Central Skull Base Osteomyelitis: Diagnostic Dilemmas and Management Issues

Sujata N. Muranjan^{1,5} · Satish V. Khadilkar² · Sanjay C. Wagle³ ·
Sunila T. Jaggi⁴

Received: 9 May 2015 / Accepted: 21 September 2015 / Published online: 25 September 2015
© Association of Otolaryngologists of India 2015

Abstract The aim of this study is to describe the clinical presentation of central skull base osteomyelitis and to discuss the classical imaging findings and various diagnostic and therapeutic challenges faced in the management of this condition. This is a retrospective analysis of inpatient case records, carried out in a multidisciplinary tertiary care hospital. The study subjects included five elderly diabetic patients presenting to the ENT surgeon or neurologist with headache followed by multiple cranial nerve paralysis with no temporal bone involvement in four patients and a past history of otitis externa in one patient. These patients were diagnosed to have an infective pathology of the central skull base detected by imaging and confirmed by biopsy in three. All were treated successfully with antibiotics administered for an average period of 6 weeks. Three patients followed up over 4 years and showed no relapses. One succumbed to other medical co morbidities after 8 months and one diagnosed a month prior is still under follow up. A symptom complex of headache and cranial neuropathies usually raises the suspicion of malignancy. Central skull base osteomyelitis, a

relatively uncommon pathology, must also be considered as a possible differential diagnosis despite absence of a definite septic focus. Imaging studies showing bony destruction and adjacent soft tissue involvement should raise the suspicion of this clinical entity. Malignancy needs to be ruled out by biopsy. Early diagnosis and prompt initiation of antibiotics administered for an adequate duration is of paramount importance in successfully treating these patients. A multidisciplinary approach is needed for a successful outcome.

Keywords Central skullbase · Osteomyelitis · Clivus · Cranial neuropathies

Introduction

Malignancy is usually suspected in patients presenting with headache, lower cranial nerve paralysis and imaging findings of central skull base destruction. A nasopharyngeal mass on endoscopy further substantiates this. However, concomitant presence of diabetes mellitus should also raise suspicion of an infective pathology. The central skull base comprises of the clivus, bordered anteriorly by the nasopharynx, posteriorly by the foramen magnum, anterolaterally by the petrous temporal bone and posterolaterally by the jugular foramen. It is a conduit for passage of the ninth, tenth, eleventh and twelfth cranial nerves. Osteomyelitis involving this area termed as central skull-base osteomyelitis (CSBO) is rare and distinct from the widely reported typical temporal bone osteomyelitis (TBO) secondary to otitis externa. Awareness of this condition and its early diagnosis is imperative since it is associated with high morbidity due to multiple cranial nerve involvement.

We present a series of five cases with this rare diagnosis.

✉ Sujata N. Muranjan
sujatamuranjan@gmail.com

¹ Department of ENT, Bombay Hospital and MRC, Mumbai, India

² Department of Neurology, Bombay Hospital and MRC, Mumbai, India

³ Department of General Medicine, Bombay Hospital and MRC, Mumbai, India

⁴ Department of Imaging, Bombay Hospital and MRC, Mumbai, India

⁵ Suman Apartments, 3rd floor, 16 B Naushir Bharucha Road, Tardeo, Mumbai 400 007, India

Materials and Methods

Case records of five patients, admitted over 7 years were retrospectively analyzed. All patients were males aged between 55 and 70 years. All had infection of bone and soft tissue of the central skull base. Of these only one had past history of otitis externa with temporal bone involvement. The diagnosis was established by clinical, radiological and histopathology findings following which antibiotics were administered for an average period of 6 weeks.

Case 1 (60/M) had right-sided headache and facial pain with reduced hearing 4 months prior to presentation. A contrast enhanced computerized tomography scan (CT scan) of the brain done at that time was normal. Diagnostic nasal endoscopy (DNE) had revealed a diffuse minimal bulge in the nasopharynx on the right side. Biopsy from this site was inconclusive. A right ear myringotomy with insertion of ventilation tube was performed. The complaints had resolved following antibiotics administered for 10 days. However, 4 months later, the patient presented with symptoms and clinical signs listed in Tables 1 and 2.

