

Skull Base Osteomyelitis - Extent, Clinical Impact and Medical Management

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Abstract

Original Research Article

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*.

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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-1

CASE NO	AGE (YRS)	SEX	SITE		CLINICAL FEATURES	TREATMENT	NERVE INVOLVED	RISK FACTOR	POST TREATMENT	
									DIABETES MELLITUS	NERVE STATUS
1.	34	M	CT :Erosion of rt petrous apex with rt Meckel's cave	SBO	Rt severe headache with b/l ear discharge Safe CSOM	Tab Ciprofloxacin 500 mg Q12 h x 3 months	Rt abducens nerve palsy,	Non-diabetic	DIABETES MELLITUS	NERVE STATUS
				No surgery					NAD	Improved
2.	47	M	Widening of rt TMJ with destruction of mandibular condyle with sequestrum, no central involvement	SBO Tplasty after 3 mths	Rt earache with ear discharge Safe CSOM	Inj Piptaz 4.5 g 8 hourly x 1week. Tab Ciprofloxacin 500 mg Q12h x 3 months	Facial nerve palsy	Diabetic	Controlled	Improved
3. VG	32	M	Sphenoid sinus[erosion of greater wing of sphenoid]	CSBO Sphenoid sinus mass biopsy	Headache , Facial pain	Inj Augmentin 1.2 g Q12h x 1 month	Facial nerve palsy	Diabetic	Controlled	Improved
4. NP	22	M	MRI:ill-defined signal in rt mastoid bone ,external auditory canal,rt carotid and anterior aspect of rt petrous apex	SBO Rt temporal/zygomatic bone biopsy	Pain in rt TMJ, rt tinnitus, Rt ear discharge	Inj Augmentin1.2 gm Q12h x 1 month	Facial nerve palsy	Non-diabetic	NAD	Improved
5. BM	64	M	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	SBO No surgery	Rt severe earache, Rt ear discharge	Inj piptaz 4.5 g 8 hourly x 2 weeks , Tab linzolid 600 mg Q12h x 2 weeks	Nil	Diabetic	Controlled	NAD
6. VR	65	F	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	CSBO NO SURGERY	Rt sided headache, diplopia, vomiting ,	Inj piptaz 4.5 gm 8 hourly x 1 month, Inj Ciprofloxacin 750 mg Q12h x 1 month,	Nil	Diabetic	Controlled	NAD

			canal and extension in rt CP angle			Tab Ciprofloxacin 500 mg Q12h for 2 months				
7. RK	38	M	CT: Moderately enhancing soft tissue opacification involving left middle ear and mastoid cavity extending inferiorly along carotid space and around spinous process with erosion most likely inflammatory soft tissue. Non visualization of lateral wall of facial nerve canal in the tympanic and mastoid segment. Focal areas of bony erosion noted involving posterior wall of external auditory canal and lateral aspect of tegmen tympanic and tegmen mastoideum	SBO Op case of Lt FND	Rt side deviation of mouth, left ear discharge, no giddiness, no nystagmus, tinnitus present	Inj piptaz 4.5 gm 8hourly x 1 month, Tab Ciprofloxacin 500 mg Q12h for 3 months	Facial nerve palsy	Diabetic	Controlled	Not improved
8. Rs	42	M	CT : 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 few mastoid trabeculae, vertical portion of facial canal, stylomastoid foramen.	SBO left find ,cortical mastoid	Lt ear discharge with decrease hearing, rt sided deviation of angle of mouth	Inj Ceftriaxone 1 gm x 1 month, Inj metronidazole 500 mg in 100 cc x 1 month, Tab Ciprofloxacin 500 mg x 3months	Facial nerve palsy	Diabetic	Controlled	Not improved
9. KS	67	M	CT : 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	SBO Left ear debridement	Left ear discharge, earache with decrease hearing	Inj Ceftazidime 1 gm bd 1 mth, Inj Piptaz 4.5 gm 8 hourly , Tab Ciplox 500 mg bd x1 month	Left facial palsy with IX ,X,XII palsy SNHL	Diabetic	Controlled	Not improved

