CT and MRI findings in skull base osteomyelitis - A pictorial essay

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Learning objectives

This article focuses on reviewing CT and MRI findings in central skull base osteomyelitis. Imaging of the skull-base in the setting of cranial neuropathy and probable infection is best achieved with MRI, which has advantage of superior soft tissue discrimination around the skull base as compared to CT [1,3] . Our purpose was to describe the characteristic clinical presentation and CT, MR imaging findings of central skull base osteomyelitis in patients without otitis externa to facilitate recognition of this unusual condition and thereby encourage prompt diagnosis and institution of appropriate intervention.
Background

Skull base osteomyelitis is a relatively uncommon condition. Most commonly encountered clinical scenario is, an elderly diabetic with inadequately treated chronic external otitis who presents with temporo-occipital pain. Persistent headache is the cardinal symptom. Atypical osteomyelitis of the skull base occurs much less frequently and may not be associated with otitis externa or sinusitis. With wide availability of CT and MRI, accurate localization of the lesion and evaluation of its relationship with adjacent neurovascular structures is possible, either modality being complimentary to each other in demonstrating full disease extent. 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 are of particular concern because they frequently mimic malignancy, which makes accurate histological diagnosis all the more important. However, once diagnosed and treated with appropriate antibiotics, it is one of the few times when CN palsies can be seen to resolve. The greatest challenge, however, remains in differentiating Skull base osteomyelitis from skull base malignancy.
Findings and procedure details

Methods:

We retrospectively reviewed medical records and imaging studies (CT and MRI) of seven patients identified as having central skull base osteomyelitis without otitis externa from Columbia-Asia hospital database. Cases were identified over the course of 2 years, from 2014 to 2016. Exclusion criteria were individuals with associated otitis externa and temporal bone osteomyelitis. Our study subjects included 6 males, 1 female and ranged in age from 45 to 75 years, with a mean age of 58 years. We obtained institutional review board approval to perform this study.

All patients were examined with CT and MR imaging before biopsy and treatment. Imaging included sagittal, axial, and coronal T1-weighted images, axial fast spin-echo T2-weighted image and axial and coronal post-contrast T1-weighted images with fat saturation. 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 and bone marrow invasion.

All patients underwent direct tissue sampling. Biopsy specimens were delivered to microbiology for culture and to pathology for histological examination. All patients had erythrocyte sedimentation rate (ESR), total leucocyte count, differential leucocyte count, blood culture tests performed. All patients were treated with broad-spectrum empiric antibiotics, and in some cases antifungal and antituberculous drugs, until cultures and antibiotic susceptibility results were obtained. One patient underwent follow-up MR imaging at our institution.

**TABLE 1: Clinical characteristics of patients with atypical central skull base osteomyelitis**

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age(years) and sex(M/F)</th>
<th>Risk factors</th>
<th>Microbiology</th>
<th>Cranial neuropathies</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>67/M</td>
<td>Diabetes mellitus, sphenoid sinusitis</td>
<td>Staphylococcus aureus</td>
<td>VI, VII, VIII</td>
</tr>
<tr>
<td>2</td>
<td>64/M</td>
<td>Diabetes mellitus</td>
<td>Pseudomas aeruginosa</td>
<td>VII, VIII, IX, X</td>
</tr>
</tbody>
</table>
TABLE 2: MR findings in atypical central skull base osteomyelitis