On admission, a nasogastric tube was inserted. Magnetic resonance imaging (MRI) revealed diffuse abnormal soft tissue in the midline in the region of the central skull base and nasopharynx extending laterally on both sides with obliteration of the fossa of Rosenmuller and Eustachian tube openings. This was iso to hypo intense on T1 weighted images with a variable signal intensity on T2 weighted images. There was intense heterogenous post contrast enhancement with some focal non enhancing necrotic

areas. There was almost complete loss of normal marrow signal in the clivus which revealed intense post contrast enhancement alongwith involvement of the occipital condyles. The soft tissue component extended along the petroclival fissure bilaterally as well as the right hypoglossal canal and jugular foramen. These findings were suggestive of an inflammatory/infective pathology involving the central skullbase with lateral extensions (Table 3). Submucosal nasopharyngeal biopsy was taken, which was reported as pyogenic abscess with lymphoid hyperplasia with no evidence of malignancy, dysplasia, tuberculosis or fungus. The culture did not grow any organisms. Antibiotics (Table 4) were given for 6 weeks and antihypertensive and oral medications for diabetes were continued. Analgesics were given for headache. Speech therapy and swallowing exercises were initiated. The symptoms gradually improved over 6 weeks and DNE done then showed considerable reduction in the nasopharyngeal bulge. The nasogastric tube was removed and the patient discharged. His voice and tongue movements were normal at 8 months follow up. The patient followed up yearly for 4 years and was symptom free.

Case 2 (60/M) was diagnosed to have diabetes a month prior. He presented to the neurologist with dysphagia of 10 days' duration for which a nasogastric tube had been inserted. He also had bilateral moderate to severe conductive hearing loss due to middle ear fluid. DNE revealed a fluctuant bulge in the nasopharynx (Fig. 1). MRI (Fig. 2) revealed a nasopharyngeal abscess with findings as listed in Table 3.

Table 1 Symptoms with duration

Case no	Age/sex	HT	DM	Symptoms	Duration	Cr Nvs
1	60/M	+	+	Right sided headache, Dysphagia, Nasal regurgitation Hoarseness, Aspiration Slurring	All symptoms of 20 days duration	9th 10th 12th
2	60/M	+	+	Dysphagia Slurring Reduced hearing both ears	12 days 10 days 20 days	9th 12th
3	72/M	+	+	Headache, Nasal blockage, Nasal discharge Neck pain Diplopia	All symptoms of 1 month duration	6th
4	55/M	+	+	Headache Dysphagia, Nasal regurgitation Hoarseness, Aspiration Slurring Diplopia, Ptosis	3 months Symptoms of 6 weeks duration	9th 10th 12th 6th 3rd
5	55/M	+	+	Headache, Dysphagia, Hoarseness Slurring Neck pain, Diplopia	All symptoms of 3 weeks duration	11th 12th 6th

HT Hypertension, DM diabetes mellitus, Cr Nvs cranial nerves

Table 2 Clinical findings

Case no	Diagnostic nasal endoscopy	Ear	Ocular movements	Palatal movements	Tongue movements	Laryngoscopy	Neck movements
1	Diffuse bulge in nasopharynx	Grommet right side Bilateral EACs—normal	Normal	Bilaterally absent, absent gag reflex	Deviation to right	Right vocal fold paralysis, pooling of saliva in right PF	Normal
2	Fluctuant bulge in nasopharynx extending bilaterally up to ET openings	Bilateral dull TMs Bilateral EACs—normal	Normal	Bilaterally reduced, Absent gag reflex	No movements, fasciculations	Normal mobility of both vocal folds, pooling of saliva in both PFs	Normal
3	Polyps, crusts in the left nasal cavity, trimmed left MT adherent to lateral nasal wall	Grommet on left side Bilateral EACs—normal	Absent movement in left lateral gaze	Normal	Normal	Normal	Painful
4	Normal	Bilateral EAC edema Bilateral TMs—normal	Absent movement in left lateral gaze	Bilaterally absent, Absent gag reflex	Reduced movement on left side with fasciculations	Left vocal fold paralysis, pooling of saliva in left PF	Normal
5	Not done	Bilateral dull TMs	Absent movement in left lateral gaze	Normal	Deviation to right	Left vocal fold paralysis, pooling of saliva in left PF	Neck stiffness

