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Endoscopic endonasal resection of craniovertebral junction osteomyelitis: illustrative cases

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BACKGROUND Operative management of craniovertebral junction (CVJ) osteomyelitis has traditionally been extracranial and focused on debriding the infection. In select patients, the endoscopic endonasal approach (EEA) with a focus on additional resection versus debridement may be preferred. The goal of this study is to present the authors' experience with the EEA with gross or subtotal resection for the treatment of osteomyelitis at the CVJ and describe their technique in the context of the literature.

OBSERVATIONS Two patients of the authors' and 6 detailed case reports in the literature were identified with a mean age of 58.9 years. Most patients (n = 5; 62.5%) underwent skull base surgery and debridement (n = 5; 62.5%). Although more common, debridement was inferior to resection in terms of neurological improvement (66.7% vs. 100.0%) postoperatively. The majority (n = 7; 87.5%) of patients underwent occipitocervical fusion.

LESSONS Osteomyelitis is an exceedingly rare lesion of the CVJ. Despite the region's delicate biomechanical stability, resection of infected bone may be superior to debridement alone in terms of clinical outcome. Given how well established the safety of the EEA is to this region, further study of outcomes with resection is warranted.

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KEYWORDS osteomyelitis; craniovertebral junction; endoscopic endonasal approach

Nontuberculous, or pyogenic, vertebral osteomyelitis is an increasingly prevalent condition, with most cases presenting in the subaxial spine.[1] Craniovertebral junction (CVJ) osteomyelitis represents a very rare subset of cervical osteomyelitis, which accounts for 6.5% of all vertebral osteomyelitis.[2] Its incidence is highest in immunocompromised individuals as well as patients diagnosed with end-stage renal disease or diabetes.[3] In these instances, *Staphylococcus aureus*[4] is most frequently encountered as the causative agent, although there have also been reports of *Streptococcus*,[5] gram-negative microorganisms, and invasive fungal species[6] as well.

A combination of neuroimaging with the isolation of blood-borne pathogens can aid in making a diagnosis.[7,8] Early diagnosis and intervention can yield good outcomes in these patients,[8] while delays can result in epidural abscess formation and subsequent death or neurological injury.[9] Patients most frequently present with neck pain, swelling, and stiffness as well as dysphagia. Patients presenting with neurological deficits because of destructive lesions of the skull base may recover function following treatment.[10] Although the literature does have reports of conservative, medical management,[11,12] there is a paucity of data on operative management of CVJ osteomyelitis and its outcomes. To address this gap in the literature, we conducted a systematic review of the literature to identify all published operative reports and analyze the presentation, operative technique, and clinical outcomes of patients with CVJ osteomyelitis.

ABBREVIATIONS CN = cranial nerve; CVJ = craniovertebral junction; EEA = endoscopic endonasal approach; MRI = magnetic resonance imaging; OC = occipitocervical.

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Illustrative Cases

Case 1

History and Examination

A 36-year-old woman presented with a desquamating rash and occipital and cervical lymphadenopathy, with complaints of persistent nuchal pain and headaches. She had a medical history of asthma, chronic hepatitis C, and intravenous drug use. She also had known osteomyelitis in the lumbar spine and retro-odontoid and retro-clival epidural abscesses. On examination, sternocleidomastoid and trapezius muscle strength was 4/5 and the patient had a positive left Hoffman's sign and generalized hyperreflexia. Magnetic resonance imaging (MRI) showed a retroclival epidural collection with a 2 × 26–mm nonenhancing fluid component extending into the cervical spine ventrally (Fig. 1). The medulla and upper cervical spinal cord showed mild posterior displacement, concerning for compression.

Operation

The patient underwent an endoscopic endonasal approach (EEA) odontoidectomy with medulla and spinal cord decompression and occipitocervical (OC) posterior fusion. In standard EEA fashion, mucosal removal, turbinate mobilization, septectomy, and drilling of the intranasal bone were used to expand access. A large nasoseptal flap was obtained and tucked into the inferior nasopharynx for protection. The nasopharynx and clivus were in view at this point. Longus coli muscles were resected to expose the bony anatomy of C1–2; then, the anterior arch of C1 was drilled until reaching the apical ligament of the odontoid process. The odontoid was first hollowed via diamond burr dill and then in-fractured from the lateral portions for total removal. The transverse ligament was visible and inflamed. The clivus was drilled until the inferior 6 mm could be removed with rongeurs. After adequate decompression of the clivus and odontoid process, the base of C2 was decompressed by drilling a 2-cm-deep, 1-cm-wide window. With bony decompression complete, the alar ligament was removed bilaterally with the soft tissue overlying the CVJ. There was a dense, adherent phlegmon overlying the dura. Resected tissue grew *Candida* glabrata when cultured. After bony and ligamentous decompression, the nasoseptal flap was placed over the defect and anchored in place with fibrin glue, nasopore splints, and fat graft.

