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CASE REPORT

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A case of atlantoaxial instability following skull base osteomyelitis: Tips for diagnosis and management

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Abstract

Skull base osteomyelitis is a rare but dangerous consequence of untreated malignant otitis externa. Pseudomonas aeruginosa is responsible for most cases with typical presentation. Here, we discuss a diabetic 54-year-old female presented with malignant otitis externa and bilateral facial paresis followed by cervical spondylitis and C1-C2 instability. Skull base osteomyelitis confirmed by clinical presentation, imaging, and laboratory data. Fortunately, she responded well to antibacterial and antifungal therapy. Due to limited data, there is no confirmed standard of treatment for cervical instability secondary to SBO. It seems antibiotic therapy is the mainstay of treatment. In case of poor response to antibiotic therapy, surgical intervention is inevitable. This article introduces the first case of SBO-related AAI successfully managed with conservative treatment.

KEYWORDS

cervical instability, osteomyelitis, otitis externa, skull base

1 | INTRODUCTION

Skull base osteomyelitis (SBO) is an uncommon condition. It can be divided into two groups using origin and bony anatomic involvement. The typical group is mainly related to malignant otitis externa, which usually involves the temporal bone. The atypical or central group commonly involves sphenoid and occipital bone without a determined otologic infection.[1]

Delay in treatment is related to poor prognosis. The physician should be familiar with this condition; otherwise, it can be missed, and extensive morbidity and mortality will be forced onto patients.[2] SBO is more common in immunocompromised patients or elderly with comorbidities like renal failure or diabetes mellitus(DM).[3] SBO is usually bacterial; the most common germ is Pseudomonas aeruginosa, especially in otic-origin infections. Due to vital vascular and neurological element proximities, complicated conditions are not rare in these patients.[4]

Here, we present a case of complicated fungal skull base osteomyelitis in a female patient with uncontrolled diabetes mellitus.

2 | CASE PRESENTATION

A 54-year-old female patient presented to the otolaryngology department with a complaint of bilateral facial palsy. The patient developed diabetes 20 years ago and was not well controlled (last HbA1c was 9.2%). She had multiple episodes of otitis externa in the preceding 6 months, which has been partially treated with short courses of oral and

topical antibiotics. She complained of severe headaches and bilateral ear pain for the last 4 months and had developed right-side facial palsy 2 months ago, followed by left-side facial palsy 2 weeks before our visit. She had low-grade fevers, and external canal redness, inflammation, and granulation tissue were evident on the ear examination. She was admitted to the infectious disease department for more evaluation. CRP and ESR were high (63 and 95, respectively). Leukocytosis was evident with a WBC count of 15,300. A smear sample of ear discharges was obtained, and after blood culture specimens, intravenous broad-spectrum antibiotics started (Meropenem 1 gr TDS and Vancomycin 1 GR BD). Brain and temporal bone CT scans and MR imaging were done. CT scan revealed evidence of skull base osteomyelitis as bilateral temporal bone sclerosis. In MR imaging, Soft tissue hyperintensity extending from the middle ear to the skull base was seen in T2 MRI with contrast enhancement after gadolinium injection (Figure 1). Brain MRI was interpreted as an inflammatory/infectious process. After 2 weeks, the patient continued to have periodic low-grade fevers and no significant decrease in inflammatory markers. The blood and discharge specimens' cultures were negative. Anti-fungal intravenous voriconazole was added, and the patient continued to receive intravenous antibiotics for additional 4 weeks, followed by oral antibiotics (Levofloxacin 750 mg daily and Voriconazole 200 mg q 12 h) after discharge. Left-side facial palsy improved completely in follow-up visits, and right-side paresis decreased but was still persistent as House Brackman grade of 3. CRP and ESR levels decreased (to 24 and 46, respectively), but she continued to complain of headaches. After 6 months, the patient was referred to the neurosurgery department, when she reported progressive cervical pain. Cervical Range of Motion was severely limited, and the patient insisted on keeping her head motionless. There was no radiating pain, and the sensory and motor examinations were normal. Deep tendon reflexes were normal, and there was no Gait or balance disturbance on examination. There was no midline tenderness. No cervical lymphadenopathy was palpated. There was no jaw tenderness or jaw movement limitation. She denied any history of trauma. Ear pain and discharges were improved. Right-side hearing loss was explicit.