TM Tympanic membrane, *EAC* external auditory canal, *PF* pyriform fossa, *ET* Eustachian tube, *MT* middle turbinate

Table 3 Extent of disease on imaging

Case no	Imaging modality	Nasopharynx	Preclival region	Clivus	Occipital condyles	Petrous apex	Hypoglossal canal	Jugular foramen	C1, C2 vertebrae
1	MRI CT	+	+	+	+	–	+	+	–
2	MRI CT	+ abscess	+	+	–	–	+	+	+
3	CT	–	–	+	–	+	–	–	+ atlanto occipital joint
4	MRI CT	+	+	+	–	+ bilateral	+	+	–
5	MRI	+	–	+	+	+ bilateral	+	+	–

Injection insulin and antibiotics (Table 4) were started. Under general anesthesia with endotracheal intubation, an incision and drainage of the nasopharyngeal abscess was done under endoscopic guidance. A wide opening was created to drain out the pus. This was sent for bacterial, mycobacterial and fungal smear and culture-sensitivity studies. Granulations from the walls of the abscess cavity were sent for histopathology. Bilateral myringotomy with

ventilation tube insertion was also done. The culture did not grow any organisms. The histopathology revealed a pyogenic abscess with no caseation, granulomas, fungus or malignancy. After 2 weeks, there was marginal improvement in the symptoms but the patient refused any further medication due to financial constraints and requested discharge against medical advice. Two months later, he followed up with worsening of complaints. A repeat MRI

Table 4 Antibiotics with duration

Case no	Antibiotic	Dosage	Duration
1	Ceftazidime	2 gm, 8 hourly	6 weeks
	Levofloxacin	500 mg, once daily	6 weeks
2	<i>1st admission</i>		
	Vancomycin	1 gm, 12 hourly	2 weeks
	Metrogyl	500 mg, 8 hourly	2 weeks
	Ceftazidime	2 gm, 8 hourly	2 weeks
	<i>2nd admission</i>		
	Piperacillin–Tazobactam	4.5 gms, 8 hourly	6 weeks
3	Fluconazole	200 mg, once daily	6 weeks
	Piperacillin–Tazobactam	4.5 gms, 8 hourly	6 weeks
	Levofloxacin	500 mg, once daily	6 weeks
4	<i>1st admission</i>		
	Piperacillin–Tazobactam	2.2 gms, 8 hourly	5 days
	Levofloxacin	250 mg, once daily	11 weeks
	Imipenem	1 gm loading dose, 500 mg, 12 hourly	6 weeks
	<i>2nd admission</i>		
5	Piperacillin–Tazobactam	2.2 gms, 8 hourly	5 weeks
	Ceftazidime	2 gm, 12 hourly	6 weeks
	Ciprofloxacin	500 mg, 12 hourly

Fig. 1 Endoscopic view showing a nasopharyngeal abscess (asterisk) and Eustachian tube opening (ET)

showed residual disease. Incision drainage was repeated but minimal pus was obtained and this time too no bacterial organisms were cultured. The fungal smear this time however was positive for yeast. Antibiotics were restarted (Table 4) and continued for 6 weeks along with antifungal

Fig. 2 Post contrast fat saturated axial T1 weighted image through the skull base showing a thick walled irregular peripherally enhancing abscess in the mid line retropharyngeal region (asterisk) with erosion of bilateral petrous apices marked by arrow

medication. Speech therapy and swallowing exercises were started. Palatal mobility gradually improved and was completely restored by 6 weeks. The nasogastric tube was removed. The tongue movements improved marginally and the patient was discharged. At 8 months follow up his swallowing was normal though his tongue movements had residual deficit and the dysarthria persisted. MRI after 11 months showed complete resolution of the disease. He followed up yearly for 4 years and showed no relapse though the dysarthria still persisted.

