

Case Report

Challenges in the Diagnosis and Treatment of Skull Base Osteomyelitis

Patorn Piromchai MD, MSc, PhD, FRCOT, FICS*, Pornthep Kasemsiri MD, FRCOT*,
Supawan Laohasiriwong MD, FRCOT*, Teeraporn Ratanaanekchai MD, FRCOT*

* Department of Otorhinolaryngology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

Osteomyelitis of the skull base involves a complex anatomy and requires multimodality management. Delayed diagnosis and treatment can lead to death. To emphasize the challenge of this condition, we underscore the difficulty distinguishing between skull base malignancy and skull base osteomyelitis. Signs of craniofacial osteomyelitis include (a) clinical symptoms of persistent discharge from the natural orifices and severe pain and (b) imaging evidence of osteolytic lesions. Empirical treatment with antibiotics should be started as soon as possible to minimize morbidity and mortality.

Keywords: Osteomyelitis, Temporal bone, Skull base

J Med Assoc Thai 2017; 100 (Suppl. 6): S259-S265

Full text. e-Journal: <http://www.jmatonline.com>

Craniofacial osteomyelitis can occur in various locations, including the mandible, frontal bone, maxilla, nasal bone, temporal bone, and skull base bones⁽¹⁾. Skull base osteomyelitis (SBO) is a rare but fatal disease, which left untreated, will deteriorate rapidly and lead to mortality. The risk factors-such as diabetes, elderly, and immuno-compromised-have been reported in earlier series⁽²⁻⁵⁾. More than half of untreated patients die⁽²⁾, but with long-term antibiotics and surgical debridement, six-month survival for treated patients is as high as 80%⁽⁶⁾.

Osteomyelitis can be defined as an inflammatory condition of the bone that begins as an infection of the medullary cavity, which rapidly involves the Haversian systems and extends to the periosteum of the affected area⁽⁷⁾. The long bones are common sites of osteomyelitis. Osteomyelitis of the skull base is rare, including osteitis of the temporal bone, bony labyrinth, the medial part of the os petrosa, the os sphenoidale occipital, the clivus, and the infratemporal fossa⁽⁸⁾.

Conditions altering the vascularity of the bone like radiation, malignancy, osteoporosis, osteopetrosis, and Paget's disease predispose the patient to osteomyelitis. Systemic diseases such as diabetes, anemia, and malnutrition can cause a

concomitant alteration in host defenses and profoundly influence the course of osteomyelitis⁽⁹⁾.

Skull base osteomyelitis can be divided into lateral SBO and central SBO. Lateral skull base osteomyelitis was defined as osteomyelitis with an auricular origin, in which the patients usually presented with otologic symptoms such as purulent otorrhea and severe otalgia. Lateral skull base osteomyelitis has been discussed under various names, including malignant otitis externa, necrotizing otitis externa, and osteomyelitis of the mastoid. Central skull base osteomyelitis has an unrelated auricular etiology. The common causes of central SBO are radiation, malignancy, and infection in the upper airway including sinuses.

There remains a lack of clarity on the presenting symptoms of this condition and a uniform management algorithm. Lateral SBO is usually managed by an otologist while central SBO is usually managed by a rhinologist given the lack of otologic symptoms. We present a case series on osteomyelitis, including central and lateral skull base osteomyelitis, their signs and symptoms, diagnosis, and treatment, and a management algorithm. Ethical approval was provided by the Khon Kaen University Ethics Committee (HE591177).

Correspondence to:

Piromchai P, Department of Otorhinolaryngology, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand.
Phone: +66-81-5444463
E-mail: patorn@gmail.com

Case Report

Case 1

A 65-year-old diabetic male was referred to our hospital having experienced a chronic ear discharge

for six months. The patient reported that water got into his ear during shower before getting a greenish discharge from his right ear and otalgia. He had no history of otorrhea, and his blood sugar was well-controlled.