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Abnormal SI in Clivus</th>
<th>Preclival ST mass</th>
<th>T1 SI in Clivus</th>
<th>T2 SI in Clivus</th>
<th>Postcontrast enhancement in ST mass</th>
<th>ST in MC</th>
<th>IC extension</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Y</td>
<td>Y</td>
<td>Low</td>
<td>High</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>2</td>
<td>Y</td>
<td>Y</td>
<td>Low</td>
<td>Heterogenous</td>
<td>N</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>3</td>
<td>Y</td>
<td>Y</td>
<td>Low</td>
<td>Low</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>4</td>
<td>Y</td>
<td>Y</td>
<td>Low</td>
<td>Heterogenous</td>
<td>N</td>
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<td>N</td>
</tr>
<tr>
<td>5</td>
<td>Y</td>
<td>Y</td>
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<td>High</td>
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<td>7</td>
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<td>Y</td>
<td>Low</td>
<td>High</td>
<td>Y</td>
<td>N</td>
<td>N</td>
</tr>
</tbody>
</table>

Note.-Signal intensity in clivus is compared with that of normal fatty marrow. SI indicates signal intensity; ST, soft tissue; CS, cavernous sinus; MC, Meckel's cave; IC, intracranial. Intracranial extension implies extension beyond CS or MC, involving dura or brain parenchyma or both.

Results:

The clinical characteristics of patients are summarized in Table 1. Headache was the chief complaint in all of our patients and without evidence of external otitis, acute otitis media, or mastoiditis. All patients had cranial neuropathy by the time they presented.
Cranial nerve (CN) III palsy was present in two patients, CN V palsy in two patients, CN VI palsy in two, CN VII palsy in five, CN VIII palsy in three, CN IX, X palsy in four and CN XI, XII palsy present in three patients (Table 1). All had underlying diabetes mellitus and three patients had a history of chronic sinusitis. Four patients had recent history of fever with elevated ESR. All had elevated white blood cell (WBC) counts ranging from $16.8 \times 10^9/L$ and $21.4 \times 10^9/L$ with a mean of $18.6 \times 10^9/L$. No patient had positive blood cultures.

In all cases, CT and MR imaging of the skull base was abnormal (Table 2). The most consistent MR finding was regional or diffuse clival hypointensity on T1-weighted images relative to normal fatty marrow, which was noted in all patients. There were also signs of pre- and paraclival soft tissue infiltration with obliteration of normal fat planes or even frank soft tissue masses (Fig 1 and 2) in all patients. Four patients had abnormal soft tissue in the cavernous sinus. T2 signal intensity of the clivus was diffusely high in four patients, heterogeneously high in two patients, and low in one patient and postgadolinium enhancement was seen in all patients. One patient had abnormal dural enhancement, and one patient had abnormal leptomeningeal enhancement as well as signal intensity abnormality in the adjacent brain parenchyma (Fig 3), reflecting local cerebritis with abscess formation. The three patients with CN XII palsy had abnormal marrow signal intensity around the hypoglossal canal as well as abnormal soft tissue infiltrating adjacent fat planes.
Fig. 1: Patient 1, 67-year-old male presenting with severe headache and sphenoid sinusitis, no improvement in symptoms in spite of treatment. A, Axial bone window of CT scan demonstrates erosions of bilateral sphenoid bones and clivus. B, Sagittal T1-weighted image demonstrates low signal intensity along the clivus. C, Axial T1-weighted image demonstrates abnormal soft tissue isointense to muscle infiltrating the nasopharyngeal soft tissues, with replacement of normal hyperintense fatty marrow of the clivus.

References: Columbia Asia Hospital, Bengaluru/India.
Fig. 2: Patient 1, D, Axial T2-weighted image demonstrates mildly increased signal intensity within the infiltrated soft tissue in comparison to the adjacent muscle. E, F, Axial contrast enhanced T1 weighted images demonstrating extensive heterogeneous enhancement of the skull base with associated soft tissue predominantly involving the basi-sphenoid, lesser & greater wings (right >left), clivus & petrous apices. Associated mucosal thickening and enhancement in bilateral sphenoid and ethmoid sinuses. G, Coronal contrast enhanced T1 weighted image demonstrates peripheral enhancement of the sella with mildly enlarged pituitary gland suggestive of hypophysitis.

References: Columbia Asia Hospital, Bengaluru/India.