Dynamic cervical radiography was done. C1- C2 instability was diagnosed as an increased Atlanta-dental interval at flexion (about 5 mm) (Figures 2, 3). Bed rest, analgesics, and a rigid cervical collar were prescribed, and a cervical spine CT scan and MRI was requested (Figure 3). Sclerosis of upper cervical vertebrae and erosions in the odontoid process was reported in the CT scan. MRI revealed bone marrow edema of bodies of upper cervical vertebrae without the involvement of intervertebral disks indicating cervical spondylitis. The patient was admitted to the infectious ward Again. CRP and ESR levels were high (49 and 61), and PPD and PCR for TB infection and wright and coombs-wright for brucellosis were tested, which were negative. Hard cervical collar was applied, and broad spectrum intravenous antibiotics were restarted (Meropenem

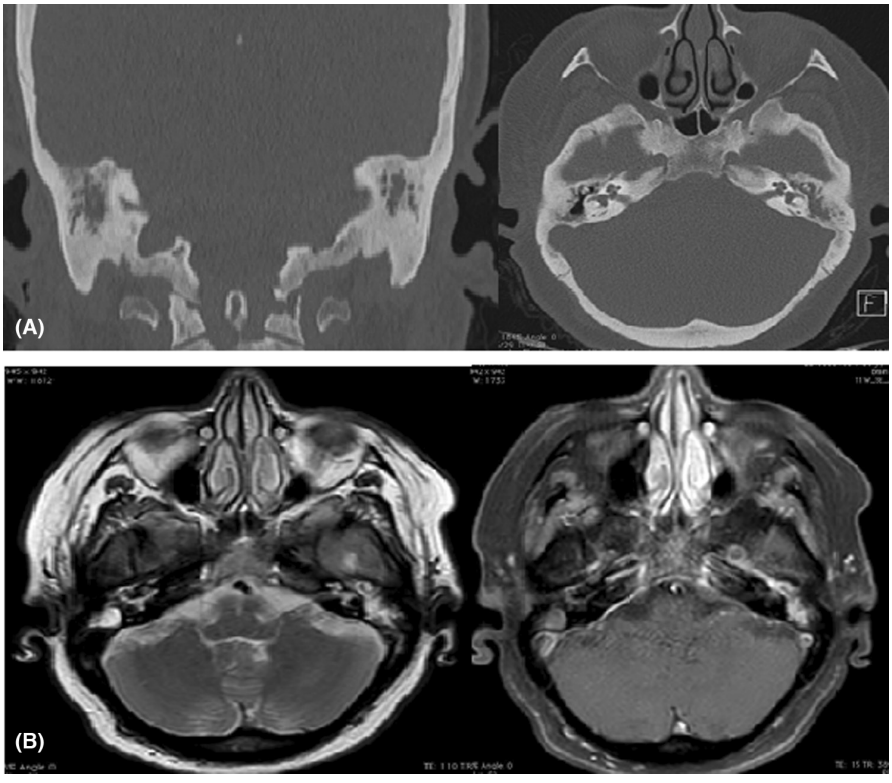

FIGURE 1 Evidence of skull base osteomyelitis in CT and MRI: A: coronal and axial CT Scan, decreased pneumatization of mastoid air cells and Bilateral petrous and clival sclerosis indicating otomastoiditis. B: T2-weighted axial MRI, Edema and effusion is noted in left middle ear and bilateral mastoid air cells with enhancement after iv contrast