Case 3 (72/M) had undergone endoscopic sinus surgery for a left maxillary sinus polyp 3 months prior in another institute and left ear myringotomy with ventilation tube insertion a month prior. He presented to the neurologist with signs and symptoms of a month's duration (Tables 1, 2). He had previously received 5 weeks of intravenous Ceftazidime and oral Ciprofloxacin but all symptoms had persisted. The CT scan revealed involvement of the central skullbase along with disease in all the paranasal sinuses suggesting inflammatory/infective pathology (Table 3). Antibiotics (Table 4) and injection insulin were started. Endoscopic sinus surgery was performed under general anesthesia, and disease was cleared from all paranasal sinuses bilaterally. The material obtained was sent for bacterial, mycobacterial and fungal smear and culture-sensitivity testing as also for histopathology. However, no organisms were cultured. Histopathology suggested sino-nasal inflammatory disease. The antibiotics were continued for 6 weeks. Post-operative nasal cleaning and douching

were done. The nasal cavity healed in 4 weeks' time. Neck, facial pain and headache resolved over 5 weeks and the left lateral rectus paralysis recovered after 8 weeks. He followed up yearly for 4 years and was symptom free.

Case 4 (55/M) had uncontrolled diabetes since 11 years and associated co-morbidities like nephropathy, retinopathy, peripheral neuropathy and coronary artery disease. He had a past history of bilateral otitis externa 5 months prior that had resolved with intravenous antibiotics. His presenting symptoms of 6 weeks' duration and clinical findings are listed (Tables 1, 2). The patient was drowsy but responsive to verbal commands. A percutaneous endoscopic gastrostomy (PEG) tube had been inserted for feeding purpose. Additionally, there was a tender, diffuse, non-fluctuant swelling of the left parotid gland with pus extruding from its duct, which was sent for culture.

An ultrasound examination revealed a bulky left parotid gland suggesting an inflammatory pathology without abscess formation. The disease extent on MRI (Fig. 3) and CT (Fig. 4) is listed in Table 3. Additionally, there was mucosal thickening of the left sphenoid and left posterior ethmoid sinuses. Antibiotics were started (Table 4) along with Insulin. The dosage was altered in view of raised serum creatinine levels. The pus grew *Klebsiella pneumoniae* and Methicillin resistant *Staphylococcus aureus* (MRSA). Injection Imipenem was started as per the sensitivity report. The patient's sensorium improved following correction of sodium levels and the parotid swelling subsided over 4 days. The patient requested discharge and

agreed to continue the injectable antibiotics locally for 5 weeks. He was advised to monitor his blood sugar. Follow-up 6 weeks later however did not show significant clinical improvement. Biopsy was not considered due to anesthesia fitness issues and in view of prior antibiotics used. Intravenous Piperacillin–Tazobactam was restarted and oral Levofloxacin continued. After 5 weeks swallowing and ptosis had improved but serum creatinine levels rose to 3.5 and the platelet count reduced to 65,000. Hence antibiotics were discontinued. Over the next 2 months, serum creatinine level and platelet count returned to normal. Five months after his first presentation to us, the ptosis had resolved completely and his voice and swallowing improved steadily. Three months later i.e. 8 months after his first presentation, however he developed breathlessness, bilateral pedal oedema and altered sensorium. Biochemical tests showed a serum creatinine of 4.5 mg/dl, deranged serum electrolytes and blood sugar of 210 mg/dl. The 2D echocardiography showed an ejection fraction of 30 %. He was intubated and kept on ventilatory support and dialysis was started but he ultimately succumbed to cardiac and renal failure after 12 days.

Case 5 (55/M) a known case of diabetes mellitus since 20 years, presented with symptoms of 3 weeks duration (Table 1). He had been diagnosed to have meningitis at another institute and had received injection Vancomycin and Amikacin as well as Meropenem. A PEG tube was inserted for feeding. He had been operated for squamous cell carcinoma of the buccal mucosa 8 months prior and had received post-operative chemotherapy and radiotherapy.

