Skull Base Osteomyelitis - Extent, Clinical Impact and Medical Management

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Abstract

Skull base osteomyelitis is a complex and fatal clinical entity that is often misdiagnosed for malignancy. Typical SBO are initiated by ear infection with Pseudomonas Aeruginosa as the usual pathogen, whereas atypical SBO centred on the sphenoid and occipital bones rather than temporal bone. Culture sensitivities will guide the choice of antibiotics, influenced by local prescribing policies. Infective causes must be included in the differential diagnosis of all patients with skull base masses, not just diabetic and immunocompromised patients, especially in the setting of headache, raised ESR and CRP, and multiple lower CNP. Accurate diagnosis and evaluation of the disease depends on appropriate physical examination and radiological assessment including both CT and MRI scans. Treatment with quinolones – especially Ciprofloxacin is the first line treatment for skull base osteomyelitis. If the diagnosis is made and aggressive treatment started early as per culture and sensitivity or empirical based treatment, for appropriate period of time, outcome has improved without any surgical intervention, neural deficit improves, although full recovery of cranial nerve function may not occur.

Keywords: Osteomyelitis, malignancy, SBO, Aeruginosa.

INTRODUCTION

Skull base osteomyelitis (SBO) is a serious, life-threatening condition seen most in elderly diabetic or immunocompromised patients.

Typical cases of skull base osteomyelitis (SBO) or MOE are initiated by ear infections in older diabetic patients, with Pseudomonas Aeruginosa as the usual pathogen [1, 2]. Whereas atypical skull base osteomyelitis, centred on the sphenoid and occipital bones rather than the temporal bone, and termed as central skull base osteomyelitis (CSBO) occurs less frequently and does not begin with otitis externa [3, 4]. It can present with headache and a variety of cranial neuropathies, often a combination of VI and lower cranial nerve (CN) neuropathies. The imaging findings frequently mimic malignancy, which makes accurate histological diagnosis all the more important.

A wide variety of soft tissue masses may be encountered in the skull base such as cholesterol granuloma, schwannoma and meningioma [5, 6]. Interestingly, they have been described to be associated with lower cranial nerve palsies [7].

As the infection spreads through the skull base bone erosion occurs with the formation of soft tissue granuloma and abscesses [8].

Despite advances in new diagnostic modalities, introduction of new antibiotics, and operative techniques, management of SBO remains a great challenge. We present 15 cases of skull base osteomyelitis with or without a history of diabetes and discuss the antimicrobial management of these cases.

MATERIAL AND METHODS

The medical records and imaging studies of 15 patients identified as having SBO were retrospectively reviewed. Cases were identified over the course of 3 years from 2015-2018. Inclusion criteria were cases of skull base infection as suggested by radiological, histological and microbiological findings.
All patients were male except two and ranged from 22-67 years in age with a mean age of 44 years. HRCT temporal bone was done for all patients. MRI images were assessed qualitatively with regard to skull base marrow signal intensity, presence of abnormal soft tissue and signal intensity of any abnormal soft tissue. Typical SBO in 12 patients except three. Four patients underwent combined 99Tc and gallium 67 scanning at the time of initial diagnosis and at follow up.

Four patients underwent direct tissue sampling from different sites eg. sphenoidal mass, temporal bone external auditory canal and skull base. Biopsy specimens were delivered to microbiology for culture and to pathology for histologic analysis. No tissue sampling was done for the remaining 11 patients as diagnosis was confirmed with imaging findings. All patients were treated with broad spectrum antibiotics based on antibiotic susceptibility results. Five patients underwent ear surgery. Two patients underwent facial nerve decompression for unsafe CSOM with grade IV LMN facial palsy. All patients were followed up for neurological improvement and recurrence for an average period of 2 years.