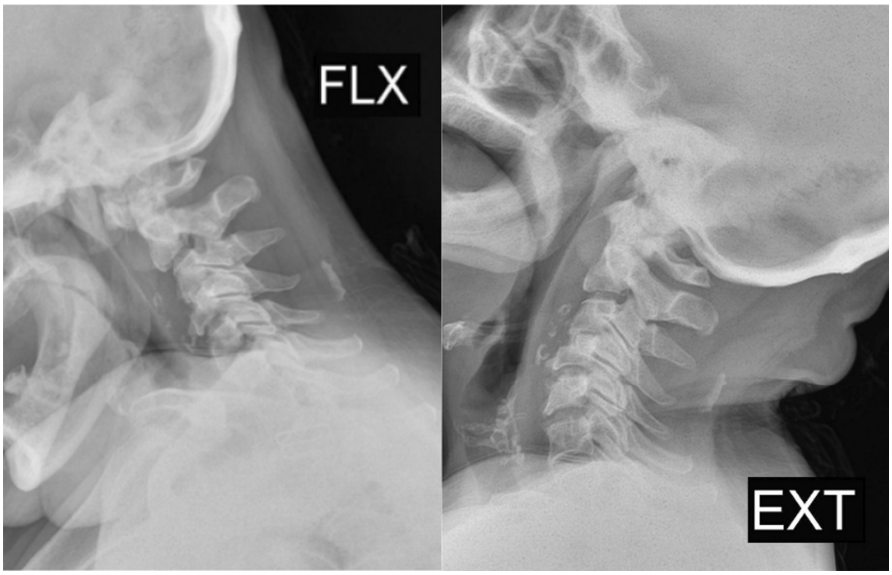

FIGURE 2 Dynamic cervical X-ray: Increasing ADI in flexion view is evident. Soft tissue edema and calcifications in prevertebral area and sclerosis in body of C3, C4, and C5