			pterygoid muscle.							
10. A SH EIK H	67	M	CT : Mildly enhancing soft tissue opacification noted of external auditory canal in its medial two-thirds with non-visualization of tympanic membrane and similar non enhancing soft tissue seen in entire middle ear cavity, aditus mastoid air ad antrum, mastoid antrum and mastoid air cells. There is associated erosion and destruction of scutum, wall of external auditory canal, styloid process. Soft tissue extending along the styloid process and superior portion of sternocleidomastoid muscle obliterating the right parapharyngeal fat and abutting the cervical internal carotid artery and internal jugular vein and right pterygoid muscle with focal erosion noted of opening of carotid canal and facial canal at stylomastoid foramen	<u>SBO</u> <u>Right</u> <u>cortica</u> <u>l</u> <u>mastoi</u> <u>d</u>	<u>RT</u> ear <u>discharge</u> <u>with</u> <u>earache,</u> <u>decrease</u> <u>hearing</u>	<u>Inj Piptaz 4.5</u> <u>gm 8 hourly x</u> <u>1 month.</u> <u>T</u> <u>Ciprofloxacin</u> <u>500 mg Q12h</u> <u>x 3 months</u>	<u>Facial</u> <u>palsy</u>	<u>Non</u> <u>diadeti</u> <u>c</u>	NAD	<u>Impro</u> <u>ved</u>
11. N SH ETT Y	65	M	MRI : Enhancing soft tissue is noted on the right side in external auditory canal, middle ear, mastoid air cells, petrous region and base of skull. Abnormal marrow signal is seen in the right petrous bone, right half of clivus inferiorly base of occipital bone on right and right occipital condyle, greater wing of sphenoid bone. The soft tissue extends into the right hypoglossal canal which is widened.	<u>SBO</u> <u>Explor</u> <u>ation</u> <u>Biopsy</u> <u>from rt</u> <u>ear</u> <u>polyp</u>	<u>Rt</u> ear <u>discharge</u> <u>with</u> <u>earache .rt</u> <u>tinnitus,</u> <u>swallowin</u> <u>g</u> <u>difficulty</u> <u>.slurred</u> <u>speech</u>	<u>Inj Piptaz 4.5</u> <u>gm 8 hourly</u> <u>for 3 weeks ,</u> <u>Inj</u> <u>Metronidazol</u> <u>e 500 mg in</u> <u>100 cc NS</u> <u>Q8h for 3</u> <u>months.</u> <u>Inj Piptaz</u> <u>2.25 gm 8</u> <u>hourly for</u> <u>land half</u> <u>month.</u> <u>Inj</u> <u>Ciprofloxacin</u> <u>750 mg Q12h</u> <u>for 3month</u>	<u>VII,VIII,I</u> <u>X.X,XI,X</u> <u>II _____rt</u> <u>cranial</u> <u>nerve</u> <u>palsy</u> <u>SNHL</u>	<u>Diabet</u> <u>ic</u>	Controll ed	<u>Impro</u> <u>ved</u>
12. SU HA S	49	M	MRI : Abnormal marrow signal appearing heterogeneously T2 hyperintense and T1 hypointense involving piterous part of right temporal bone, right half of clivus, right basiocciput and right occipital condyle. It shows heterogenous post contrast enhancement. Abnormal heterogenous enhancement along course of right trigeminal nerve within right	<u>No</u> <u>surger</u> <u>y</u> <u>SBO</u>	<u>B/L</u> ear <u>discharge</u> <u>with retro</u> <u>orbital</u> <u>pain, with</u> <u>diplopia</u>	<u>Inj piptaz 4.5</u> <u>gm 8 hourly x</u> <u>2 months,</u> <u>Inj</u> <u>Vancomycin</u> <u>1 gm Q12h</u> <u>for 1 month</u>	<u>.VI</u> <u>.IX.X,XI,</u> <u>XII nerve</u> <u>palsy</u>	<u>Nondi</u> <u>abetic</u>	NAD	<u>Impro</u> <u>ved</u>