Four patients had simple fluid collections in the mastoid air cells or middle ear cavity or both. This fluid was assumed to be secondary to Eustachian tube dysfunction in the
setting of abnormal nasopharyngeal sub-mucosal inflammatory soft tissue or reactive adenoidal hypertrophy or both rather than a reflection of temporal bone infection, because no patients had symptoms referable to the external or middle ear or mastoid.

Fig. 3: Patient 2, 64-year-old male with history of left-sided facial weakness and severe headache since one month. A, Axial bone window of CT scan demonstrates extensive bony destruction is noted in the left lateral skull base with with erosions of the left lateral margin of the clivus and destruction of the inferior aspect of the left petrous temporal bone. B, Axial T1-weighted image demonstrates replacement of normal hyperintense fatty marrow of the clivus with adjacent abnormal soft tissue isointense to the muscles. C, Axial T2-weighted image demonstrates heterogenous signal intensity of the clivus, mildly increased soft tissue signal intensity in comparison to the adjacent muscle plane. There is fluid in the left mastoid air cells and middle ear cavity, possibly secondary to Eustachian tube dysfunction/obstruction. D, Axial contrast enhanced T1 weighted image demonstrates extensive abnormal enhancement in the skull base crossing the midline with multiple tiny pockets of air noted in the prevertebral region on either side of the midline suggestive of a prevertebral abscess with significant surrounding inflammatory change. E, F, Sagittal and coronal contrast enhanced T1 weighted images demonstrate abnormal marrow enhancement is also noted within the clivus, C1 and C2 vertebral bodies. Normal flow voids in the petrous ICAs with normal enhancement.
**Fig. 4:** Patient 3, 45-year-old male with history of severe headache, right hemiparesis and diminished vision in the right eye. A, Axial bone window of CT scan demonstrates permeative destruction of bilateral sphenoid bones, petrous apices and clivus. B, Axial T1-weighted image demonstrates hypointensity involving the clivus, bilateral petrous apices and sphenoid bones. T1 hypointense well-defined lesions are seen in the right cerebellar hemisphere. C, Axial T2 weighted image demonstrates hypointense signal involving the clivus, bilateral petrous apices and sphenoid bones. T2 hyperintense well-defined lesions are seen in the right cerebellar hemisphere. D, E, F, Axial and sagittal contrast enhanced T1 weighted images demonstrate postcontrast enhancement along the soft tissue of clivus, sphenoid and ethmoid sinuses, bilateral petrous apices. Soft tissue enhancement in the posterosuperior nasopharynx. Additionally, there is perineural extension along the cranial nerves in the right cavernous sinus, right orbital apex, right forearm ovale, rotendum, right CP angle cisternvencasing the cisternal segment of the 7th/8th nerve complex with extension to the midbrain, pons, medulla and cerebellum hemisphere. Multiple ring-enhancing lesions measuring 2 to 3 cm in the cerebellum hemisphere, pons, medulla and right midbrain.

**References:** Columbia Asia Hospital, Bengaluru/India.
Fig. 5: Patient 4, 55-year-old male with history of severe headache, bulbar palsy. Suspected case of sepsis. A, Axial bone window of CT scan demonstrates permeative destruction of the clivus, left petrous apex, body and greater wing of left sphenoid. B, Axial T1-weighted image demonstrates hypointense soft tissue in the left side of skull base involving the parapharyngeal and carotid spaces. C, Axial T2-weighted image demonstrates heterogenous signal intensity in the soft tissue in the left side of skull base. D, E, F, axial and coronal contrast enhanced T1 weighted images demonstrate enhancing illdefined soft tissue in left side of skull base involving parapharyngeal space and carotid space encasing the internal carotid artery and jugular veins. Small nonenhancing sliver of fluid seen within the centre of the lesion. Anteromedially, the lesion extends to the lateral parapharyngeal wall on the left side, with abnormal enhancement seen upto the level of the superior endplate of C3. Posteriorly, the lesion invades body of the sphenoid and greater wing posteriorly, clivus and left petrous apex with permeative pattern of bone destruction. The foramen Ovale and spinosum on the left side is involved and widened. The soft tissue is also extending to the left hypoglossal canal and jugular fossa.