**Sampling**
The demographic characteristics, clinical presentation and management of 15 patients who were included in the study were as follows:

<table>
<thead>
<tr>
<th>CASE NO</th>
<th>AGE</th>
<th>SEX</th>
<th>SITE</th>
<th>CLINICAL FEATURES</th>
<th>TREATMENT</th>
<th>NERVE INVOLVED</th>
<th>RISK FACTOR</th>
<th>POST TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>34</td>
<td>M</td>
<td>CT : Erosion of rt petrous apex with rt Meckel’s cave</td>
<td>SBO</td>
<td>Rt severe headache with b/l ear discharge Safe CSOM</td>
<td>Tab Ciprofloxacin 500 mg Q12 h x 3 months</td>
<td>Rt abducens nerve palsy,</td>
<td>Non-diabeti c</td>
</tr>
<tr>
<td>2.</td>
<td>47</td>
<td>M</td>
<td>Widening of rt TMJ with destruction of mandibular condyle with sequestrum, no central involvement</td>
<td>SBO</td>
<td>Rt earache with ear discharge Safe CSOM</td>
<td>Inj Piptaz 4.5 g 8 hourly x 1 week. Tab Ciprofloxacin 500 mg Q12h x 3 months</td>
<td>Facial nerve palsy</td>
<td>Diabet ic</td>
</tr>
<tr>
<td>3.</td>
<td>32</td>
<td>M</td>
<td>Sphenoid sinus[erosion of greater wing of sphenoid]</td>
<td>CSBO Sphe noid sinus mass biopsy</td>
<td>Headache Facial pain</td>
<td>Inj Augmentin 1.2 g Q12h x 1 month</td>
<td>Facial nerve palsy</td>
<td>Diabet ic</td>
</tr>
<tr>
<td>4.</td>
<td>22</td>
<td>M</td>
<td>MRI: ill-defined signal in rt mastoid bone, external auditory canal,rt carotid and anterior aspect of rt petrous apex</td>
<td>SBO</td>
<td>Pain in rt TMJ, rt tinnitus, Rt ear discharge</td>
<td>Inj Augmentin1.2 gm Q12h x 1 month</td>
<td>Facial nerve palsy</td>
<td>Non-diabeti c</td>
</tr>
<tr>
<td>5.</td>
<td>64</td>
<td>M</td>
<td>CT:mild enhancing lesion in lateral part of external auditory canal extending to infraaural, sub cutaneous tissue, extraaural region, Erosion of posterior and inferior wall of EAC</td>
<td>SBO No surgery</td>
<td>Rt severe earache, Rt ear discharge</td>
<td>Inj piptaz 4.5 g 8 hourly x 2 weeks, Tab linozolid 600 mg Q12h x 2 weeks</td>
<td>Nil</td>
<td>Diabet ic</td>
</tr>
<tr>
<td>6.</td>
<td>65</td>
<td>F</td>
<td>CT : Enhancing lesion involving skull base on rt side medial to rt styloid process and lateral to clivus with extension along the jugular foramen, hypoglossal</td>
<td>CSBO NO SURGERY</td>
<td>Rt sided headache, diplopia, vomiting</td>
<td>Inj piptaz 4.5 gm 8 hourly x 1 month, Tab Ciprofloxacin 750 mg Q12h x 1 month</td>
<td>Nil</td>
<td>Diabet ic</td>
</tr>
<tr>
<td>No.</td>
<td>Name</td>
<td>Age</td>
<td>Gender</td>
<td>CT Description</td>
<td>MRI Description</td>
<td>Treatment</td>
<td>Investigation</td>
<td>Improvement</td>
</tr>
<tr>
<td>-----</td>
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<tr>
<td>7.</td>
<td>RK</td>
<td>38</td>
<td>M</td>
<td>Moderately enhancing soft tissue opacification involving left middle ear and mastoid cavity extending inferiorly along carotid space and around spinoous process with erosion of mastoid trabeculae, vertical portion of facial canal, stylo mastoid foramen.</td>
<td>Bilateral mastoid air cells with erosion of mastoid trabeculae</td>
<td>Tab Ciprofloxacin 500 mg Q12h for 2 months</td>
<td>Facial nerve palsy</td>
<td>Improved</td>
</tr>
<tr>
<td>8.</td>
<td>Rs</td>
<td>42</td>
<td>M</td>
<td>Non enhancing soft tissue opacification left middle ear extending into Prussac’s space with mild soft tissue opacification of mastoid air cells with erosion of mastoid trabeculae. Vertical portion of facial canal, stylo mastoid foramen.</td>
<td>Ill-defined soft tissue surrounding the left mastoid bone with involvement of the external pinna and extending into the external auditory canal causing mild erosive changes of the anterior and lateral margins of the left mastoid bone.</td>
<td>Inj Ceftriaxone 1 gm x 1 month, Inj Metronidazole 500 mg in 100 cc x 1 month, Tab Ciprofloxacin 500 mg x 3 months</td>
<td>Facial nerve palsy, Diabetic</td>
<td>Not improved</td>
</tr>
<tr>
<td>9.</td>
<td>KS</td>
<td>67</td>
<td>M</td>
<td>Ill-defined soft tissue surrounding the left mastoid bone with involvement of the external pinna and extending into the external auditory canal causing mild erosive changes of the anterior and lateral margins of the left mastoid bone. MRI: There is moderately enhancing soft tissue involving the left external ear middle ear cavity, mastoid air cells on the left side. The soft tissue is seen extending anteriorly into the mandibular fossa with erosion of the posterior cortex of the mandibular condyle with its anterior subluxation that further extending anteriorly into the infratemporal fossa around the zygomatic arch and the left TM joint abutting the lateral</td>
<td>Left ear discharge, earache with decrease hearing</td>
<td>Left facial palsy with IX, X, XII palsy, SNHL</td>
<td>Not improved</td>
<td></td>
</tr>
<tr>
<td>SBO Explor Biopsy from rt ear polyp</td>
<td>Facial palsy</td>
<td>Inj Piptaz 4.5 gm 8 hourly for 1 month, T Ciprofloxacin 500 mg Q12h x 3 months</td>
<td>NAD</td>
<td>Improved</td>
<td></td>
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<tr>
<td>RT ear discharge with earache, rt tinnitus, swallowing difficulty, slurred speech</td>
<td>No surgery, SBO</td>
<td>Inj Piptaz 750 mg Q12h for 3 months</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inj Piptaz 2.25 gm 8 hourly for 1 month</td>
<td>Inj Ciprofloxacin 750 mg Q12h for 3 months</td>
<td></td>
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</table>
**RESULTS**