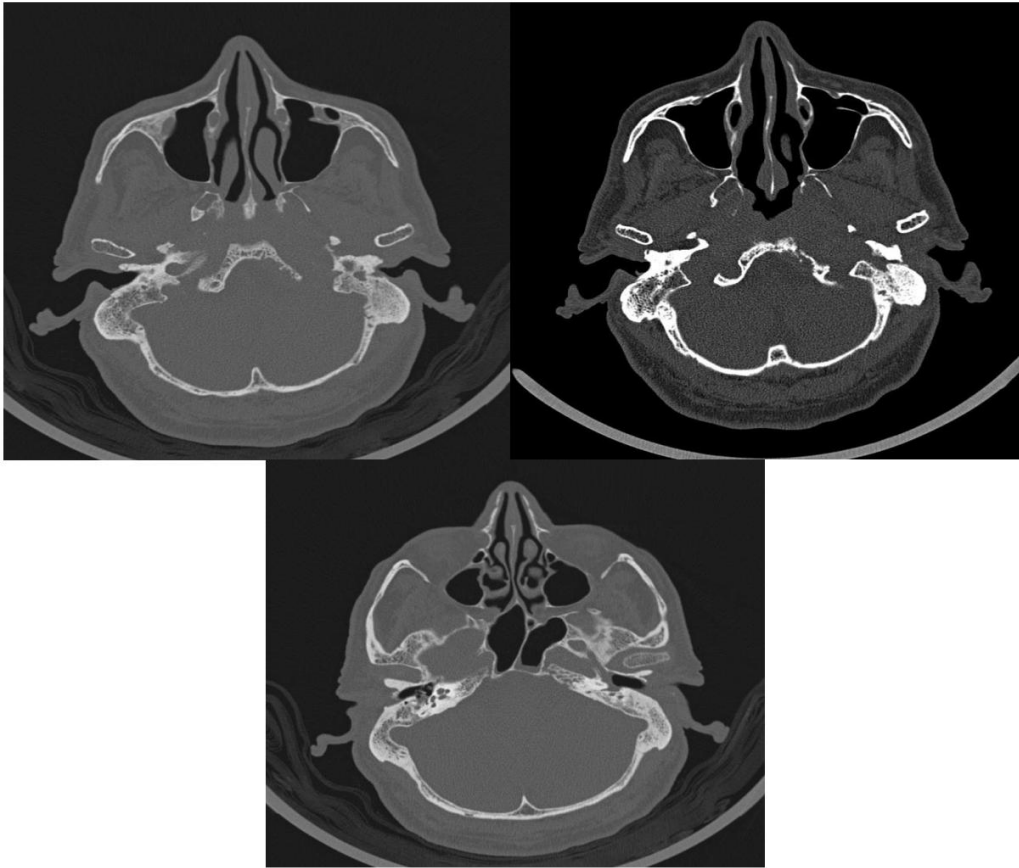
			Meckel's cave along with mildly enhancing adjacent dural thickening. CT : Inflammatory soft tissue seen involving the right mastoid ear cavity with extension in mesotympanum and epitympanum with destruction of tympanic membrane. Soft tissue is extending in hyper pneumatized petrous bone involving the peritubal area and apical region with erosion of posterior wall of petrous apex, right lateral wall of clivus.							
13. SP	60	M	<i>MRI: abnormal soft tissue density seen in middle ear ,mastoid cavity secondary to skull base osteomyelitis due to eustachian tube blockage,soft tissue density in left parapharyngeal space incasing left internal carotid artery and internal jugular vein.</i>	SBO No surgery	ear ache ,b/l decrease hearing,,left ear discharge	Inj Ciplox 500 mg 12 hourly ,,inj fortum 1 gm 12 hourly for 1 month,tab Ciplox 500 mg 12 hourly,tab clindamycin 600 mg 12 hourly x 1 month.	nil	Non diabetic	nil	Nil
14. K. PA ND UR AN G	62	M	CT:Area of the permeative lytic destruction of the skull base of the left middle fossa involving the body and left greater wing of sphenoid,the dorsum sella ,left occipital condyle,the left atlanto-occipital joint.	Endoscopic biopsy of skull base lesion FUNGAL SBO	Headache, left sided facial pain	Inj amphotericin B ,Syp Posaconazole 5ml 6 hourly x 2 weeks ,inj Moxclav 1.2 gm 12 hourly for 1 month.	nil	diabetic	Improved	Nil
15 SA NJU SU MA NT	40	F	MRI:permeative destruction by abnormal isointense heterogeneously enhancing soft tissue in the body of sphenoid bone,its greater wing,clivus with perineural spread of infection along vidian nerve and mandibular nerve.	CSBO	Rt sided facial pain and headache	Inj ceftriaxone 1 gm 12 hourly x 2 weeks , inj Ciplox 500 mg 12 hourly ,,inj Piptaz 4.5 gm 8 hourly for 1 month,tab Ciplox 500 mg	nil	Non diabetic	Nil	nil'