FIG. 1. Case 1. Postoperative radiograph of OC fusion. Following odontoidectomy, the radiograph showed stabilization of the craniovertebral junction.

Having ensured adequate medullary decompression, the patient was carefully flipped to the prone position on an open Jackson table under continuous neuromonitoring. The proper alignment of the CVJ was confirmed via lateral radiograph and the Mayfield head holder was locked in place. Ensuring adequate alignment, a standard posterior cervical dissection was performed. A generous exposure of the occiput and the C1–4 vertebrae was achieved. A standard occipital plate was used with bicortical purchase ensured for screw placement. Lateral mass screws were placed at C3, and C2 screws were placed across the pedicles. We avoided the use of C1 screws because it is known that placement increases the risk of vertebral artery injury[13] and they are generally unnecessary in the setting of adequate fixation below the atlas, such as ours. Instrumentation configuration was verified with fluoroscopy, and then rods were contoured into the appropriate shapes and placed and secured with set caps. A mix of demineralized bone matrix and bioactive glass was placed for OC fusion. The patient was stable throughout both portions of the surgery based on neuromonitoring feedback.

Postoperative Course

Postoperative MRI revealed that the left lateral mass screw had close proximity to the left vertebral artery in the setting of a new mild cranial nerve (CN) VII palsy on postoperative day 4, which raised concern for stroke. A diagnostic angiogram was carried out to rule out vertebral artery damage, with another MRI showing no evidence of infarction. The CN VII palsy was likely secondary to phlegmonous inflammation of the nerve as it entered the clivus. This improved shortly after workup, on postoperative day 7. Otherwise, the patient tolerated the procedure well, with improvement from presentation. Her postoperative neurological examination showed resolution of the CN VII palsy, no facial droop, and facial symmetry. She remained stable at 6 months of follow-up. Follow-up radiographic films showed preserved alignment of the CVJ (Fig. 2). The C0–1 segmental Cobb angle was –2°, the C1–2 segmental Cobb angle was –37°, and the C0–2 regional lordosis measured 40°. These were all within 1.25 standard deviations of asymptomatic adult normative data.[14,15] Unfortunately, the patient's bacteremia recurred 2 years later, and she died of septic shock from pneumonia. Imaging at this time confirmed that osteomyelitis did not recur.

Case 2

History and Examination

A 57-year-old male presented initially with nasopharyngeal carcinoma for radiation and chemotherapy treatment. Afterward, he developed radionecrosis of the skull base with secondary *Pseudomonas aeruginosa* meningitis and presented with altered mental status, increasing confusion, headache, neck pain, and right ear discharge. An

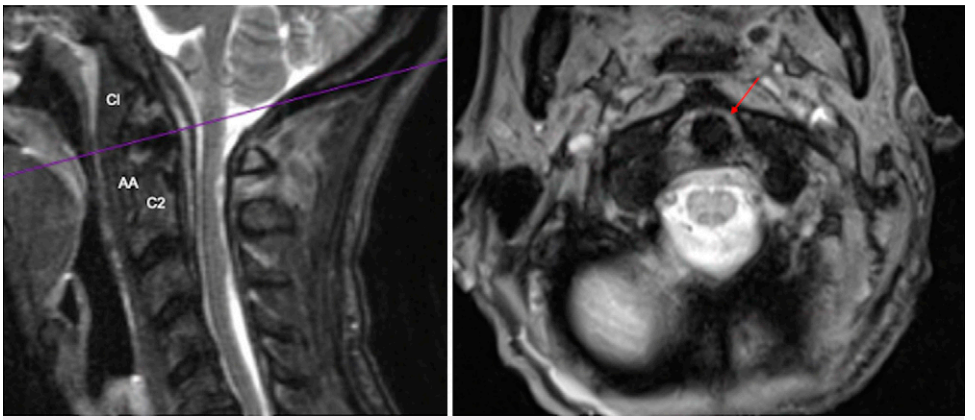

FIG. 2. Case 1. Preoperative MRI (**left**) showing osteomyelitis of the clivus (Cl), anterior arch (AA) of C1, and the odontoid of C2. Transverse plane (*purple line*). Axial MRI (**right**) showing the epidural abscess. Retroclival epidural abscess (*red arrow*).

