Cranial Osteomyelitis: A Comprehensive Review of Modern Therapies

Martin M. Mortazavi[1,2], Muhammad Adnan Khan[1], Syed A. Quadri[1], Sajid S. Suriya[1,2], Kian M. Fahimdanesh[3], Salman A. Fard[1,2], Tania Hassanzadeh[4], M. Asif Taqi[1,2], Hannah Grossman[5], R. Shane Tubbs[1,6]

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: Nonsinorhino-otogenic
PSBO: Posterior skull base osteomyelitis
SBO: Skull base osteomyelitis
SPECT: Single-photon emission computed tomography
SRO: Sinorhino-otogenic
SSI: Surgical site infections
Tc 99m: Technetium 99m
WBC: White blood cell

From the [1]National Skull Base Center, Thousand Oaks, California; [2]California Institute of Neuroscience, Thousand Oaks, California; [3]University of California Irvine Medical Center, Irvine, California; [4]University of Arizona College of Medicine, Tucson, Arizona; [5]Los Robles Hospital and Medical Center, Thousand Oaks, California; and [6]Seattle Science Foundation, Seattle, Washington, USA

To whom correspondence should be addressed: Martin M. Mortazavi, M.D.

[E-mail: m_mortazavi@hotmail.com]

Citation: World Neurosurg. (2018) 111:142-153.
https://doi.org/10.1016/j.wneu.2017.12.066

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

1878-8750/$ - see front matter

BACKGROUND: **Cranial osteomyelitis is a rare but potentially life-threatening condition that requires early diagnosis with prompt and appropriate management by neurosurgeons to prevent further central nervous system complications.**

METHODS: **The literature in the Medline database was comprehensively reviewed with the keywords "cranial osteomyelitis," "skull base osteomyelitis (SBO)," "central skull base osteomyelitis," and "temporal bone osteomyelitis." Items in the reference list of each article relevant to the objective of this study were reviewed.**

RESULTS: **This review produced 183 articles: 13 book chapters, 24 case reports, 17 case series, 98 original articles, 30 review articles, and 1 meta-analysis. We classified cranial osteomyelitis as sinorhino-otogenic, including anterior, middle, and posterior skull base osteomyelitis; and non-sinorhino-otogenic, including iatrogenic, posttraumatic, hematologic, and osteomyelitis with other causes.**

CONCLUSIONS: **New diagnostic modalities, the introduction of broad-spectrum antibiotics, and recent advances in neurosurgical procedures have led to a decrease in the rate of treatment failure in cranial osteomyelitis. Early recognition of initial nonspecific symptoms is key to diagnosing and managing this treatable but life-threatening condition. Early identification of the causative pathogen, appropriate broad-spectrum antibiotic therapy over a period of 8–20 weeks, and aggressive surgical debridement are essential for managing cranial osteomyelitis. On the other hand, inadequate treatment is responsible for refractory cases and poses a great diagnostic challenge. A new classification dividing cranial osteomyelitis into sinorhino-otogenic versus nonsinorhino-otogenic groups could prove valuable for clinical communication and treatment.**

INTRODUCTION

In 1959, Meltzer and Kelemen were the first to describe skull base osteomyelitis (SBO) in a patient with pyocyaneus chondritis and osteomyelitis of the external auditory canal (EAC).[1] Cranial osteomyelitis includes a spectrum of various causes.[2,3]

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 SBO," 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.[2,4-6] 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.[2] 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.[22,24] 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.[2,18,21-23,28] 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 abscess, leading to significant morbidity and mortality.[21-23,28-31] 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.[32-33] 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.[30-31]

2) MSBO. Although relatively uncommon, MSBO is a frequent clinical entity among SBO cases, associated with significant functional morbidity and mortality.[15,34] 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.[36,37] Many studies suggest that *Pseudomonas aeruginosa* infection is a leading cause of MOE and MSBO, responsible for up to 98% of all cases.[38] However, MSBO can also develop as a complication of paranasal sinusitis,

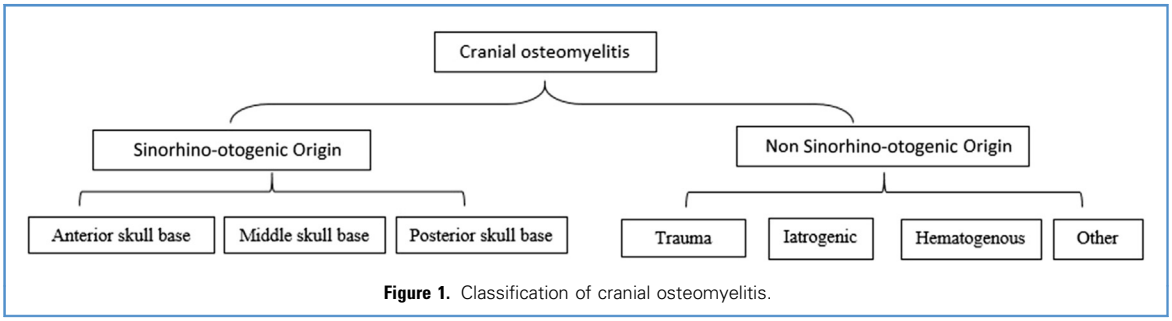

Figure 1. Classification of cranial osteomyelitis.