Cranial Osteomyelitis: A Comprehensive Review of Modern Therapies

Martin M. Mortazavi1,2, Muhammad Adnan Khan1, Syed A. Quadri1, Sajid S. Suriya1,2, Kian M. Fahimdansheh3, Salman A. Fard1,2, Tania Hassanzadeh6, M. Asif Taqi1,2, Hannah Grossman5, R. Shane Tubbs1,6

Key words  
- Central skull base osteomyelitis  
- Cranial osteomyelitis  
- Iatrogenic osteomyelitis  
- Posttraumatic osteomyelitis  
- Skull base osteomyelitis (SBO)  
- Temporal bone osteomyelitis

Abbreviations and Acronyms
- ASBO: Anterior skull base osteomyelitis  
- CT: Computed tomography  
- CRP: C-reactive protein  
- EAC: External auditory canal  
- ESR: Erythrocyte sedimentation rate  
- MOE: Malignant otitis externa  
- MRI: Magnetic resonance imaging  
- MSBO: Middle skull base osteomyelitis  
- NSRO: Non sinonhino-otogenic  
- PSBO: Posterior skull base osteomyelitis  
- SBO: Skull base osteomyelitis  
- SPECT: Single-photon emission computed tomography  
- Tc 99m: Technium 99m  
- WBC: White blood cell

INTRODUCTION

In 1959, Meltzer and Kelemen were the first to describe skull base osteomyelitis (SBO) in a patient with pyocyanes chondritis and osteomyelitis of the external auditory canal (EAC). Cranial osteomyelitis includes a spectrum of various causes. Despite advances in neurosurgical procedures, introduction of new antibiotics, and new diagnostic modalities, management of cranial osteomyelitis remains a great challenge. The aim of this article is to catalog various types of osteomyelitis along with modern management of the disease.

METHODS

The published literature in PubMed, Medline, and EMBASE was comprehensively reviewed. Cross-checking of references identified additional relevant references. “Cranial osteomyelitis,” “skull base osteomyelitis (SBO),” “central skull base osteomyelitis,” and “temporal bone osteomyelitis” were used as search terms. The final decision to include or exclude reviews and data extraction were completed by the authors, and any disagreements were settled by discussion. Articles related to the keywords were thoroughly searched and later the articles focusing mostly on cranial/calvarial, infectious, iatrogenic, posttraumatic, tuberculous pediatric-clival, Garré and sclerosing osteomyelitis and their diagnostic modalities and treatment were included. No date restrictions were imposed. Studies with the possibility of blurred/mixed and confusing data were excluded. Moreover, the animal data studies were also excluded to maintain the study totally human focused.

RESULTS

A total of 2522 articles were initially recovered. Of these articles, 183 were included on the basis of their relevance to
skull osteomyelitis and our objectives. These articles comprised 13 book chapters, 24 case reports, 17 case series, 98 original articles, 30 review articles, and 1 meta-analysis. The relevant available information was then used to describe the classification, prevalence, risk factors, clinical course, diagnostic modalities, and investigative techniques along with management in all classifications. On the basis of the information available, we propose a new classification of cranial osteomyelitis into sinorhino-otogenic (SRO) and non-SRO (NSRO) categories. The SRO group is subdivided into anterior SBO (ASBO), middle SBO (MSBO), and posterior SBO (PSBO) and the NSRO group into iatrogenic, posttraumatic, hematologic, and osteomyelitis with other causes (Figure 1).

**Causes and Risk Factors of Cranial Osteomyelitis**

The most common causes of cranial osteomyelitis in developing countries are paranasal sinusitis, direct head injuries, and scalp infections. Postoperative craniotomy-related infections are the predominant source of cranial osteomyelitis in developed countries. 2-4 SBO mainly involves the middle skull base and usually occurs as a complication of malignant otitis externa (MOE) or chronic mastoid infections or secondary to sphenoidal sinusitis. 7-9

Cranial osteomyelitis is also influenced by systemic diseases that decrease bone vascularity, change the course of disease, and alter host defense mechanism. 2-10-17 The causative infections and predisposing comorbidities are summarized in Tables 1 and 2. Common organisms causing cranial osteomyelitis are summarized in Table 3.

**Classification of Cranial Osteomyelitis**

Depending on the originating site of infection, cranial osteomyelitis can be classified primarily into 2 broad clinical entities: SRO origin and NSRO origin (see Figure 1).