Three months prior to presentation, he went to the local primary hospital. The otolaryngologist found a mass in his right external auditory canal. Computed tomography (CT) of the temporal bone revealed a right middle ear enhanced soft tissue density lesion with a slightly lateral displacement of the right ear ossicle and subtle bony erosion of the floor of the middle ear. Topical antibiotics were given, but the discharge continued to drain from his right ear.

On arrival at our hospital, he had no fever, his blood pressure was slightly high (153/77 mmHg). Otologic microscopy revealed aural polyps originating from the superior part of the middle ear extending to the external auditory canal. There was no pus discharge and no evidence of cholesteatoma. A punch biopsy of the aural polyps was performed, and otic steroid with anti-infective preparation prescribed (viz., furaltadone, polymyxin B, neomycin, fludrocortisone, and lidocaine).

The pathological report showed submucosal granulation, subacute inflammation, and fibrosis. At one month, the aural polyps persisted, and the patient continued to have otalgia. Systemic ciprofloxacin antibiotic was added in conjunction with an otic solution.

Two months after treatment, the patient returned with persistent otalgia. On the otologic microscopy examination, the aural polyps disappeared, and the tympanic membrane was intact. We performed a follow-up CT scan and found a soft tissue mass at the right temporo-mandibular joint and nasopharynx involving the middle ear with bony destruction. A biopsy of the nasopharynx was performed. The audiogram revealed right moderately-severe mixed hearing loss.

Two weeks after biopsy, the pathological report showed chronic inflammation. The patient indicated that the ear pain was increased on the left side. The audiogram revealed bilateral, moderately-severe, mixed hearing loss. At this point, the patient had diagnosed skull base osteomyelitis and was admitted for intravenous antibiotics. A baseline gallium scan was performed (Fig. 1).

In the ward, the patient was given intravenous clindamycin and ceftazidime for 4 weeks. Adjunct hyperbaric oxygen therapy was given 11 times. Fiber

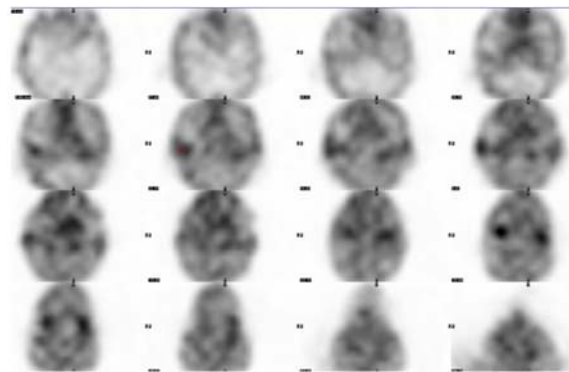


Fig. 1 Faint Ga-67 uptake at right petrous, right mandibular condyle, and right TMJ. Physiologic Ga-67 uptake at lacrimal glands, salivary glands.

optic endoscopy revealed a reduction in the area of granulation tissue in the nasopharynx. After complete treatment, the patient was symptom-free and discharged with oral ciprofloxacin and clindamycin.

The oral antibiotics were given for 3 months. A follow-up Gallium scan revealed resolution of the osteomyelitis. The hearing level based on the audiogram improved from moderately-severe to moderate sensorineural hearing loss. No additional complications were reported.

Case 2

A 40-year-old male presented with a swollen left cheek and toothache that he had for two months. Gum biopsy revealed an infected radicular cyst with verrucous proliferation and mild atypia. His cheek was still painful. Moreover, 2-cm diameter lymphadenopathies were present on the left neck. He underwent partial resection of the antero-inferior portion of the maxilla with neck dissection. Pathology reported chronic inflammation with squamous epithelial hyperplasia, parakeratosis, fibrosis, and chronic osteomyelitis with fibrosis on the maxillary specimen. Lymph nodes revealed reactive hyperplasia. Augmented penicillin was administered after surgery. One year later, the patient complained of left aural fullness and nasal obstruction. Nasal endoscopy revealed an ulcerative lesion anterior to the left Eustachian tube and marked swelling of the mucosa on the left nasal cavity. CT revealed fullness of the left Rosenmüller fossa, and destruction of the body of the sphenoid bone and pterygoid plate (Fig. 2).