MRI was obtained which showed osteomyelitis of the occipital condyles, anterior ring of C1, and C2–3 vertebral bodies as well as the C2–3 disc space. This was suggestive of skull base osteomyelitis with caudal extension to involve the CVJ manifesting as C1–3 spondylodiscitis. The patient was initially treated with cefepime, but subsequently had a new-onset seizure with monoclonal jerking of all extremities. Cefepime was discontinued and the patient was started on meropenem but developed acute kidney injury due to antibiotics and contrast administration. At this point, it was determined that surgery was necessary.

Operation

The patient underwent an EEA bilateral exenteration of the nasopharynx with clivectomy via a transpterygoid approach to remove the necrotic tissue and to graft vascular tissue in the avascular area of necrosis (Video 1, Fig. 3). Because of the patient's neoplastic disease and health status, nearly the entire nasopharynx was necrotic. A broad nasoanterior window was made via extensive resection of the nasopharynx from each eustachian tube down to the clivus. Samples were sent, which confirmed necrosis and infection. With the pterygopalatine fossae dissected out via sphenoidotomy, vidian nerves needed to be sacrificed since the vidian canal was not flush with the floor of the sphenoidal recess. This facilitated broad exposure of the middle cranial fossa to gain access to the clivus. The base of the clivus, noted to be necrotic, was drilled down to the dura, exposing the internal carotid artery and paraclival arteries bilaterally. The clivectomy was extended from the foramen lacerum to the foramen magnum. Phlegmon was noted near the cartilage of foramen lacerum bilaterally. Longus coli muscles and parapharyngeal contents were resected bilaterally until bleeding tissue was encountered bilaterally. The inferior nasopharynx was then resected down to the anterior ring of C1, preserving the eustachian tubes, until bleeding tissue was located. Nasoseptal reconstruction was performed using an anterolateral thigh musculofascial free flap that was anastomosed and tunneled into the nasopharynx. The patient was stable throughout all portions of the surgery based on neuromonitoring feedback.

VIDEO 1. Clip showing EEA clivectomy and nasopharyngeal exenteration using the transpterygoid approach. Pre- and postoperative presentation and outcome following treatment of CVJ osteomyelitis in the setting of widespread necrosis of the area from radiation. Click here to view.

Postoperative Course

Postoperative head and sinus computed tomography scans were performed with no concern. Of note, the patient had significant postoperative delirium and accidentally pulled out their merocele packing and left nasal trumpet on the first postoperative day. Infectious disease specialists recommended meropenem for a duration of 1 month following discharge. The patient had been followed by palliative medicine prior to their surgery and they were taking 5 mg of oxycodone daily at the time of discharge. Postoperative MRI revealed debridement of infected tissue and proper installation of the free flap. Sensorineural hearing loss that had been present for 11 months prior to surgery remained. Additionally, the patient developed new-onset

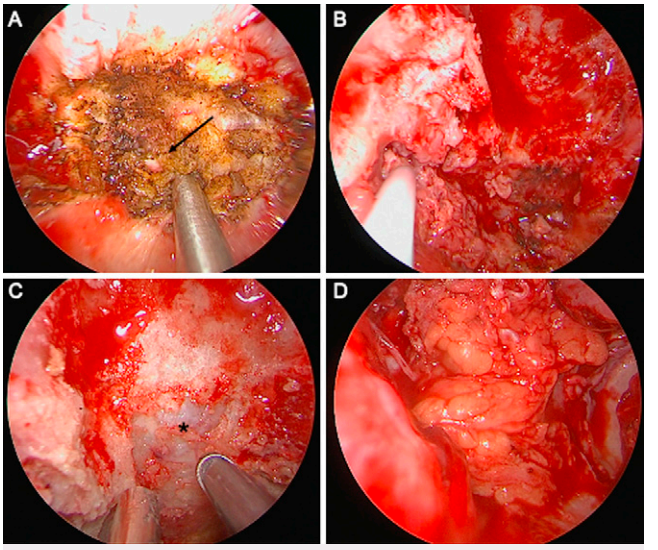

FIG. 3. Case 2. Photographs demonstrating purulence (*arrow*, **A**), micro-Doppler localizing of the paraclival internal carotid arteries (**B**), clivectomy with the dura exposed (*asterisk*, **C**), and vascularized anterolateral thigh flap for nasopharyngeal reconstruction (**D**).

bilateral CN VI palsy 3 months postoperatively that manifested as diplopia, which has been stable for 6 months with only mild improvement in the mobility of the left eye.