**SRO Origin.** We differentiate the SRO origin of osteomyelitis into 3 types to guide with definitive diagnosis and selection of appropriate therapy.

1) ASBO. ASBO develops as a complication of paranasal sinusitis, acute bacterial rhinitis, skull base trauma, or previous surgical procedures, or it can be idiopathic. 17-18 The most common causative pathogens are Staphylococcus aureus, streptococci, and anaerobes. 19 Prasad et al. 20 determined that chronic rhinosinusitis is the main source of frontal bone osteomyelitis. Undertreatment of infection is also an important risk factor for recurrence of ASBO. 20 However, direct extension involving the external wall of the frontal bone leads to bone erosion, subperiosteal abscess, epidural empyema, subdural collections, meningitis, and encephalitis. 21-24 On the other hand, hematogenous spread can also occur by valveless diploic veins causing sagittal sinus thrombophlebitis, brain abscess, and subdural empyema. 22-25 This process leads to bone sequestration, which assists in harboring bacteria, and also produces an area of low oxygen tension. This area effectively reduces the bactericidal activity of leukocytes and the rate of diffusion of the antibiotic into the dead bone. These pathologic changes make it impossible for the antibiotic to reach the site of infection, despite a therapeutic serum concentration. 24-25 Frontal osteomyelitis is generally a polymicrobial infection; however, if the intracranial complications are the initial presentation of frontal osteomyelitis, then, anaerobic or fungal infections are the leading cause. 21,22,26-27

Clinically, ASBO can present acutely as fever, frontal headache, frontal edema, retro-orbital pain, photophobia, purulent rhinorrhea, seizures, and focal neurologic signs. 21,22,23,26,28 However, chronic ASBO is characterized by progressive frontal headache along with decreased mentation, sinocutaneous fistulas, and infectious complications such as meningitis and extradural, subdural, or intraparenchymal abscesses, leading to significant morbidity and mortality. 21-23,28-30 ASBO is frequently a complication of frontal sinusitis or posttraumatic infection. Other less frequent risk factors are osteocartilaginous necrosis secondary to chronic intranasal cocaine abuse, dental abscess, or delayed complications of neurosurgery. 20-31 Another rare clinical entity that causes frontal bone osteomyelitis and is commonly found in the adolescent and young adult group is Pott puffy tumor. 30-31 This disease is characterized by forehead-localized nonneoplastic swelling caused by a subperiosteal abscess associated with osteomyelitis of the frontal bone secondary to either direct or hematologic spread of the infection. 20-31

2) MSBO. Although relatively uncommon, MSBO is a frequent clinical entity among SBO cases, associated with significant functional morbidity and mortality. 21-24 In 1838, Toulmouche 35 was the first to report a case of progressive temporal bone osteomyelitis. However, Chandler in 1968 introduced the term malignant otitis externa. 23-24 Many studies suggest that Pseudomonas aeruginosa infection is a leading cause of MOE and MSBO, responsible for up to 98% of all cases. 20 However, MSBO can also develop as a complication of paranasal sinusitis,
chronic mastoiditis, suppurative otitis media, and odontogenic infections.39-40
Many other pathogens can also cause MSBO, including Staphylococcus aureus, Staphylococcus epidermidis, Proteus spp, Klebsiella spp, Candida ciferri, Candida parapsilosis, Scedosporium apiospermum, mucormycosis, Aspergillus fumigatus, and Aspergillus niger.41-43

Pathologically, MSBO is a progressive infection spread from the EAC to the middle skull base through the fissures of Santorini and the osseocartilaginous junction.44 The facial nerve is the cranial nerve most commonly involved. As a result of the spread to the jugular foramen, cranial nerves IX, X, or XI are the next most commonly affected.44-45 Anterior spread of the infection can involve the parotid gland and temporomandibular joint. Septic thrombosis of the sigmoid sinus and internal jugular vein, meningitis, cerebral abscess formation, and contralateral side spread with cervical spine involvement can also complicate the course of infection.39-46