Multiple sites biopsy were performed. All specimens revealed marked chronic inflammation with squamous hyperplasia at the sphenoid mucosa and

pterygoid plate. The patient received antibiotic and hyperbaric oxygen therapy 20 times (2.4 ATA, 90 minutes) but the symptoms did not improve. He continued to have pain with irregular nasal mucosa of the left nasal cavity. CT was requested for re-evaluation and it showed an increase of ill-defined infiltrative lesions at the bilateral ethmoid sinuses, sphenoid sinus, left maxillary, nasal cavity, and bilateral orbital apex. Bony destruction involved the nasal septum, pterygoid plate, sphenoid bone, and middle cranial base on the left side (Fig. 3).

The patient underwent complete resection of the left maxillary sinus for a definite diagnosis. The pathologist reported verrucous carcinoma. A residual tumor presented at the middle cranial base and was considered a high-risk surgery because of potential for

morbidity and mortality, so radiotherapy was requested since complete resection of the tumor at the cranial base was not possible (Fig. 3). Unfortunately, the patient was lost to follow-up and the radiotherapy was not initiated.

Case 3

A 56-year-old diabetic male with hypertension and chronic kidney disease presented with left ear pain with discharge and headache for one month. The local otolaryngologist requested a CT scan without contrast (due to renal impairment) which revealed a left nasopharyngeal mass. He had a swollen left ear canal with pus discharge. Nasal endoscopy was performed, and biopsy of the left nasopharyngeal mass was done under local anesthesia. Oral ciprofloxacin and tramadol for pain were given. The pathology was negative for malignancy. The swelling of the ear canal improved and the audiometry revealed normal hearing in the right ear and moderate mixed hearing loss of the left ear (PTA 53 dB with type B tympanogram).

The patient came for a second biopsy under general anesthesia during which he developed left facial palsy (grade 5) before being admitted. Other cranial nerves were intact, and the facial palsy was thought to result from the invasiveness of a malignancy. The pathology result, however, was negative for cancer.

Due to the high prevalence of nasopharyngeal carcinoma in the region and possible submucosal types of cancer, a second CT scan was requested to evaluate the suspected tumor and to take a more accurate biopsy by image-guided navigation. The second CT scan revealed a mass at the bilateral nasopharynx (left more than right). The lesion extended to the left parapharyngeal space, left middle ear canal, and C1/C2 joint space. Bony erosions were found at the left petrous apex, the anterior portion of the clivus, the greater wing of the left sphenoid bone, and the left facial canal. No neck lymphadenopathies were found (Fig. 5).

Another nasopharyngeal biopsy under image-guided navigation was performed. Soft, friable tissue was observed with white mucoid pus seeping from the biopsied tissue. The fluid was sent for culture and the tissue for histopathology. The patient was given empirical treatment of ceftazidime for necrotizing otitis externa. The culture from the biopsied tissue came back as *Enterobacter spp.* sensitive to cefotaxime, ceftazidime, and ciprofloxacin but resistant to amoxiclavulanate. The haemoculture was negative and so was the fluid gram stain, acid fast bacilli (AFB) stain,

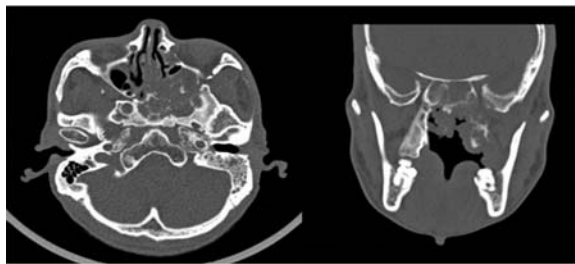


Fig. 2 CT scan showed the destruction of body of sphenoid bone and pterygoid plate on left side.