At presentation, he was febrile and drowsy but obeying commands. There was neck stiffness with a positive

Fig. 3 T1 weighted axial image revealing loss of normal marrow signal in the clivus (asterisk) with peri clival soft tissue

Fig. 4 Axial CT scan showing ill-defined bone destruction involving the anterior and right lateral margin of the clivus marked by arrow

Kernig's sign. Local examination of the oral cavity indicated that the previous surgical reconstruction had taken up well. A healed scar of neck dissection was seen with no palpable lymph nodes. The other positive clinical signs are listed in Table 2.

His total WBC count was 8300, blood sugar 220 mg/dl and Sodium 126 mEq/l. The CSF study showed proteins of 118, sugar of 38 with a white blood cell count of 501 and adenosine deaminase of 6. The MRI showed post-operative changes in the left infratemporal fossa and maxillary sinus along with findings suggestive of CSBO with extent as listed in Table 3. It also showed meningitis with a communicating hydrocephalus. Injection Ceftazidime and Ciprofloxacin were started and continued for 6 weeks (Table 4). The blood sugar was monitored closely. His regular anti hypertensive medication and Insulin were continued along with sodium supplementation. He received regular physiotherapy and speech therapy along with swallowing exercises.

Two weeks later his voice and swallowing improved and he was able to take some food orally. At the time of discharge at 6 weeks he was able to swallow all food orally and the PEG tube was removed. His left lateral rectus paralysis however persisted. He is scheduled for follow up after a month.

Discussion

Skullbase osteomyelitis (SBO) usually occurs in the temporal bone secondary to otitis externa. An atypical form now termed central skull base osteomyelitis (CSBO) is centered on the sphenoid and occipital bones rather than the temporal bone [1]. The first report of SBO in patients without external otitis or any other contiguous infection was made by Sie et al. [2] and the term "Atypical skull base osteomyelitis" was used to describe it [3]. The disease usually occurs in elderly diabetics, as was seen in all our cases. Previous work has supported diabetes mellitus as a predisposing factor in the development of malignant otitis externa due to defects in chemotaxis and phagocytosis of polymorphonuclear leukocytes (PMNs), monocytes, and macrophages. The oxidative burst and killing function of PMNs has been shown to be reduced in diabetics [4]. These patients may initially have headache as the only symptom, with cranial neuropathies occurring much later [5]. This pattern was seen in three of our cases. Persistent headache in a diabetic patient should therefore not be ignored and warrants an imaging study.

CSBO may present without any contiguous focus of infection in the ear, nose or sinuses [6]. This was seen in Cases 1, 2 and 5. Cases 3 and 4 had an obvious focus of infection in the paranasal sinuses. The latter also had an

Fig. 5 Post contrast axial T1 weighted image showing enhancing abnormal marrow signal in the clivus (*arrow*) and associated abnormal enhancing soft tissue in the right para clival region and along the petrous apex (*asterisk*)

additional left parotitis and past history of otitis externa. Past history of otitis externa even if apparently resolved before onset of presenting symptoms should raise suspicion of an underlying infective cause.

Imaging plays an important role in diagnosing SBO. MRI depicts soft tissue involvement; CT scan, bony erosions. In very early stages, a CT scan may fail to demonstrate any findings as was seen in our first case. Rowlands et al. [7] have also described a case wherein an early CT scan failed to demonstrate any bony destruction. Although MRI can show bony texture changes, its main value lies in establishment of the ill-defined, diffuse process of soft tissue surrounding the involved bones [8]. The MRI findings in SBO are classical. Highly sensitive but non-specific MR findings of osteomyelitis include marrow T1 hypointensity and T2 hyperintensity [9]. Chang et al. reported clival marrow and preclival soft tissue abnormalities in all their cases [1]. Our MRI findings also showed the abnormal soft tissue to be iso to hypo intense on T1 weighted images with variable signal intensity on T2 weighted images with intense but heterogeneous post contrast enhancement and almost complete loss of normal marrow signal in the clivus (Fig. 5). All patients had radiological evidence of fluid in the middle ear and mastoids. This is secondary to Eustachian tube dysfunction as a result of nasal/nasopharyngeal mucosal inflammation and impaired palatal mobility following lower cranial nerve paralysis. There was no evidence of temporal bone infection in Cases 1, 2, 3 and 5. Case 4 had otorrhoea with external auditory canal edema but there was no accompanying otalgia.