MSBO primarily involves the temporal and sphenoid bones.57-62 Typically, MSBO involving the temporal bone presents with severe and deep otalgia, spiking fever, aural fullness, and foul purulent discharge.49 Conductive deafness, headache, and temporomandibular joint pain may also be present.50 On examination, wooly induration of the pinna, preauricular cellulitis, and a tender EAC with granulation tissue are the cardinal findings. In later stages, there can be involvement of the mastoid bone with granulation tissue and cutaneous fistula.59-60 Cohen and Friedman suggested the following diagnostic criteria: pain, exudate, edema, granulation tissue of EAC, and positive technetium 99m (Tc 99m) scan.23 Sphenoid SBO specifically presents with unremitting headaches in the absence of localized ear and sinus infection, posing a diagnostic challenge. If it is not treated promptly, a variety of cranial neuropathies, most commonly abducens palsy, can ensue rapidly as a result of the extension of infection to the brainstem.34 Subtemporal spread of infection involves the facial nerve, where further posteromedial spread can involve the jugular foramen, carotid space, sigmoid sinus, and hypoglossal canal.52 This situation implicates the cranial nerves exiting the jugular foramen, the glossopharyngeal, vagus, and accessory nerves (Vernet syndrome), and also the hypoglossal nerve exiting through the hypoglossal canal (Collet-Sicard syndrome).63 Complications such as meningitis, brain parenchymal involvement, abscess formation, venous sinus thrombosis, and lateral medullary syndrome can also result from the spread of infection.51-55

Gradenigo syndrome or petrous apicitis is rarely seen since the introduction and widespread use of antibiotics. However, it is a serious and potentially fatal intracranial complication of acute otitis media, acute mastoiditis, and cholesteatoma.53 It can also be caused by extradural inflammation at the petrous apex of the temporal bone involving the trigeminal ganglion and abducens nerve.54 Gradenigo syndrome consists of the triad of suppurative otitis media, ipsilateral abducens nerve palsy secondary to involvement of the nerve as it passes through the Dorello canal, and unilateral retro-orbital pain, or pain in the cutaneous distribution of the ophthalmic and maxillary divisions of the trigeminal nerve as a result of the extension of inflammation into the Meckel cave.53-56 Other symptoms can include severe headache, photophobia, meningeval signs, fever, diplopia, and reduced corneal sensitivity.55-57 The most common etiologic pathogens are Staphylococcus aureus, Streptococcus pneumoniae, group A streptococci, Pseudomonas, and nontypeable Haemophilus influenzae.58 Traditionally, Gradenigo syndrome has been treated by surgery; however, surgery is reserved for refractory cases. A pus sample is obtained by mastoid drainage or in life-threatening complications.58 Recent advances in imaging with new antibiotic treatment availability allow conservative treatment to produce complete recovery without major surgery.58-60

3) PSBO. PSBO is a very rare condition that occurs in the setting of direct spread of an infection involving the paranasal sinuses, EAC, mastoid, middle ear, or oral cavity.59-61 Noninfectious causes are extremely rare and can be secondary to posttraumatic and iatrogenic causes.59,61-66 Various pathogens such Pseudomonas, streptococcal pneumonia, Streptococcus spp, and Staphylococcus aureus are most frequently involved; fungal or mixed bacterial infections have also been documented, although less commonly.67-69 Factors such as delayed

| Table 2. The Main Routes of Infection in Cranial Osteomyelitis |
| Routes of Infection and Their Causes |
| Contiguous Spread from Local Infection | Direct Inoculation from Iatrogenic or Posttraumatic Condition | Hematogenous Dissemination from Remote Source of Infection |
| Chronic mastoiditis | Neurosurgical site infections | Lung infection |
| Paranasal sinus infections | Gunshot wounds | Spine infection |
| Malignant otitis externa | Postcraniofacial injuries | Peripheral arthritis |
| Scalp infections | Cephalohematoma | Meningitis |
| Penetrating scalp wound and laceration | Cephalohematoma | Cryptogenic infection |

| Table 1. Systemic Comorbid Conditions in Cranial Osteomyelitis |
| Systemic Comorbid Conditions |
| Nutritional imbalance | Immunocompromised state |
| Diabetes mellitus | Malignancy |
| Renal failure | Postradiation exposure |
| Hepatic failure | Paget disease |
| Chronic hypoxia | Osteoporosis |
| Small-vessel disease | Prolonged hospital stay |
| Osteopetrosis | Advanced age |
| Smoking/tobacco use | |
Table 3. Common Pathogens Causing Cranial Osteomyelitis in Different Locations of Skull Base