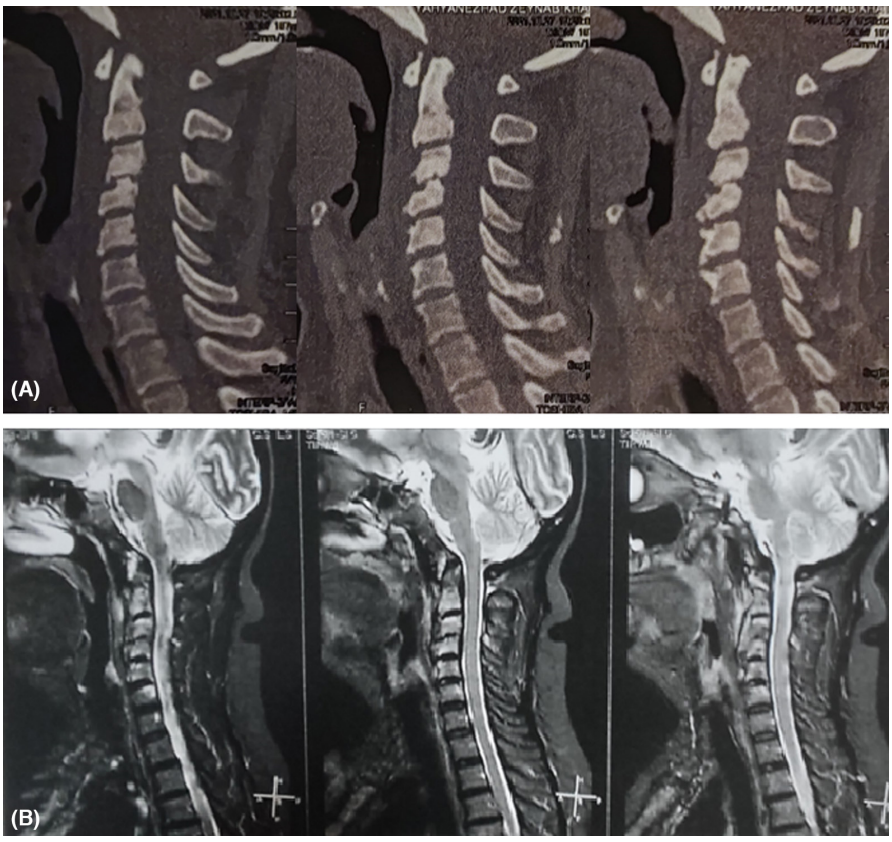

FIGURE 3 Evidence of cervical spondyilitis and C1-C2 Instability. A. CT scan revealing erosions and sclerosis in body of C2 to C5 vertebrae and posterior aspect of Odontoid process. B. Cervical MRI, STIR sequence, C1-C6 body hyperintensities and mild surrounding soft tissue edema in favor of inflammation

and Vancomycin) in addition to intravenous antifungal (IV Voriconazole 200 mg q 12 h), which continued for 4 weeks. Then, oral antibiotics continued for 12 months. After discharge, the patient was visited every month. The pain was reduced gradually, and no new neurological deficit was found in her follow-up. After 12 months cervical MRI and dynamic cervical X-ray showed significant improvement in edema and instability. At 1-year imaging, cervical spine edema and spondylitis disappeared in MRI, and C1-C2 stability was retained (Figure 4).

3 | DISCUSSION

Skull base osteomyelitis (SBO) is a rare condition. Origins of infection in the skull are usually malignant otitis externa (MOE), paranasal sinusitis, odontogenic infections, and chronic mastoiditis. The primary germ causing SBO is P. aeruginosa in overall. In fungal SBOs, Aspergillus is the leading pathogen. MOE involving the temporal bone is the most common cause of SBO. MOE mainly involves the sphenoid and temporal bone. Although male-to-female