References: Columbia Asia Hospital, Bengaluru/India.
Fig. 6: Patient 5, 54-year-old male with history of tuberculosis, present complaint of headache and difficulty in swallowing. A, Axial bone window of CT scan demonstrates permeative destruction of lower clivus and bilateral petrous apices. B, Axial T1-weighted image demonstrates hypointense diffuse abnormal thickening of the nasopharynx with abnormal marrow signal appearing hypointense along the lower clivus. C, Axial T2 weighted image demonstrates hyperintense diffuse abnormal thickening of the nasopharynx in comparison to adjacent muscle plane. There is fluid in the bilateral mastoid air cells and middle ear cavity, possibly secondary to Eustachian tube dysfunction/obstruction. D, E, F, Axial, sagittal and coronal contrast enhanced T1 images demonstrate thick peripheral enhancement with a central non enhancing component involving the central skull base suggestive of abscess. Posteriorly, the abscess extends into the extra-axial compartment of the posterior fossa in the region of the right cerebello-pontine angle. There is involvement of the inferior aspect of the clivus.

References: Columbia Asia Hospital, Bengaluru/India.

Diagnosis was made by sampling of preclival soft tissues by surgical biopsy in all of them. Causative organism was successfully recovered in all patients (Table 1). The osteomyelitis was bacterial in five cases, and fungal in two cases.
All patients responded well to 6 weeks of intravenous antibiotic/antifungal therapy, with resolution of symptoms and normalization of WBC count and ESR. All patients had residual cranial nerve dysfunction despite successful treatment of their infection, although some patients had improvement or resolution of particular deficits.

Follow-up MR imaging was available for only one patient. These follow-up studies demonstrated a decrease in abnormal pre- and paraclival soft tissue, as well as improvement in abnormal clival signal intensity.
Conclusion

Discussion

Osteomyelitis of the central skull base is an uncommon condition that is potentially life threatening if not promptly recognized and properly treated (1). It often presents subtly and nonspecifically with persistent headache and eventual development of cranial neuropathy. Patients with this condition seem to have a predisposition to infection because of an underlying condition such as diabetes mellitus, corticosteroid use, HIV infection, or chronic inflammatory sphenoid sinus disease. The specific details of an individual case can be expected to vary, given the rarity of the condition. The region in which this condition arises is an anatomical "minefield," and presenting symptoms will vary according to the precise location of infection (19).

The most common organism involved in skull base osteomyelitis arising from otitis externa is *Pseudomonas aeruginosa* (1). In these typical cases of skull base osteomyelitis, patients usually present with otitis externa, but are then found to have involvement of the marrow of the mastoid and petrous parts of the temporal bone and the adjacent soft tissues of the infratemporal fossa (6). In our series of atypical skull base osteomyelitis involving primarily the sphenoid bone, we observed two cases of *Pseudomonas*, with Gram-positive organisms being more common. Two of our patients had an invasive fungal skull base infection caused by an *Aspergillus* species, presumably secondary to an underlying fungal sinus infection. Isolated reports of atypical skull base osteomyelitis secondary to fungal infection have previously implicated *Mucormycosis* and *Aspergillus* (7, 8).

Imaging of the skull base in the setting of cranial neuropathy and probable infection is best accomplished with MR. MR has the advantage of superior soft tissue discrimination without the beam-hardening artifacts of CT and is particularly useful for assessing soft tissue planes around the skull base and abnormalities of the medullary cavity of bone. Highly sensitive but nonspecific MR findings of osteomyelitis include marrow T1 hypointensity and T2 hyperintensity (5), imaging findings that were observed in our study. Clival enhancement can be seen with both infectious and neoplastic processes, but it should not be observed under normal circumstances. The use of fat suppression on the postgadolinium study is of course necessary to assess skull base enhancement accurately (17).