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<th>Infection in Different Location of Skull</th>
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<td>Fungi: <em>Candida</em> species, <em>Candida parapsilosis</em>, <em>Aspergillus</em> spp, and <em>mucormycosis</em></td>
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<td>Mixed bacterial and fungal infections: occasionally</td>
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Clinically, traumatic cranial osteomyelitis presents as chronic infection and is usually milder than the acute variant. However, osteomyelitis reported after scalp avulsion can show the findings of acute osteomyelitis. The diagnostic workups include checking erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels and performing imaging modalities and bone biopsy. Bone magnetic resonance imaging (MRI) and bone single-photon emission computed tomography (SPECT) are considered the most sensitive techniques. Needle biopsy is the most accurate diagnostic tool. *Staphylococcus aureus* is the most common pathogen, followed by other organisms including *Proteus mirabilis*, *Peptostreptococcus* spp, *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Mycobacterium tuberculosis*, *Klebsiella* spp, *Pseudomonas* spp, and *Bacteroides* spp.

3) Hematologic Cranial Osteomyelitis. Osteomyelitis can also result from hematogenous spread after bacteremia or fungemia. It can occur in immunosuppressed patients who have prolonged neutropenia, leukemia, corticosteroid use, critical illness requiring intensive care, chemotherapy, AIDS, or diabetes mellitus. These chronic infections are difficult to diagnose and have life-threatening complications with poor prognosis. The most common pathogens include *Pseudomonas aeruginosa*, *Salmonella* spp, *nontuberculous Mycobacterium* spp, *Treponema pallidum*, and fungal causes including *Cryptococcus* neoformans, *Aspergillus* spp, *blastomycosis*, and *mucormycosis*.

Aspergillus is the most common fungal cause of cranial osteomyelitis in immunosuppressed patients, usually involving the temporal bone at the base of the skull. However, cranial osteomyelitis can also occur in immunocompetent patients. *Mucormycosis* is another common fungal cause of this condition. Very rarely, *blastomycosis* and *Cryptococcus* neoformans can involve skull bones, causing osteomyelitis, most often in the temporal bone. A high index of suspicion and recognition of atypical clinical features of specific organisms are required for diagnosing and treating hematogenously spread osteomyelitis.

Cranial osteomyelitis caused by *Salmonella* spp is extremely rare and can occur in...
both immunocompetent and immunosuppressed patients. A few cases of cranial osteomyelitis caused by disseminated Mycobacterium infection have been reported in patients with advanced AIDS. Disseminated disease is universally fatal, with a mean survival time of 6 months from initial diagnosis.

4) Other Causes of Cranial Osteomyelitis. Tuberculous Osteomyelitis. Primary tuberculous osteomyelitis, both of the skull vault and skull base, is a common cause of cranial osteomyelitis in many regions of the world. Because of widespread malnutrition, poor socioeconomic conditions, and immunodeficiency syndromes in the developing world, the incidence of calvarial TB is on the increase. It usually presents as painless or sometimes painful scalp swelling with a discharging sinus, subgaleal collections, and a variable amount of extradural granulation tissue. It usually involves multiple cranial bones. The radiologic forms of calvarial TB are diffuse TB of the cranium or circumscribed lesions of the sclerotic and lytic type. If the extrapulmonary source is not found, this may lead to delay in starting the treatment. Posttraumatic tuberculous osteomyelitis of the cranial vault has also been reported. It is suggested that the increased vascularity and transitory decrease in resistance at the trauma site may result in the inoculation of the bacilli.

Clival Osteomyelitis. Clival osteomyelitis is a very rare condition observed in the pediatric population. It usually occurs secondary to the direct spread of an infection from contiguous structures, the paranasal sinuses, or adjacent bones of the skull base. A few case studies have reported pathogens such as Enterococcus faecium, methicillin-resistant Staphylococcus aureus, and an anaerobe, Fusobacterium necrophorum. Infection can also be transmitted from the lymphatic tissue in the pharynx through the fossa navicularis magna to the skull base. The lymphoid tissue of the pharyngeal tonsil and emissary veins in the fossa navicularis are a potential route for the spread of infection and subsequently lead to clival osteomyelitis. Because numerous important structures lie adjacent to the clivus, any progression of disease can lead to an intracranial complication.