Patient’s clinical characteristics and management were as summarized in Table-1. Patients presented with ear discharge except three (case 3, 6 and 15 central skull base osteomyelitis). They presented with headache and without evidence of otitis externa or mastoiditis. Underlying Diabetes mellitus was present in 9 patients. VII Cranial nerve palsy was present in 6 patients and cranial nerve IX, X and XII were affected in 3 patients. 5 patients were without any nerve involvement.

Two patients 7 and 8 showed fluid in middle ear, this was secondary to eustachian tube dysfunction as a result of nasal/nasopharyngeal mucosal inflammation and impaired palatal mobility causing lower cranial nerve palsy.
Axial CT sections of skull bone window (Fig-1) and soft tissue window (Fig-2) showing erosion of the clivus with small extra axial collection along the left side of clivus and bilateral otomastoiditis (Fig-3)

Fig-4: Coronal section of skull through the TM joint showing complete destruction of mandibular right condyle with widening of right TM joint and small sequestrum

Fig-5: Axial section of skull bone window showing the mild irregular solid periosteal reaction along the clivus
In all cases contrast enhanced CT imaging was performed (Table-1). The most consistent CT findings were soft tissue opacification in middle ear, mastoid air cells with focal area of bony erosion in posterior wall of EAC. One patient showed soft tissue density in mastoid cavity with erosion at petrous apex and widening of cavernous sinus, half of clivus, basiocciput and occipital condyle. MRI findings: T2 hyperintense non enhancing signal was noted within mastoid air cells and middle ear cavity. Abnormal marrow signal, appearing heterogeneously T2 hyperintense and T1 hypointense involving petrous part of temporal bone, half of clivus, basiocciput and occipital condyle. It showed heterogeneous contrast enhancement.
In cases 3, 4, 11 and 14; we obtained tissue biopsy from different sites where malignancy had been excluded. 14 patients received intravenous antibiotics except 1 (case 1). Case 1 received Tablet Ciprofloxacin 500 mg PO 12 hourly for 3 months. 5 patients (case 2, 6, 7, 10, 15) received Injection Piptaz 4.5 gm 12 hourly followed by Tablet Ciprofloxacin 500 mg PO for 3 months. Case 5, 11 and 12 received Tablet Linezolid 600 mg, Injection Ciprofloxacin and Injection Vancomycin 1 g respectively. Case 3 and 4 received Injection Augmentin 1.2 g for 1 month. Total 8 patients received ciprofloxacin for 3 month. Case 8 and 9 received injection Ceftriazone 1 g for 1 month followed by injection Metro 500 mg for 1 month. Case 14 is the
case of fungal skull base osteomeliitis. Patient received inj Amphotericin B and syrup Posaconazole. 7 patients (1, 2, 3, 4, 10, 11 and 12) nerve improvement noticed after empirical broad spectrum antibiotics. Three patients showed no nerve improvement.