Varied differential diagnoses exist in patients presenting with lower cranial nerve paralysis. When initial imaging illustrates a destructive or diffusely infiltrative central skull base lesion, neoplastic processes such as nasopharyngeal carcinoma, lymphoma or leukemia need to be considered. Inflammatory pseudotumor, granulomatosis with polyangiitis (Wegener's), tuberculosis, sarcoidosis, fibrous dysplasia and Paget disease may also present in a similar manner [1]. Diagnosis of CSBO is often delayed, as imaging findings can mimic central skull base malignancy and biopsies may show nonspecific and non-diagnostic inflammatory changes [10]. In Case 1, there was delay in diagnosis when the first biopsy report was inconclusive. A delay was also reported by Cavel et al. [8] and was attributed to lack of specific signs as well as to the clinical and imaging traits shared by CSBO and malignant processes. Since the imaging findings frequently mimic malignancy [11] accurate histological diagnosis becomes all the more important. We had obtained tissue biopsy in Cases 1, 2 and 3 where malignancy had been excluded.

Antimicrobial therapy forms the cornerstone of management of CSBO. In Cases 1 and 2, despite histopathology reporting a pyogenic abscess, no organisms were cultured. All the patients had received antibiotics prior to presentation at our institute. This could be the reason why no organisms were cultured in Cases 1, 2 and 3. Antibiotics were therefore started empirically. This empirical approach is supported by the recommendations of Djalilian et al. [12] for the treatment of culture-negative SBO. *Pseudomonas* is the common causative organism in SBO but the possibility of polymicrobial infection has to be borne in mind and broad-spectrum antimicrobial therapy should therefore be instituted. In our series, Cases 1 and 5 showed a good response to intravenous Ceftazidime whereas Cases 2, 3 and 4 responded well to Piperacillin–Tazobactam. It is also important to use antibiotics like Quinolones that penetrate bone. Cases 1, 3 and 4 received Levofloxacin for 6 weeks and Case 5 Ciprofloxacin. The immunocompromised state in diabetics can be a predisposing factor to fungal infections as seen in Case 2 where oral Fluconazole was added following a positive fungal culture.

The current recommendations in the setting of new diagnosis of SBO include 6 weeks to many months of antibiotics [13]. The therapeutic response is usually seen 2–3 weeks following antibiotic administration. This is definitive evidence that the underlying pathology is infective in nature. Cases 1, 2, 3 and 5 showed improvement in their symptoms after 2 weeks of antibiotics. These were then continued for 6 weeks. Since antibiotics needed to be given for a prolonged period, we had secured intravenous access in three of our patients by means of a peripherally inserted central venous catheter (PIC) that was inserted

under fluoroscopic guidance by the interventional radiologist. In Case 5 a central line was inserted.

Few hurdles were faced in managing these patients. Initially, we were not sure of the diagnosis in Case 1. We had therefore reviewed the outside histopathology slides to ascertain that a malignancy had not been missed. After treating the next two patients with more or less identical clinical presentation, we established our diagnostic criteria for these cases presenting with headache, lower cranial nerves paralysis and classical MRI findings. For reasons stated, we could not obtain tissue biopsy in the fourth case. In Case 5, though there was a past history of buccal mucosa malignancy, the MR findings were classical for CSBO. We therefore did not attempt a tissue biopsy and antibiotics were started promptly based on the MRI report. Recent studies have considered the possibility that prompt administration of antibiotics might obviate the need for tissue biopsy in some patients [8].