We noted clival marrow and preclival soft tissue abnormalities in all of our cases. It is unclear whether the preclival soft tissue abnormalities were due to direct extension of the inflammatory process inferiorly from the sphenoid sinus or whether it was an anterior
extension of the process from the clivus itself. The anterior cortex of the clivus was grossly intact in all cases, but this does not preclude anterior spread of infectious organisms. Sagittal T1-weighted images of the clivus were the most useful for detecting abnormalities of the clival marrow, whereas axial T1-weighted images offered the best evaluation of the pre- and paraclival soft tissues. The coronal plane and administration of gadolinium offered the best assessment of Meckel's cave and the cavernous sinus, as well as skull base dura and inferior temporal lobes.

Processes to be considered in the clinical and imaging differential diagnosis of central skull base osteomyelitis include neoplastic, pseudoneoplastic, and nonneoplastic entities. Neoplastic processes such as squamous cell carcinoma of the head and neck, lymphoma, and hematogenous metastasis can involve the clivus, preclival soft tissues, and sphenoid sinus. Neoplasms such as squamous cell carcinoma or minor salivary tumor with skull base extension would generally result in a more focal destructive mass, rather than the diffuse infiltrative pattern observed in our cases. Lymphoma, however, could appear identical on imaging studies. Leukemia would be expected to give a more diffuse pattern of marrow involvement (ie, not only clivus, but also the calvarium and cervical spine), and would be unlikely to demonstrate the associated soft tissue changes. Nasopharyngeal carcinoma can be diffusely infiltrative but usually has an identifiable mucosal mass lesion, and the nasopharyngeal mucosa was intact in all of our cases. Elevation of the ESR would not be expected in the setting of skull base neoplasm, and this can be a helpful clinical feature in limiting the differential diagnosis. Several other processes, including inflammatory pseudotumor, Wegener granulomatosis, other granulomatous diseases such as tuberculosis and sarcoid, fibrous dysplasia, and Paget disease can potentially mimic the imaging appearance of skull base osteomyelitis and must also be considered. Inflammatory pseudotumor and Wegener granulomatosis could demonstrate the MR findings seen in the cases presented here. Tuberculosis would be expected to be more focally destructive of bone but could certainly be a cause of central skull base osteomyelitis and could demonstrate imaging findings similar to those presented here. Sarcoidosis can affect bone and soft tissue, but the diffuse marrow abnormality and contiguous non-nodal soft tissue abnormality would be highly unusual. Fibrous dysplasia and Paget disease can result in abnormal marrow signal intensity on MR images, but they have a typical CT appearance, cause bone expansion rather than erosion, and would not be expected to have an associated soft tissue abnormality.

A tissue sampling procedure is often required for definitive diagnosis of this condition, because the imaging appearance alone is highly suggestive but non-specific for skull base osteomyelitis. A definite diagnosis was made by endoscopic sphenoidotomy or open craniotomy. Potentially complicating diagnosis is the fact that a low burden of infectious organisms within the clival bone or pre-clival soft tissues can lead to a false-negative biopsy. New modalities such as MR-guided biopsy of soft tissue surrounding the skull base may prove to be useful under these circumstances (9). Blood tests consistently demonstrate elevated acute-phase reactants, in particular the ESR, whereas
leucocytosis is less reliable (as is a lack of fever), although often seen at least to a moderate degree. One would not expect elevated acute-phase reactants with malignancy, so, given the potentially similar radiological findings, this may be a useful discriminator. Monitoring of the ESR is one of the key investigations that can help to guide how long antibiotic therapy is continued, and its normalization would appear to be a good indicator that the infection has resolved (16).