These patients responded well to an average of 6 weeks of intravenous antibiotic therapy with resolution of discharge and nerve improvement from grade 4 to grade 2. No recurrences were observed in the follow up period of 3 years. 4 patients who underwent 99Tc and 67G scanning at the time of initial diagnosis they also followed up. It was thought that these scans would serve as a baseline for future assessment of therapeutic response and patients demonstrated improvement in inflammatory changes on follow up scans obtained at the conclusion of antibiotic therapy.

Follow up MRI imaging performed for two patients demonstrated a decrease in abnormal pre and para-clival soft tissue, as well as improvement in clivus signal intensity abnormalities.

**DISCUSSION**

The case presentations above illustrate the complexities involved in the diagnosis and management of skull base infection associated with multiple lower CNP. C reactive protein and ESR are nonspecific, being elevated in inflammation, infection and or carcinoma. ESR is more sensitive to chronic inflammation and has been shown to be elevated after CRP has fallen. Therefore diagnosis of skull base osteomyelitis should be considered early especially in the presence of non-remitting otalgia in all elderly patients with a history of ear disease.

*Pseudomonas aeruginosa* is the most common pathogen implicated in osteomyelitis secondary to malignant otitis externa. This too seems true for central SBO, although other organisms have been reported, including *Aspergillus* gram-positive organisms, *mycobacterium*, and *Candida*.

Culture sensitivities will guide the choice of antibiotics, influenced by local prescribing policies. But classically, first line treatment is oral Ciprofloxacin. Cases 1, 2, 6, 7, 8, 9, 10 and 11, total 8 patients received Ciprofloxacin for 3 months. When multiple CNP are present, then other intravenous antibiotics are used. The length of antibiotics required is dictated by the patient’s clinical picture and inflammatory markers.

A number of regimes have been documented in the literature. 3 of our 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 Djalllian et al., for the treatment of culture-negative SBO. The duration of time antibiotics administered is variable among the cases reported, but in each case treatment was given for at least 1 month and up to 6 months. The Bone Infection Unit in Oxford, United Kingdom, often recommends up to 6 weeks of intravenous treatment followed by 6 to 12 months of oral medication, guided by clinical response. The current recommendations in the setting of new diagnosis of SBO include 6 weeks to many months of antibiotics. 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, 4, 5, 6, 10, 11 and 12 showed improvement in their symptoms after 3 weeks of antibiotics. These were then continued on treatment for an average for 3 months. Since antibiotics needed to be given for a prolonged period, we had secured intravenous access in 11 patients (cases 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12).

Duration and cost of treatment were the other difficult issues. Each patient had at least 1 hospital admission for a minimum period of 1 month. Patients required extensive counselling regarding this. 9 patients improved successfully with recovery of facial palsy and have remained symptoms-free with no relapses over a period of 3 years.

**SUMMARY**

Treatment with quinolones – especially Ciprofloxacin shows high rate of cure in a debilitating illness such as SBO thus reduces high morbidity and mortality. If the diagnosis is made and aggressive treatment started early as per culture and sensitivity or empirical based treatment, for appropriate period of time, outcome has improved without any surgical intervention, neural deficit improves, although full recovery of cranial nerve function may not occur.

Infective causes must be included in the differential diagnosis of all patients with skull base masses, not just diabetic and immunocompromised patients, especially in the setting of headache, raised ESR and CRP, and multiple lower CNP. These lesions can cause severe damage including cranial neuropathy, hearing loss, vestibular dysfunction, swallowing problems, dysarthria, hoarseness, headache, facial weakness, and ophthalmic disorders. Such lesions occur in one of the most inaccessible areas of the body. The complex anatomy of the vital structures at the skull base makes surgical resection or biopsy of lesions involving this area extremely difficult. Accurate diagnosis and evaluation of the disease depends on appropriate physical examination and radiological assessment including both CT and MRI scans. Managing these cases requires aggressive and prolonged treatment to reduce risks of infection dissemination. Response to treatment is indicated by resolution of symptoms. Monitoring of the ESR is one of the key investigations that can help to guide how long antibiotics therapy is continued and its normalization would appear to be a
good indicator that the infection has resolved. Close cooperation between an otolaryngologist, radiologist, microbiologist, and infectious diseases consultant is essential in the management of these difficult cases.

**REFERENCES**