture swabs are recommended to obtain a diagnosis. We perform debridement of obviously necrotic tissue with preservation of critical neurovascular structures. The tissue is usually inflammatory and includes a large portion of the central skull base so a large initial resection is usually not indicated. Multiple cultures are obtained and a trial of medical therapy and control of the underlying disease is instituted. If there is progression of disease or no response despite medical therapy, more aggressive debridement of the soft tissue and bone are performed, which may include bringing in local tissue such as a nasoseptal flap to bring in a healthy blood supply and protect critical neurovascular structures. It is our experience that patients with persistent disease have underlying infection of the bone that requires more aggressive debridement especially of the clivus and sphenoid bone.

In our series, our patients with staphylococcus positive cultures had a decreased need for subsequent operative debridement. This preliminary evidence suggests that patients with cultures positive for pseudomonas or aspergillus may require more aggressive therapy to manage disease. This would include more frequent surgical debridement combined with long-term antimicrobial therapy.