Contrast-enhanced imaging studies such as MRI and computed tomography (CT) scans with contrast are required to assess the extent of the disease process. Clival osteomyelitis is treated by intravenous administration of broad-spectrum antibiotics over a period of 4–8 weeks. Surgical drainage via the posterior pharyngeal wall is necessary in patients who are unresponsive to antibiotic therapy.

Garré Osteomyelitis. Garré osteomyelitis is a rare chronic disease characterized by a unique proliferative subperiosteal reaction in the pediatric population. It was first described by Carl Garré in 1893. This disease is also known as Garré chronic sclerosing osteomyelitis because it comprises chronic sclerosing osteomyelitis with proliferative periostitis, ossifying periostitis, or other forms of osteomyelitis. It predominantly affects the mandible and long bones, with rare calvarial involvement. However, Klisch et al. suggested that calvarial sclerosing osteomyelitis has to be included as a differential diagnosis of skull osteolytic and sclerosing lesions with persistent swelling of the head. The imaging findings are not specific and predominantly show sclerosis of the bone and calvarial thickening. Treatment strategies can involve conservative approaches with antibiotic therapy but sometimes surgery is required to achieve a permanent cure.

Melioidosis. Melioidosis is caused by Burkholderia pseudomallei, a ubiquitous soil saprophyte, and is characterized by multiple abscesses in different organs of the body. Although uncommon, cranial melioidosis can present with either isolated involvement of brain parenchyma in the form of intracerebral abscesses or with osteomyelitis without extension into the extradural space. Diabetes mellitus is a well-documented risk factor for melioidosis. Other risk factors include alcoholism, renal disease, immunosuppression, and thalassemia. Cranial melioidosis presentation potentially mimics tuberculosis both clinically and radiologically. However, its varying presentation can mimic Guillain-Barré syndrome, limb weakness, and cranial nerve palsies.

This condition is relatively asymptomatic, especially in the context of an extradural empyema; however, it can present with fever, headache, ataxia, and generalized tonic clonic seizures.

Modern Management Strategies

Diagnostic Modalities. The diagnosis of cranial osteomyelitis, in general, can be
based on history, physical examination, laboratory findings, tissue sampling, and imaging studies. Laboratory workup is not always helpful. ESR, CRP, procalcitonin, and white blood cell (WBC) count can be mildly increased. In suspicious cases, tissue sampling is often required for definitive diagnosis because imaging studies are not specific except in giving the location of infection. Tissue can be sampled by CT-guided fine needle aspiration, endoscopic sphenoidotomy, magnetic resonance-guided biopsy, or open craniotomy. Tissue sampling with histopathology and microbiology is also helpful to rule out malignant disease.

Imaging studies are generally used to establish the location and extent of infection. These modalities include contrasted CT, MRI with contrast, gallium 67 scintigraphy, and indium 111 WBC (In-111 WBC) scan, and Tc 99m bone scintigraphy. CT with contrast is sensitive to bone erosion or periosteal remodeling; however, it is a poor choice for monitoring intracranial extension, bone marrow involvement, and treatment response. In iatrogenic osteomyelitis, plain radiographs and CT lack initial sensitivity but can later show destruction in osteomyelitis (Figure 3). In cranial melioidosis, CT lacks sensitivity, particularly in the initial stages of the disease. CT is no longer diagnostic of active osteomyelitis after surgery or trauma.

MRI is more sensitive than CT for early detection of cranial osteomyelitis and determines the full extent of adjacent soft-tissue involvement (Figure 4). In the setting of extensive disease, the imaging of cranial osteomyelitis is best achieved with MRI. Clival marrow and preclival soft-tissue abnormalities are the usual MRI findings. However, it is uncertain whether these changes in preclival soft tissue are caused by direct extension of an infection from the sphenoid sinus or extension from the clivus itself. MRI T2-weighted scans show classic signs of cranial melioidosis, which include calvarial osteomyelitis, leptomeningeal enhancement, ring-enhancing lesions, edema, abscesses, and a predilection for brainstem involvement.

For patients with cranial osteomyelitis who have not undergone previous skull base surgery, MRI with contrast and In-111 WBC bone SPECT scintigraphy are the most sensitive techniques for detecting osteomyelitis. Seabold et al. and Weber et al. showed that bone SPECT scintigraphy is superior to CT for detecting cranial osteomyelitis. Anatomic localization of the disease can be further improved with positron-emission tomography. In patients with preexisting cranial bone abnormalities resulting from surgical procedures or trauma, SPECT and Tc 99m methylene diphosphonate bone scans have been proved to be the most accurate methods. These techniques are also useful for assessing ongoing active cranial osteomyelitis after treatment. Gallium scintigraphy and inflammatory parameters such as CRP, procalcitonin, WBC, and ESR are among the modalities for evaluating treatment response and assessing recurrence and prognosis in cranial osteomyelitis, because they rapidly revert to normal as the disease resolves.