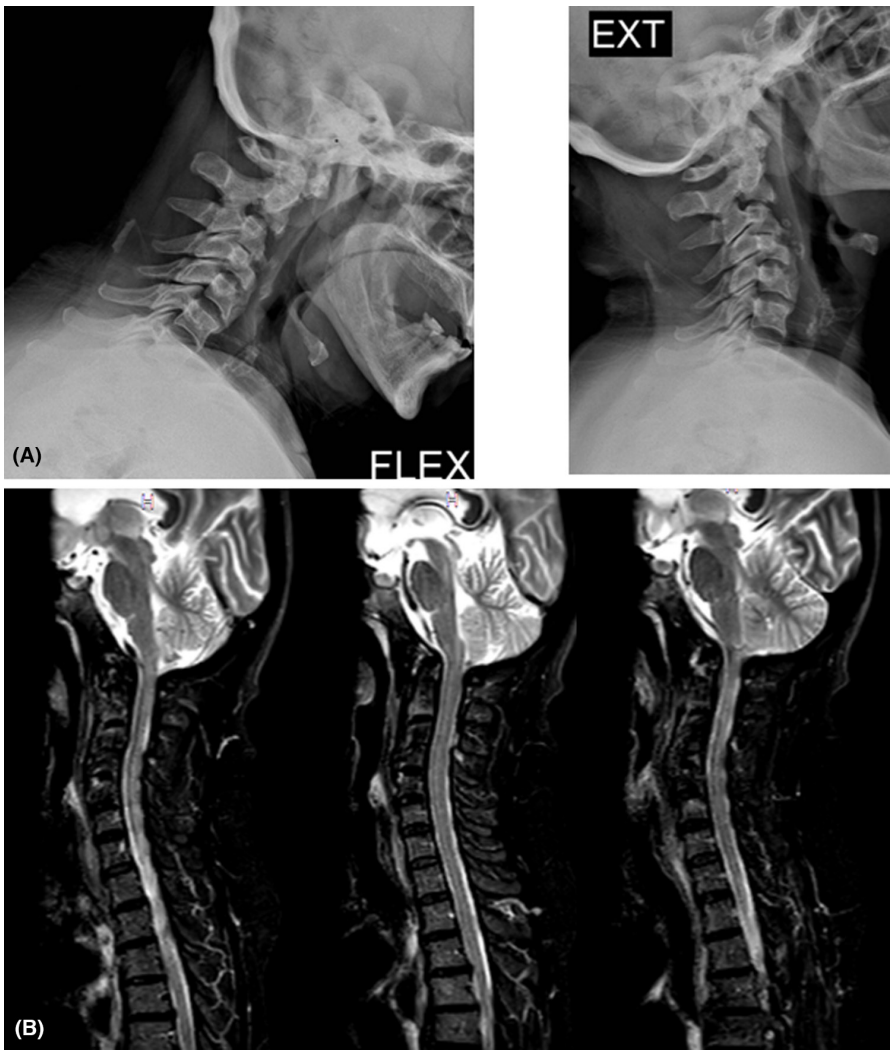

FIGURE 4 Improved cervical spondylitis and atlantoaxial instability in follow-up imaging. A. Dynamic cervical X-ray decreased C1-C2 subluxation. B. Cervical STIR MRI showing improved edema of cervical vertebral bodies

ratio is more than 1 in MOE, it seems that SBO prevalence is the same in both sex.[5] MOE finds its way to the skull base from the external auditory canal (EAC) through the osseocartilaginous junction of the EAC and Santorini fissure. Skull base extension can affect cranial base foramina, leading to cranial neuropathies and temporomandibular joint involvement.[6,7] The mastoid and middle ear cleft are known as the lateral temporal bone, and the petrous apex is the medial temporal bone; both can be involved during MOE course.[8] The main complaint in MOE is disproportional otalgia. Tender EAC, preauricular cellulitis, and pinna woody induration are the most common signs in MOE.[9,10]

On imaging, patients with the erosion of the mastoid part of the facial canal are seven times more at risk of incidence of facial paresis.[11] The most common cranial neuropathy in SBO is facial nerve involvement in the stylomastoid foramen. Jugular foramen involvement and lower cranial neuropathies manifestation are less common. Spreading to petrous apex can lead to 5th and 6th cranial nerves paresis.[6,12] WBC count, ESR, and CRP can be elevated. These inflammatory markers can be helpful as markers of treatment response.[13] MRI and SPECT are better studied for detecting the first stages of SBO. CT scan is not sensitive for detecting early SBO phases. However, it can help reveal periosteal reactions and bony erosions in the base of the skull.[14,15] Tissue samples are essential for treatment. Using broad-spectrum antibiotics must be culture based; otherwise, they may not be effective. The best prognosis achieves through early diagnosis and intervention.

In immune-compromised patients, improving the immune system should be considered. In a diabetic patient, strict blood sugar level control is essential.[8,16] Diabetes mellitus increases infection rate, but no data suggest more prolonged antibiotic therapy in these patients.[17] Hyperbaric oxygen (HBO) therapy is an adjunct treatment for refractory SBO. It can be used in a daily manner for several weeks. Important side effects are perforation of the tympanic membrane and barotrauma.[18,19] Surgical debridement is helpful in extensive fungal SBOs, but in usual cases, the surgical role is limited to biopsy. In some cases of MOE, bone and granulation tissue debridement may be needed. Meatoplasty is indicated in extensive EAC

involvement. Broad-spectrum antibiotics are the mainstay of treatment, and surgical intervention could be helpful in refractory conditions.[20,21]

Pseudomonas is the most commonly diagnosed germ in MOE, and it is a part of the normal flora of the ear canal; therefore, microbiologic studies cannot be helpful in determining a definitive diagnosis. Studies have shown that a large number of MOE patients have negative cultures in Iran.[22] It is well known that culture results in immunocompromised patients can be misleading. In 2017, an important study conducted in Iran recommended the use of empirical antifungal therapy to treat patients who did not respond to conventional antibacterial therapy.[2] In cases in which debridement has not been performed, they recommended a longer duration of treatment and follow-up. We have referred to studies that have been conducted in Iran.[23]