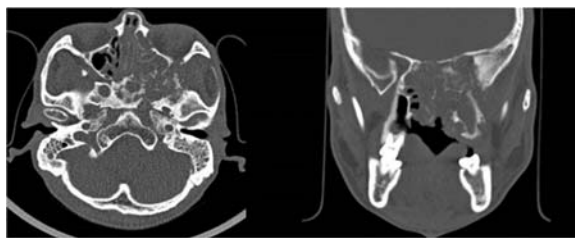


Fig. 3 CT scan showed bone destruction involving nasal septum, pterygoid plate, sphenoid bone, and middle cranial base on left side.

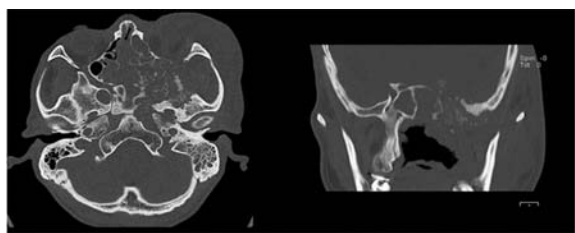


Fig. 4 CT scan showed residual tumor with bony destruction at left middle cranial.

and modified AFB stain. A gallium scan was performed (Fig. 6).

The histopathology indicated chronic inflammation. The patient received morphine for severe headache. After receiving ceftazidime for six weeks, a gallium scan was repeated. Since improvement was observed, he was discharged. Ten days later he had right ear discharge with hearing loss and a perforated tympanic membrane on the right. He refused re-admission so oral ciprofloxacin was prescribed. The right ear discharge decreased, but his hearing deteriorated. After two months, he did not come for follow-up. Data from the national house registry revealed that he had died 10 months later. The exact cause of death was not documented.

Discussion

An inadequately treated chronic infection of the craniofacial region can cause a bony infection called osteomyelitis. The bony infection is a severe form of infection and needs aggressive intervention. After treatment, patients are usually left with a scar and deformity. Since the craniofacial skeleton is associated with personal appearance, the management of craniofacial osteomyelitis is challenging and must be managed differently from other parts of the body. In 1760, Sir Percival Pott was the first surgeon to report osteomyelitis of the frontal bone resulting in a swelling on the forehead⁽¹⁰⁾.

Osteomyelitis is defined as an inflammatory condition of the bone that commences as an infection of the medullary cavity, rapidly involving the Haversian systems, and eventually involving the periosteum of the infected areas⁽¹⁾. Invasion of bacteria into the cancellous bone results in compression of blood vessels secondary to inflammation and edema of the marrow space. Severe compromise of the blood supply results in the development of ischemic and necrotic bone⁽¹¹⁾. Immobility of the stagnant blood serves as a critical nidus for the development of infection.

Diagnosis of SBO is usually difficult. The common type is a severe form of necrotizing otitis externa. Levenson's criteria are used for diagnosis of necrotizing otitis externa. The criteria include refractory otitis externa, severe nocturnal otalgia, and purulent otorrhea associated with *Pseudomonas* infection and granulation of tissue in an immuno-compromised or diabetic patient. Facial nerve palsy, swallowing problems, and hoarseness may occur if the cranial nerve is involved⁽¹²⁾. Inflammatory change and granulation are noted in the external ear canal. Pain is often

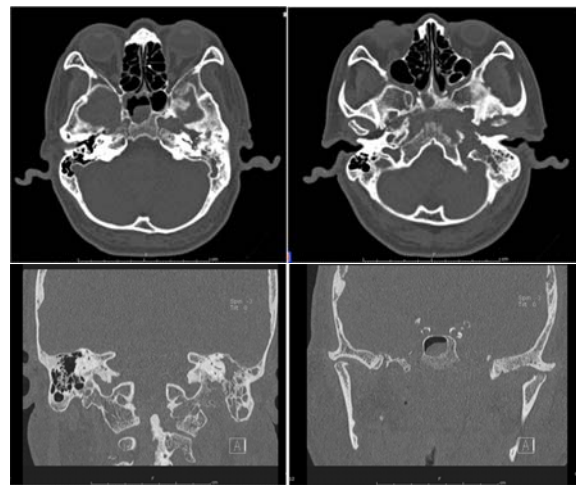


Fig. 5 CT scan showed bony erosion of left petrous apex, anterior portion of clivus, greater wing of left sphenoid bone and left facial canal.