Discussion

Observations

Vertebral osteomyelitis at the CVJ may behave differently than subaxial cases in terms of clinical presentation, course, and outcomes following operative management. Our review of the literature yielded 6 case reports in addition to our 2 patients (mean age: 59 years; age range: 36–78 years; 75.0% male) (Table 1). The infection was primarily bacterial (87.5%), and the most common pathogen was *Staphylococcus aureus* (50.0%). Patients presented with primarily new-onset weakness (62.5%), CN palsies (25.0%), and headache (25.0%). Headache is a relatively unique symptom for osteomyelitis, and otherwise not classic in the presentation for vertebral osteomyelitis. In addition to the CVJ, paravertebral soft tissue was involved in most cases, with the prevertebral space affected in 1 patient (12.5%).

Of the 5 patients undergoing cranial surgery, endoscopic was the more preferred route, with 3 of 5 (60%) patients receiving an endonasal decompression. Three patients underwent spine surgery only and extracranial approaches to the atlantoaxial and craniovertebral region. Of all cases, debridement (n = 5/8; 62.5%) was more common than gross or subtotal resection (n = 3/8; 37.5%). Seven of 8 patients (87.5%) underwent OC fusion, although only 66.7% of patients where the EEA was utilized underwent fusion. Fusion did not affect CVJ stability rates postoperatively, as all patients at the most recent follow-up had no documented abnormal motion at the site. The postoperative complication rate was 62.5% and the 90-day mortality rate was 12.5%. Clinical improvement was defined as (1) neurological improvement from baseline presentation and (2) no new or worsening neurological deficits up to and including death across the literature and our institution's patients on (3) 6-month follow-up neurological examination. The only approach that did not result in full clinical improvement was EEA, with 66.7% of cases improving. Across all cases, debridement appeared to be inferior to gross or subtotal resection regardless of approach in terms of clinical improvement (66.7% vs 100.0%).

Limitations

There are a few limitations to the current study. Despite decades of collection and publication, there still is not a significant number of patients to make statements of association about craniovertebral osteomyelitis. However, these illustrative cases in the context of all case reports available in the literature is a step in the right direction to better guide operative treatment. There is also a file-drawer effect, where negative cases of surgery are not published, and this might overstate the efficacy of surgery.

Lessons

Although the use of intravenous antibiotics may successfully treat some patients with this condition, when conservative management fails to clear osteomyelitis, it is possible that vertebrae and intervertebral discs can undergo ischemic necrosis, leading to osteonecrotic destruction.[16] This can therefore lead to rather significant rates of spinal deformity, with some reports as high as 44%.[17] This may threaten the intricate and vital biomechanics of the CVJ, which are compromised when there is deformity, let alone the threat of compression of the spinal cord and/or

TABLE 1. Summary of studies included

Author(s), Year	Age (yrs), Sex	Pathogen	Skull Base Osteomyelitis Location(s)	Vertebral Osteomyelitis Location(s)	(Micro)surgical Approach	Resected Anatomy	OC Fusion	Last FU
Goulart et al., 2015[2]	50, M	*Staphylococcus aureus*	Occipital condyles	AA joints, C1–2 vertebral bodies, paravertebral soft tissue	Posterior decompression	NA; d/b	Occiput-C4	5 mos
Reid & Holman, 2007[5]	58, M	*S. aureus*	Lt occipital condyle	Odontoid lt AA joint	Transoral, transpalatal decompression	C1 anterior arch, odontoid	Occiput-C4	6 mos
Ducic, 2019[10]	68, M	*S. aureus*	Clivus	C1 anterior arch, odontoid	Transoral, transpalatal	NA; d/b	Yes (levels not specified)	10 mos
Sibai et al., 2009[20]	56, M	*S. epidermidis, Corynebacterium*	Occipital bone, occipital condyles	C1 LMs, odontoid	Posterior decompression	NA; d/b	Occiput-C7	1 yr
Aranibar et al., 2015[21]	70, F	MRSA	Lt occipital condyle	AA joints, C1–2 vertebral bodies	Anterior cervical transtubular	NA; d/b	Occiput-C5	1 yr
Suresh et al., 2022[30]	76, M	*S. aureus, Pseudomonas aeruginosa*	Clivus, lt occipital condyle	Lt C1 LM, AA joint	Endoscopic transmastoid/-sphenoid	NA; d/b	Occiput-C3	2 mos*

AA = atlantoaxial; d/b = debridement; FU = follow-up; LA = left anterior; LM = lateral mass; MRSA = methicillin-resistant *Staphylococcus aureus*; NA = not applicable.
* Death.

medulla.[18,19] Therefore, the threshold for surgical intervention in this case may be much lower and thus earlier than for traditional axial, vertebral osteomyelitis.