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 were 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

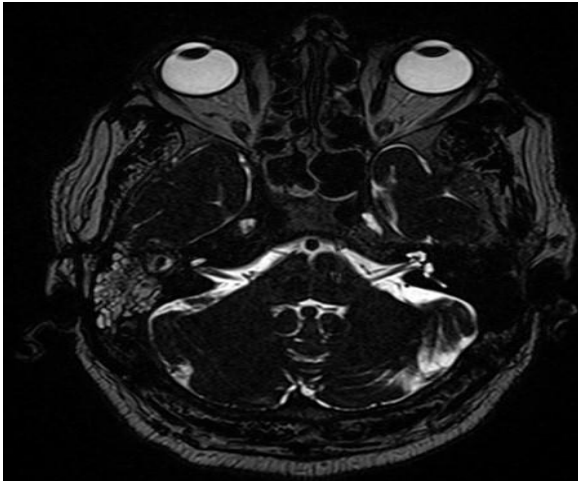


Fig-6: 3D-CISS axial image showing the thickening and enhancement (Fig-7) of the right 7th and 8th nerve complex

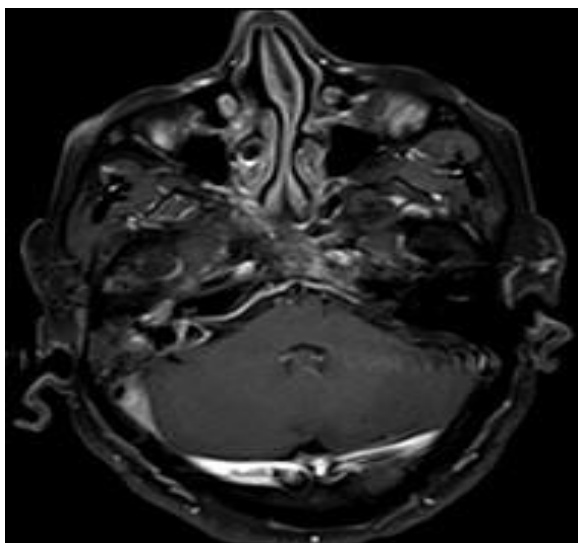


Fig-7: post contrast T1 weighted axial image showing diffuse pachymeningeal thickening and enhancement in the prepontine region along the clivus



Fig-8: Axial CT section bone window image showing the erosion of the left greater wing of sphenoid in skull base osteomyelitis

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.