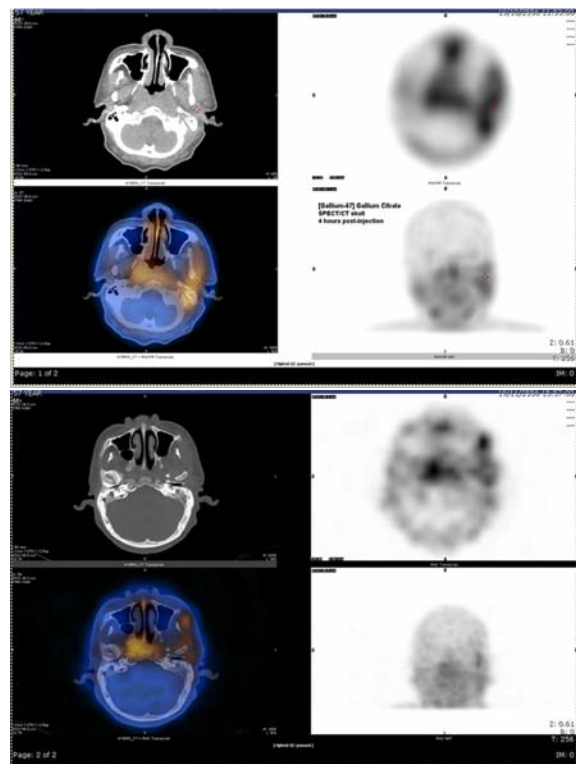


Fig. 6 Gallium scan during treatment and after six weeks of intravenous antibiotic treatment.

disproportional to the changes observable during otoscopy. SBO should be considered in cases with severe pain that do not respond well to medication or present with cranial nerve palsy beyond the facial nerve. In the central type, there may be no evidence of active

otitis externa or granulation in the external ear canal. Resolution seemed apparent several months before the development of cranial nerve palsy and SBO^(13,14). Cardinal symptoms of central SBO include persistent headache with or without neurological deficits. Cranial nerves that are commonly involved include CN VI, IX, X, and XI. SBO should be differentiated from nasopharyngeal cancer, metastatic lesion, and chronic granulomatous disorder.

ESR is usually elevated in SBO such that it is useful for discriminating cancer and serves as a guide when antibiotics are being considered as an intervention. The normalization of ESR indicates resolution of the infection.

Computed tomography findings may demonstrate the bony erosion; however, Rowlands et al⁽¹³⁾ conducted an initial CT scan and failed to demonstrate bony destruction. Seabold et al found no CT evidence of bone erosion in 13 out of 35 patients with biopsy-confirmed cranial osteomyelitis⁽¹⁵⁾. The bony erosion findings may also persist after the SBO is inactive, so the use of CT for follow-up is not recommended.

MRI and gallium bone scan are the standard investigations for diagnosis and used to assess the severity and extent of SBO. Typical MRI findings include marrow T1 hypointensity and T2 hyperintensity; although these are not specific^(16,17). In the central type, the involvement of clivus is common. MRI is also a useful and reliable tool for monitoring the response to treatment and evaluating recurrence; however, gallium bone scan is best used to delineate the transition from active to inactive SBO.

Skull base biopsy-including microbiological analysis-is the essential investigation for diagnosis and differential diagnosis in such patients. Although *Pseudomonas aeruginosa* is the most common pathogen in SBO, mucormycosis, and *Aspergillus spp.* are also found especially in the central type^(18,19).