Typical SBO mainly involves the temporal bone, and the atypical entity may affect the occipital bone, especially the clivus. The clival area is connected to the fourth thoracic vertebra via epidural space.[24,25] Clinical presentation can be different due to the extension of the infection. If it extends superiorly, cranial neuropathy, facial pain, and headache are the prominent symptoms. Inferior extension of SBO to the paravertebral region can affect the occipitoatlantoaxial junction. It may present cervical pain, fever, suboccipital region tenderness, paresis, and craniovertebral junction instability.[26,27,28]

With aggressive treatment, the neurologic morbidity rate has been reported in 31% of cases and mortality in about 10%. Diabetes mellitus is related to poorer prognosis.[29,30]

Atlantoaxial instability, in our case, can be compared with Grisel syndrome. This syndrome is secondary to an infection in the head and neck regions, leading to nontraumatic rotatory atlantoaxial subluxation. It is more common in the pediatric population and presents with torticollis. Adult cases are rare.[31] The exact mechanism is unknown; however, it has been hypothesized that hyperemia secondary to infection spread through pharyngovertebral veins to periodontoid veins and cervical lymphadenitis may have roles in transient ligament laxity.[32,33] In Grisel syndrome also, early detection is essential and delayed diagnosis after 3 weeks may increase the need for fusion surgery. It seems that with inflammatory process resolution, stability will be recovered. Recommended treatment is conservative management consisting of bed rest, anti-inflammatory therapy, muscle relaxants, and antibiotic therapy. Failure of conservative management necessitates surgery and appropriate fusion.[31,32,33]

Determining the optimal time to do surgery could be challenging. In case of progressive deformity, progressive neurologic decline, and refractory pain or instability

TABLE 1 A summary of previously reported AAI following skull base osteomyelitis

Year	author	Age	Sex	Co-morbidity	Neurological examination	Discharge smear/culture	Response to antibiotic therapy	Surgical intervention
2020	Low et al.[34]	67	Male	DM type 2	Limited cervical ROM	MSSA P.A	Poor response	Occipitocervical arthrodesis
2020	Chefi et al.[19]	35	Male	Negative	Normal	Coagulase-negative staphylococci	Poor response	Occipitocervical arthrodesis
2022	Current study	54	female	DM type 2	Limited cervical ROM, Cervical pain	Negative smear and culture	Good response	No

Abbreviations: AAI, atlantoaxial instability; DM, diabetes mellitus; ROM, range of motion; MSSA, methicillin-resistant staphylococcus aureus; P.A, pseudomonas aeruginosa.

despite appropriate antibiotic therapy, surgical management is inevitable.[19,34] A summary of previous similar cases in the literature is shown in Table 1.

In our case, there was no absolute indication for early surgery, so we chose non-surgical treatment and close follow-up. In addition to AB therapy, an orthosis was prescribed for the patient.

Although bone scans are not essential for diagnosing MOE and SBO, especially in typical manifestations, they can assist us in determining the appropriate time for terminating treatment in follow-up,[23] and this may be a limitation of our study.

4 | CONCLUSION

Skull base osteomyelitis is a rare but severe disease. Symptoms usually are not specific. It can be life-threatening if not diagnosed early and treated appropriately. Skull base foramina, cranial nerves, and vascular structure can be involved. Infection extension to the craniovertebral junction may lead to bone and ligament injuries and instability. In this case, proper antibiotic therapy with appropriate orthosis lead to the good outcome, but in some cases, fusion may be inevitable. This article introduces the first case of SBO-related AAI successfully managed with conservative treatment.