In our cases the presence of fever, the lack of any history of neoplasia, the presence of factors that pre-dispose to infection, and signs of infection such as elevated ESR and WBC counts were very helpful in raising the suspicion for skull base osteomyelitis and indicating the need for prompt tissue sampling. It is interesting that abnormal blood cultures were remarkably absent in our patients.

Other imaging techniques can help support the diagnosis of skull base osteomyelitis. Technetium scans may be helpful for initial diagnosis, although they may remain "hot" for months following resolution of infection (10). Gallium scan abnormalities have been shown to be useful to monitor response to treatment and evaluate recurrence (3). CT findings are generally unhelpful for monitoring response to treatment, because the CT scan may not even be abnormal initially or, if abnormal, may remain abnormal for as longs as 2 years after treatment (6).

Several potentially serious complications can arise as a result of skull base osteomyelitis, including cranial neuropathy, soft tissue involvement of the cavernous sinus with or without cavernous sinus thrombosis, and meningeal and brain parenchymal extension. Cranial nerve involvement is commonly seen because of the proximity of the clivus to the brain stem, basal cisterns, cavernous sinuses, and skull base foramina. A recent study of 21 patients with combined CN VI and XII palsies implicated a process involving the clivus in 18 cases (11). We observed that cranial neuropathies resolved slowly in patients, despite successful treatment of infection. Analyzing this can be difficult because function may return due to compensation of the contralateral side rather than true resolution of the affected side. The literature implies that this recovery is variable, and certainly not universal. However, this potential is relevant when counseling the patient and in aiding therapy (such as speech and language therapy) involved in the aftercare of the patient (3,17). Various nuclear medicine imaging techniques have been advocated in suspected SBO including gallium-67 scintigraphy, indium-111 white blood cell scans, technetium-99m methylene diphosphonate (MDP) bone scans, and single-photon emission computed tomography (SPECT). The latter two techniques may have an advantage over CT and MRI in detecting postoperative osteomyelitis and may be more useful in the follow-up of patients on antibiotics because marrow signal change may persist for up to 6 months after successful treatment (10,12).

The abnormal soft tissue in the cavernous sinuses in four of our patients with central skull base osteomyelitis is presumably secondary to direct extension of the process from...
the clivus or sphenoid sinus or both. Septic cavernous sinus thrombosis is also a known complication of ethmoid or maxillary sinuses infection (13). Intracranial extension beyond just the cavernous sinuses was seen in one patient along with dural involvement and leptomeningeal involvement. Other complications of skull base osteomyelitis reported in the literature have included epidural abscess of the cervical spine as a result of spread of infection through the prevertebral space (14) and petroclival abscess (15).

Conclusion

Atypical central skull base osteomyelitis is usually centered on the clivus rather than the temporal bones and presumably arises in old aged, immunocompromised persons most cases from paranasal sinus inflammatory disease rather than otitis or mastoiditis, although it may also be hematogenous in origin. Unlike typical skull base osteomyelitis, symptoms of ear involvement are absent. Maintaining high index of suspicion is of utmost importance in making timely diagnosis of skull base osteomyelitis. Unexplained headaches associated with neurologic deficits should alert physician to possible presence of osteomyelitis. Our patients mostly presented with headache and cranial neuropathy with or without fever, and all had clival and preclival abnormalities on CT and MR images, best appreciated on T1-weighted and postcontrast images. Early tissue sampling along with prompt and appropriate treatment can prevent further morbidity. Follow-up MR imaging in one of our patients showed progressive resolution of abnormal clival and pre-clival signal intensity abnormalities; however, some cranial nerve deficits did persist clinically but contralateral compensation was usually present. We, from our study emphasize that this diagnosis should be considered in an immunocompromised patient in the setting of headache, cranial neuropathy, an elevated ESR, and abnormal clival imaging so that biopsy specimens are submitted for culture and not just for cytologic and pathologic assessment and early and vigourous treatment is initiated.
References