The treatment of choice in SBO is intravenous antibiotics. Oral antibiotics-such as ciprofloxacin-can be used in a few cases with minor symptoms. SBO should be treated with antibiotics for at least 6 weeks because bone tissue uptake of antibiotics is a function of vascularity, small vessel disease-especially among diabetics-further compromises antibiotic uptake and tissue distribution^(12,20,21).

Hyperbaric oxygen may play a role in the management of chronic, refractory SBO^(22,23); however, a Cochrane review concluded that not enough data are available to provide recommendations⁽²⁴⁾. The role of

surgery is confined to biopsy and possible drainage when an associated abscess is present⁽⁵⁾.

Early diagnosis and early management with effective antibiotic therapy may result in resolution of cranial nerve palsy albeit slow. Unfortunately, permanent neurological sequelae and mortality are consequences of delayed diagnosis and treatment.

Conclusion

We presented a subgroup of patients with craniofacial osteomyelitis at the skull base. Clinical symptoms of persistent discharge from natural orifices and severe pain combined with imaging evidence of osteolytic lesion are serious signs of potential craniofacial osteomyelitis. Empirical treatment with antibiotics should be started immediately to minimize morbidity and mortality.

What is already known on this topic?

Craniofacial osteomyelitis is a bony infection of the craniofacial skeleton.

Skull base osteomyelitis is a subset of craniofacial osteomyelitis.

Inadequately treated sufferers of craniofacial osteomyelitis can result in disfigurement.

What this study adds?

Clinical symptoms of persistent discharge from natural orifices and severe pain combined with the imaging evidence of osteolytic lesions are signs of craniofacial osteomyelitis.

Empirical treatment with antibiotics should be started immediately to minimize morbidity and mortality.

Acknowledgements

The authors thank (a) the patients at Srinagarind Hospital who are represented in this case series; (b) the Center of Cleft Lip-Cleft Palate and Craniofacial Deformities, Khon Kaen University under Tawanchai Royal Grant Project for support; and, (c) Mr. Bryan Roderick Hamman for assistance with the English-language presentation of the manuscript.

Potential conflicts of interest

None.

References

1. Prasad KC, Prasad SC, Mouli N, Agarwal S. Osteomyelitis in the head and neck. *Acta Otolaryngol* 2007; 127: 194-205.
2. Chandler JR. Malignant external otitis. *Laryn-*