AUTHOR CONTRIBUTIONS

Faramarz Roohollahi: Resources; writing – original draft. **Arad Iranmehr:** Visualization; writing – review and editing. **Ehsan Fatahi Andabili:** Conceptualization; data curation; project administration; supervision; writing – review and editing.

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CONFLICT OF INTEREST

The authors report there are no competing interest to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request. We will answer an email request in 48 hours. The email of corresponding author is "fattahimd@gmail.com".

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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REFERENCES

1. Chapman PR, Choudhary G, Singhal A. Skull base osteomyelitis: a comprehensive imaging review. *Am J Neuroradiol*. 2021;42(3):404-413.
2. Draf W, Regli F. To the differential diagnosis of cranial nerve lesions: the progressive necrotising external otitis (author's transl). *J Neurol*. 1975;210(3):219-226.
3. Burns TC, Mindea SA, Pendharkar AV, Lapustea NB, Irime I, Nayak JV. Endoscopic transnasal approach for urgent decompression of the craniocervical junction in acute skull base osteomyelitis. *J Neurol Surg Reports*. 2015;76(01):e37-e42.
4. Trück J, Thompson A, Dwivedi R, Segal S, Anand G, Kelly DF. Nonotogenic skull base osteomyelitis in children: two cases and a review of the literature. *Pediatr Infect Dis J*. 2015;34(9):1025-1027.
5. Khan M, Quadri S, Kazmi A, et al. A comprehensive review of skull base osteomyelitis: diagnostic and therapeutic challenges among various presentations. *Asian J Neurosurg*. 2018;13(04):959-970.
6. Unnikrishnan R, Faizal BP, Pillai MG, Paul G. Villaret's syndrome—a rare presentation of skull base osteomyelitis. *Case Report Amrita J Med*. 2013;9:1-44.
7. Slattery WH III, Brackmann DE. Skull base osteomyelitis: malignant external otitis. *Otolaryngol Clin North Am*. 1996;29(5):795-806.
8. Prasad SC, Prasad KC, Kumar A, Thada ND, Rao P, Chalasani S. Osteomyelitis of the temporal bone: terminology, diagnosis, and management. *J Neurol Surg Part B Skull Base*. 2014;75(05):324-331.
9. Schweitzer VG. Hyperbaric oxygen management of chronic staphylococcal osteomyelitis of the temporal bone. *Am J Otol*. 1990;11(5):347-353.
10. Marshall AH, Jones NS. Osteomyelitis of the frontal bone secondary to frontal sinusitis. *J Laryngol Otol*. 2000;114(12):944-946.
11. Dabiri S, Karrabi N, Yazdani N, et al. Facial nerve paralysis in malignant otitis externa: comparison of the clinical and paraclinical findings. *Acta Otolaryngol*. 2020;140(12):1056-1060. doi:10.1080/00016489.2020.1808242
12. Adams A, Offiah C. Central skull base osteomyelitis as a complication of necrotizing otitis externa: imaging findings, complications, and challenges of diagnosis. *Clin Radiol*. 2012;67(10):e7-e16.
13. Guillén A, Brell M, Cardona E, Claramunt E, Costa J. Pott's puffy tumour: still not an eradicated entity. *Childs Nerv Syst*. 2001;17(6):359-362.
14. Seabold JE, Simonson TM, Weber PC, et al. Cranial osteomyelitis: diagnosis and follow-up with In-111 white blood cell and