Duration and cost of treatment were the other difficult issues. Each patient had undergone at least two hospital admissions and one had defaulted in completing the full antibiotic course. The patients required extensive counseling regarding this.

Cases 1, 2 and 3 were treated successfully and have remained symptom-free with no relapses over a period of 4 years. Case 4 with multiple medical co morbidities succumbed to cardiac and renal failure 8 months after his first presentation to us. Case 5 was discharged a month prior and is due for follow up.

Key Messages

An elderly diabetic presenting with persistent headache warrants appropriate clinical and radiological assessment, keeping the diagnosis of central skullbase osteomyelitis (CSBO) in mind. MRI is the radiological investigation of choice that accurately delineates soft tissue and marrow involvement. CT scan determines bony erosion. The diagnosis of CSBO needs to be substantiated by histopathology and microbiology to exclude malignancy. Appropriate antibiotics have to be started at the earliest and continued for at least 6 weeks. Proper follow up is needed to detect relapses. A multidisciplinary approach with involvement of the neurologist, otorhinolaryngologist, intensivist, neuroradiologist and speech therapist is paramount for optimum management and successful outcomes in these patients.

Acknowledgments Dr. Unnikrishnan K. Menon, Associate Prof., ENT Department, Amrita Institute of Medical Sciences and Research Centre, Kerala for critical review and valuable inputs.

Compliance with Ethical Standards

Conflict of interest Dr. Sujata Muranjan declares that she has no conflict of interest. Dr. Satish Khadilkar declares that he has no conflict of interest. Dr. Sanjay Wagle declares that he has no conflict of interest. Dr. Sunila Jaggi declares that she has conflict of interest.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

References

1. Chang PC, Fischbein NJ, Holliday RA (2003) Central skull base osteomyelitis in patients without otitis externa, imaging findings. *Am J Neuroradiol* 24:1310–1316
2. Sie KC, Glenn MG, Hillel AH, Cummings CW (1991) Osteomyelitis of the skull base, etiology unknown. *Otolaryngol Head Neck Surg* 104:252–256
3. Malone DG, O'Boynick PL, Ziegler DK, Batnitzky S, Hubble JP, Holladay FP (1992) Osteomyelitis of the skull base. *Neurosurgery* 30:426–431
4. Sreepada GS, Kwartler JA (2003) Skull base osteomyelitis secondary to malignant otitis externa. *Curr Opin Otolaryngol Head Neck Surg* 11:316–323
5. Grobman LR, Ganz W, Casiano R, Goldberg S (1989) Atypical osteomyelitis of the skull base. *Laryngoscope* 99:671–676
6. Chandler JR (1989) Malignant external otitis and osteomyelitis of the skull. *Am J Otol* 10:108–110
7. Rowlands RG, Lekakis GK, Hinton AE (2002) Masked pseudomonas skull base osteomyelitis presenting with a bilateral Xth cranial nerve palsy. *J Laryngol Otol* 116:556–558
8. Cavel O, Fliss DM, Segev Y, Zik D, Khafif A, Landsberg R (2007) The role of the otorhinolaryngologist in the management of central skull base osteomyelitis. *Am J Rhinol* 21(3):281–285
9. Erdman WA, Tamburro F, Jayson HT, Weatherall PT, Ferry KB, Peshock RM (1991) Osteomyelitis: characteristics and pitfalls of diagnosis with MR imaging. *Radiology* 180:533–539
10. Subburaman N, Chaurasia MK (1999) Skull base osteomyelitis interpreted as malignancy. *J Laryngol Otol* 113:775–778
11. Clark MP, Pretorius PM, Byren I, Milford CA (2009) Central or atypical skull base osteomyelitis: diagnosis and treatment. *Skull Base* 19:247–254
12. Djalilian HR, Shamloo B, Thakkar KH, Najme RM (2006) Treatment of culture-negative skull base osteomyelitis. *Otol Neurotol* 27:250–255
13. Patmore H, Jebreel A, Uppal S, Raine CH, McWhinney P (2010) Skull base infection presenting with multiple lower cranial nerve palsies. *Am J Otolaryngol* 31:376–380