In developing countries where these advanced diagnostic tools are not available, the relevant investigation generally performed after a clinical diagnosis includes high-resolution CT, culture and sensitivity of the pus from discharging sinuses, biopsy from the granulation tissue for histopathologic examination, and routine blood examination including blood sugar and human immunodeficiency virus testing.

Multiple factors are involved in the delayed diagnosis of the disease. Several granulomatous diseases and other inflammatory conditions such as Wegener granulomatosis, tuberculosis, sarcoidosis, fibrous dysplasia, Paget disease of bone, and inflammatory conditions such as Wegener granulomatosis, tuberculosis, sarcoidosis, fibrous dysplasia, Paget disease of bone,
and eosinophilic granuloma of the cranium can mimic findings of SRO SBO on imaging studies and must also be considered. Commonly, the disease may be misdiagnosed as tumor on CT and MRI. The bone erosion and marrow infiltration along with a masslike soft-tissue swelling may raise the suspicion for underlying malignant lesion such as nasopharyngeal carcinoma or skull base metastases. Consequently, further delays in diagnosis can occur as tissue samples from surgical biopsies may be sent for histology only and yield nondiagnostic results. Inadequate or partial treatment of primary origin of infection, failure to respond to antimicrobial treatment, and fungal infection in susceptible individuals are responsible for chronic and refractory disease and pose a great diagnostic challenge. High suspicion should be maintained after a failure of antibacterial therapy in a patient who has classic signs and symptoms with negative cultures or in patients who initially respond to antimicrobial therapy but later experience recrudescence.

**Therapeutic Techniques.** **Antibiotic Therapy.** The mainstay of treatment for cranial osteomyelitis is a course of culture-guided antibiotics and early aggressive surgical removal of infectious sequestra. Different studies have recommended various treatment durations of broad-spectrum antimicrobial agents ranging from 6 to 20 weeks, with an initial 6 weeks of intravenous therapy. However, culture-directed antimicrobial therapy for a minimum of 3 months remains the general protocol because treatment may take up to several months for complete resolution. Because of the high prevalence of *Pseudomonas aeruginosa*, double coverage is required. Recent data show that carbapenems and ciprofloxacin are suitable for adjunctive therapy. Empirical therapy with vancomycin should also be considered for adequate methicillin-resistant *Staphylococcus aureus* coverage. Johnson et al. reported that broad-spectrum antifungal coverage must be considered in refractory cases in the setting of appropriate empirical antibacterial therapy. However, empirical antifungal therapy has not been recommended in the literature. Byth et al. recommended the use of high-dose amphotericin B or liposomal amphotericin B, a new lipid formulation with lower toxicity and equal efficacy. Empirical antifungal therapy should be directed toward *Escherichia coli* and *Staphylococcus aureus*. In these cases, suction-irrigation systems, or washin washout indwelling antibiotic irrigation methods have shown favorable results and can save 50% of the infected bone flaps. The length of antibiotic treatment for traumatic open contaminated skull fractures is a highly debated subject in neurosurgery. The extensive review of controversies in antibiotic management of traumatic open skull fractures by Mortazavi et al. found that antibiotic treatment is highly effective in traumatic skull fracture cases. The distinction is that antibiotic use for an open contaminated skull fracture is treatment of contaminated tissue rather than prophylaxis. In addition, the review found that 7–10 days of antibiotic resulted in fewer late infections than did short-term treatment (24–72 hours).