Tc-99m methylene diphosphonate bone SPECT, CT, and MR imaging. *Radiology*. 1995;196(3):779-788.
15. Weber PC, Seabold JE, Graham SM, Hoffmann HH, Simonson TM, Thompson BH. Evaluation of temporal and facial osteomyelitis by simultaneous In-WBC/Tc-99m-MDP bone SPECT scintigraphy and computed tomography scan. *Otolaryngol Neck Surg*. 1995;113(1):36-41.
16. Minutilli E, Pompucci A, Anile C, et al. Cutaneous fistula is a rare presentation of Pott's puffy tumour. *J Plast Reconstr Aesthetic Surg*. 2008;61(10):1246-1248.
17. Johnson AK, Batra PS. Central skull base osteomyelitis: an emerging clinical entity. *Laryngoscope*. 2014;124(5):1083-1087.
18. Mader JT, Lone JT. MEO cure with HBO as adjuvant therapy arch. *ORL*. 1982;108:38-40.
19. Chefi MA, Amri K, Mallat Y, Nouisri L. Osteomyelitis of the skull base and the cervical vertebrae. A case report and literature review. *Otolaryngol Case Reports*. 2020;14:2019-2021. doi:10.1016/j.xocr.2019.100149
20. Alva B, Prasad KC, Prasad SC, Pallavi S. Temporal bone osteomyelitis and temporoparietal abscess secondary to malignant otitis externa. *J Laryngol Otol*. 2009;123(11):1288-1291.
21. Hsiao YC, Lee JC, Kang BH, Lin YS. Idiopathic osteomyelitis at the base of the skull. *South Med J*. 2006;99(10):1121-1124.
22. Soheilipour S, Meidani M, Derakhshandi H, Etemadifar M. Necrotizing external otitis: a case series. *B-Ent*. 2013;9(1):61-66.
23. Hasibi M, Ashtiani MK, Motassadi Zarandi M, et al. A treatment protocol for management of bacterial and fungal malignant external otitis: a large cohort in Tehran, Iran. *Ann Otol Rhinol Laryngol*. 2017;126(7):561-567. doi:10.1177/0003489417710473
24. Chaljub G, Van Fleet R, Guinto FC Jr, Crow WN, Martinez L, Kumar R. MR imaging of clival and paraclival lesions. *AJR Am J Roentgenol*. 1992;159(5):1069-1074.
25. Clark MPA, Pretorius PM, Byren I, Milford CA. Central or atypical skull base osteomyelitis: diagnosis and treatment. *Skull Base*. 2009;19(04):247-254.
26. Singh A, Al KM. Skull base osteomyelitis: diagnostic and therapeutic challenges in atypical presentation. *Otolaryngol Neck Surg*. 2005;133(1):121-125.
27. Zigler JE, Bohlman HH, Robinson RA, Riley LH, Dodge LD. Pyogenic osteomyelitis of the occiput, the atlas, and the axis. a report of five cases. *J Bone Joint Surg Am*. 1987;69(7):1069-1073.
28. Medvedev G, Palacios E, Jones W. Iatrogenic occipital osteomyelitis. *Ear Nose Throat J*. 2009;88(1):720-721.
29. Chang PC, Fischbein NJ, Holliday RA. Central skull base osteomyelitis in patients without otitis externa: imaging findings. *Am J Neuroradiol*. 2003;24(7):1310-1316.
30. Blitzer A, Lawson W, Meyers BR, Biller HF. Patient survival factors in paranasal sinus mucormycosis. *Laryngoscope*. 1980;90(4):635-648.
31. Barcelos ACES, Patriota GC, Netto AU. Nontraumatic atlantoaxial rotatory subluxation: grisel syndrome. case report and literature review. *Glob Spine J*. 2014;4(3):179-185.
32. Das S, Chakraborty S, Das S. Grisel syndrome in otolaryngology: a case series with literature review. *Indian J Otolaryngol Head Neck Surg*. 2019;71(1):66-69.
33. Spennato P, Nicosia G, Rapanà A, et al. Grisel syndrome following adenoidectomy: surgical management in a case with delayed diagnosis. *World Neurosurg*. 2015;84(5):1494. e7-1494. e12.
34. Low G, Leong A, George R, Tan G. C1/C2 osteomyelitis secondary to malignant otitis externa complicated by atlantoaxial subluxation—a case report and review of the literature. *AME Case Reports*. 2020;4:19-19. doi:10.21037/acr.2020.03.04

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