Fig 9: Pre-treatment image shows hypoglossal nerve paralysis

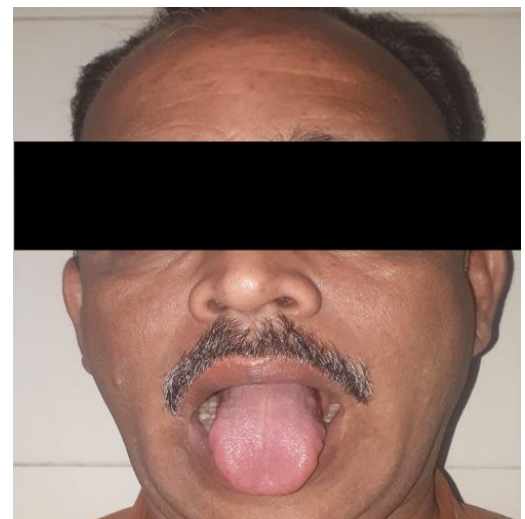


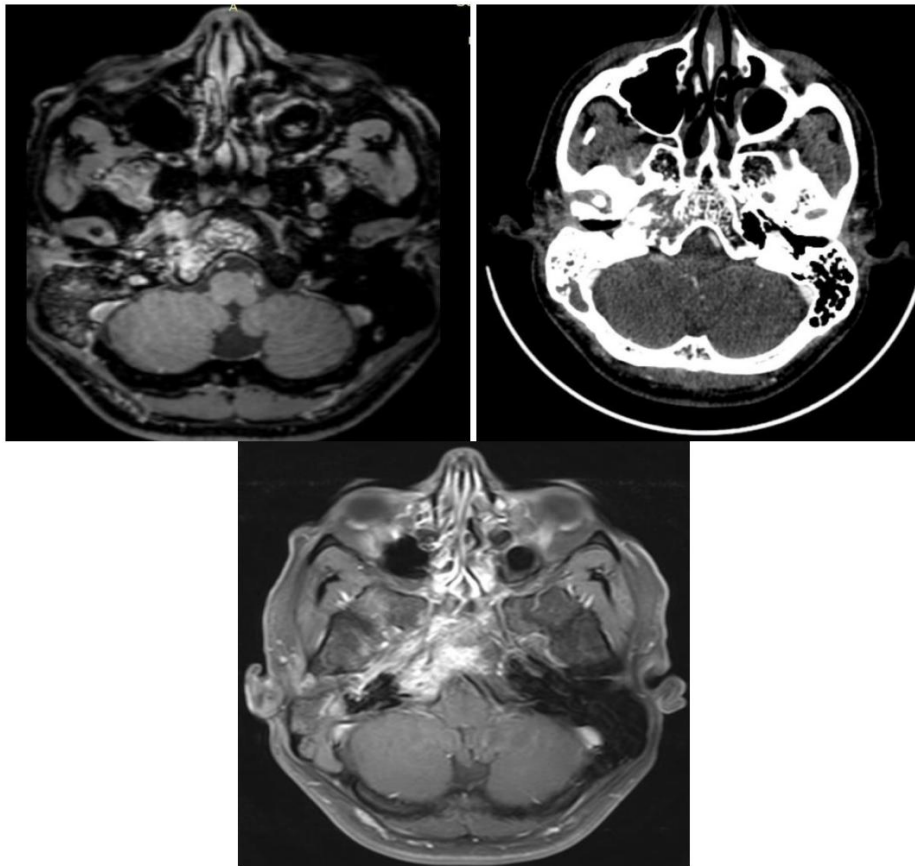
Fig-10: Post-treatment image shows complete recovery in case 11



Fig 11: Pre-treatment image shows right lateral rectus paralysis



Fig-12: Post-treatment image shows complete recovery in case 11



Case No-11, Axial CT section (Fig -11 and Fig-12, showing erosion at petrous apex and corresponding MR image (Fig-13) showing 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 osteomyelitis. 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 [9]. ESR is more sensitive to chronic inflammation and has been shown to be elevated after CRP has fallen [10]. 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 [11]. This too seems true for central SBO, although other organisms have been reported, including *Aspergillus* [12], gram-positive organisms, [13] mycobacterium, and *Candida* [14].

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 Djalilian et al., [15] 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 [16]. 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.

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