Vertebral osteomyelitis at the CVJ is a dangerous and difficult-to-treat pathology. At our institution, our go-to approach is EEA with gross or subtotal resection, followed by OC fusion for stability. In the literature, the most common approach documented is an extracranial debridement.[2,20,21] EEA for access to this distant skull base location and atlantoaxial spine is well described in the literature, reporting decreased morbidity and mortality, although only 1 case of CVJ was previously managed with this technique.[3,22–30] Direct anterior visualization via EEA provides the surgeon with an extraordinarily detailed view of lesions in the CVJ, although access below C2 is limited. However, in this case series, 1 patient operatively managed via EEA died in Suresh and colleagues' case report.[30] We tend to believe that this mortality following this approach in the 1 patient presented may be due to the extensive contiguous spread of osteomyelitis in the central skull base. It is known that this variant of skull base osteomyelitis has significant rates of mortality and morbidity.[31–33] This may be due to the intricate anatomy in this region, including the cerebellopontine angle, CN VII, trigeminal ganglion, and cavernous sinuses disposing to significant vulnerability for inflammation and other pathology (e.g., thrombo- or septic/mycotic embolism) of vital neurovascular components. The transoral approach must also be considered, although it is more invasive, and thus may lead to more complications, including mortality.[34,35]

Lateral and posterior subcranial approaches to the CVJ appear to be the most-used approach in this series; however, it is restricted from much of the skull base. This limits effective debridement or resection of diseased bone to the atlantoaxial region of the spine. Fusion of the cervical spine and occiput appears to be used nearly ubiquitously, considering that resection of the odontoid, anterior arch of C1 and clivus may exacerbate preexisting instability often related to inflammation.[36] It is known that this procedure is feasible, safe, and effective for preserving CVJ stability in the setting of resection of this area.[37–40] However, a few cases in this review did not undergo OC fusion and had unaffected CVJ stability postoperatively. It is hard to generalize this finding or predict which patients will be successful, and therefore we tend to recommend OC fusion in cases where there may be severe infection or extensive resection of the CVJ.

It is reasonable that debridement was the most common procedure as opposed to gross or subtotal resection. Not only is it less invasive but it tends to preserve the stability of the CVJ. However, it is worth mentioning that our findings may demonstrate that debridement is an inferior approach to resection of infected bone in this area. This may be because debridement of bone with concomitant antibiotic courses may take a longer time to eliminate the infection. We recommend resection in cases where the infection is severe enough to threaten the cervicomedullary junction and other neuroanatomy and to the extent that stabilization of the CVJ is feasible and preferable for the patient. Altogether, it appears that resection with the EEA and OC fusion may lead to preferable outcomes in craniovertebral osteomyelitis constrained to the posterior skull base. Although some patients experienced some fluctuation of neurological function postoperatively, this is generally transient and improves over time. With universally maintained alignment, neurological improvement, and long-term stability, gross or subtotal resection of infected bone may be indicated in select cases.

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Disclosures

Dr. VanKoevering reported being a cofounder of MakeMedical LLC, which creates medical simulators for educational purposes and is not in any way relevant to the content. Dr. Viljoen reported personal fees from Medtronic and grants from Medtronic outside the submitted work. Dr. Prevedello reported consulting for Stryker, Medtronic, and Integra LifeSciences, and royalties from Mizuho, ACE Medical, and KLS Martin. Dr. Grossbach reported personal fees and grants from Depuy, Medtronic, and 3M outside the submitted work. No other disclosures were reported.

Author Contributions

Conception and design: Keister, Kreatsoulas, VanKoevering, Viljoen, Prevedello. Acquisition of data: Keister, Vignolles-Jeong, Grossbach. Analysis and interpretation of data: Keister, Vignolles-Jeong, Kreatsoulas, VanKoevering, Grossbach. Drafting of the article: Keister, Vignolles-Jeong, Kreatsoulas. Critically revising the article: all authors. Reviewed submitted version of the manuscript: Vignolles-Jeong, Kreatsoulas, VanKoevering, Viljoen, Prevedello, Grossbach. Approved the final version of the manuscript on behalf of all authors: Keister. Statistical analysis: Keister. Study supervision: VanKoevering, Viljoen, Prevedello, Grossbach.

Supplemental Information

Video

Video 1. https://vimeo.com/769916458.

Previous Presentations

This work was presented at the 2022 CNS Annual Meeting in San Francisco, CA, in October 2022.

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