The antibiotic therapy for cranial melioidosis is still being debated. These antibiotics include ceftazidime or carbapenems for up to 6 weeks for the eradication phase and oral quinolone or cotrimoxazole for 6 months for the maintenance phase in patients with cranial melioidosis. Surgical Treatment. Surgical treatment generally involves debridement, removal of necrotic bone and culture of necrotic tissue, removal and culture of the infected bone, dead space management, and maintaining bone stability. The targeted and aggressive treatment of the source of the original infection, either simultaneously or as soon as possible to prevent further dissemination of infected material, is of the mainstays of successful management and outcome. In cases of MOE, the role of surgery is mainly limited to biopsy, debridement of EAC, and possible drainage of an associated abscess. In cases of PSBO, surgical drainage can be performed via the posterior pharyngeal wall in patients who are unresponsive to antibiotic therapy. In addition to antibiotic therapy in Pott puffy tumor, the surgical treatment includes external debridement of infected bone of the cranial base and removal of sequestra. It is usually performed under general anesthesia.
approaches such as trephination, frontal sinus obliteration, craniotomy, and endoscopic sinus surgery.163,164

In the management of iatrogenic osteomyelitis, after debridement and removal of infected bone flaps, delayed cranioplasty is recommended.164,165 However, in patients with uncomplicated postcraniotomy infections, simple surgical debridement is sufficient with preservation of bone flaps.164,165 Posttraumatic open displaced skull fractures into the brain parenchyma are a distinct entity needing special attention. Despite extensive debridement and irrigation, micropieces of contaminated bone often remain within the brain parenchyma and cause late intracerebral infection, even prolonging intravenous antibiotic treatment. Therefore, attention and special care should be given in cases of traumatic skull fracture.

Adjunct Therapy in Refractory Cases. Hyperbaric oxygen therapy is a particularly useful adjunct to antibiotics and surgical therapies and is vital for managing chronic refractory cases. It is also useful in complicated postcraniotomy cranial osteomyelitis with or without bone flap that requires repeat surgery. Treatment failures can occur in both bacterial and fungal SBO as a result of tissue hypoperfusion and hypoxia, especially in diabetic patients with microvascular disease. Hyperbaric oxygen therapy leads to increase oxygen tension in the wound, enhances the oxidative killing of pathogens, and promotes angiogenesis and osteogenesis. Mader and Love166 suggest that it requires daily treatments for several weeks; however, its side effects include oxygen toxicity, barotrauma, and tympanic membrane perforation.

Therapeutic Approach for Immunosuppressant Patients. The management of cranial osteomyelitis in immunosuppressed patients is multidisciplinary. Complete and wide surgical debridement with prolonged parenteral antimicrobial therapy is the treatment of choice if feasible, along with hyperbaric oxygen for refractory patients. Recently, the incidences of chronic and subacute forms of SBO have increased as a result of inappropriate and unnecessary use of antibiotics, especially in the immunosuppressed.167 The treatment of Pseudomonas in immunosuppressed patients includes combination antimicrobial therapy such as ciprofloxacin and ceftazidime.168 Third-generation cephalosporins and quinolones are the drugs of choice for treating systemic salmonellosis.169 However, the treatment regimen for Mycobacterium kansasi infections comprises isoniazid, rifampin, and ethambutol for 18–24 months.170 For fungal cranial osteomyelitis, amphotericin B is the drug of choice, despite its systemic toxicity.171 In view of the side effects, few studies have been conducted on newer antifungal agents such as miconazole, fluconazole, and itraconazole. Liposomal Amphotericin B and γ interferon are the new alternative therapies.169-172 Prevention of aspergillosis in immunocompromised patients has gained some attention. Prophylactic amphotericin B nasal spray or itraconazole in high-risk patients can prevent colonization.173

Aside from treatment, strict glucose control in diabetic patients, improvement of immune status, and resolution of chemotherapy-induced neutropenia are vital for successful resolution.169,172-174 Although diabetes increases susceptibility to infection, no association between diabetes and longer duration of antimicrobial therapy has been shown.175 During treatment, it is important that the reporting radiologist and physician can detect signs of improvement on radiologic images. These changes often lag significantly behind clinical improvement, resulting in premature discontinuation of antimicrobial treatment, leading to occurrence of refractory and chronic osteomyelitis.176

CONCLUSIONS

We present one of the most extensive reviews on cranial osteomyelitis and offer a classification on the basis of the origin of infection. On the basis of location and cause, we have introduced a new classification of cranial osteomyelitis: SRO versus NSRO. This classification can be valuable for assessing the clinical course of this condition and the diagnostic and therapeutic challenges for its management. Thorough diagnosis with prompt and aggressive treatment is necessary, and complete resolution of the infection is important to decrease morbidity and mortality among patients.

REFERENCES


MARTIN M. MORTAZAVI ET AL. CRANIAL OSTEOMYELITIS

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