- goscope 1968; 78: 1257-94.
3. Rubin GJ, Branstetter BF, Yu VL. The changing face of malignant (necrotising) external otitis: clinical, radiological, and anatomic correlations. *Lancet Infect Dis* 2004; 4: 34-9.
 4. Patmore H, Jebreel A, Uppal S, Raine CH, McWhinney P. Skull base infection presenting with multiple lower cranial nerve palsies. *Am J Otolaryngol* 2010; 31: 376-80.
 5. Ducic Y. Management of osteomyelitis of the anterior skull base and craniovertebral junction. *Otolaryngol Head Neck Surg* 2003; 128: 39-42.
 6. Blyth CC, Gomes L, Sorrell TC, da Cruz M, Sud A, Chen SC. Skull-base osteomyelitis: fungal vs. bacterial infection. *Clin Microbiol Infect* 2011; 17: 306-11.
 7. Fitzgerald RH Jr, Brewer NS, Dahlin DC. Squamous-cell carcinoma complicating chronic osteomyelitis. *J Bone Joint Surg Am* 1976; 58: 1146-8.
 8. Ridder GJ, Breunig C, Kaminsky J, Pfeiffer J. Central skull base osteomyelitis: new insights and implications for diagnosis and treatment. *Eur Arch Otorhinolaryngol* 2015; 272: 1269-76.
 9. Prasad SC, Prasad KC, Kumar A, Thada ND, Rao P, Chalasani S. Osteomyelitis of the temporal bone: terminology, diagnosis, and management. *J Neurol Surg B Skull Base* 2014; 75: 324-31.
 10. Banooni P, Rickman LS, Ward DM. Pott puffy tumor associated with intranasal methamphetamine. *JAMA* 2000; 283: 1293.
 11. Strumas N, Antonyshyn O, Caldwell CB, Mainprize J. Multimodality imaging for precise localization of craniofacial osteomyelitis. *J Craniofac Surg* 2003; 14: 215-9.
 12. Chandler JR, Grobman L, Quencer R, Serafini A. Osteomyelitis of the base of the skull. *Laryngoscope* 1986; 96: 245-51.
 13. Rowlands RG, Lekakis GK, Hinton AE. Masked pseudomonal skull base osteomyelitis presenting with a bilateral Xth cranial nerve palsy. *J Laryngol Otol* 2002; 116: 556-8.
 14. Clark MP, Pretorius PM, Byren I, Milford CA. Central or atypical skull base osteomyelitis: diagnosis and treatment. *Skull Base* 2009; 19: 247-54.
 15. Seabold JE, Simonson TM, Weber PC, Thompson BH, Harris KG, Rezai K, et al. Cranial osteomyelitis: diagnosis and follow-up with In-111 white blood cell and Tc-99m methylene diphosphonate bone SPECT, CT, and MR imaging. *Radiology* 1995; 196: 779-88.
 16. Malone DG, O'Boynick PL, Ziegler DK, Batnitzky S, Hubble JP, Holladay FP. Osteomyelitis of the skull base. *Neurosurgery* 1992; 30: 426-31.
 17. Erdman WA, Tamburro F, Jayson HT, Weatherall PT, Ferry KB, Peshock RM. Osteomyelitis: characteristics and pitfalls of diagnosis with MR imaging. *Radiology* 1991; 180: 533-9.
 18. Lee JH, Park YS, Kim KM, Kim KJ, Ahn CH, Lee SY, et al. Pituitary aspergillosis mimicking pituitary tumor. *AJR Am J Roentgenol* 2000; 175: 1570-2.
 19. Chan LL, Singh S, Jones D, Diaz EM Jr, Ginsberg LE. Imaging of mucormycosis skull base osteomyelitis. *AJNR Am J Neuroradiol* 2000; 21: 828-31.
 20. Grobman LR, Ganz W, Casiano R, Goldberg S. Atypical osteomyelitis of the skull base. *Laryngoscope* 1989; 99: 671-6.
 21. Magliulo G, Varacalli S, Ciofalo A. Osteomyelitis of the skull base with atypical onset and evolution. *Ann Otol Rhinol Laryngol* 2000; 109: 326-30.
 22. Sie KC, Glenn MG, Hillel AH, Cummings CW. Osteomyelitis of the skull base, etiology unknown. *Otolaryngol Head Neck Surg* 1991; 104: 252-6.
 23. Amedee RG, Mann WJ. Osteomyelitis of the skull base—an unusual manifestation. *Am J Otol* 1989; 10: 402-4.
 24. Narozny W, Kuczkowski J, Stankiewicz C, Kot J, Mikaszewski B, Przewozny T. Value of hyperbaric oxygen in bacterial and fungal malignant external otitis treatment. *Eur Arch Otorhinolaryngol* 2006; 263: 680-4.
 25. Ganhewa AD, Kuthubutheen J. A diagnostic dilemma of central skull base osteomyelitis mimicking neoplasia in a diabetic patient. *BMJ Case Rep* 2013; pii: bcr2012007183.

ความท้าทายในการวินิจฉัยและรักษากระดูกฐานสมองอักเสบ

ภาธร ภิมยศไชย, พรเทพ เกษมศิริ, สุภาวรรณ เลหาศิริวงศ์, ธีรพร รัตนเอนกชัย

การอักเสบของกระดูกฐานสมองมีความซับซ้อนสูงและมีวิธีการรักษาที่จำเพาะ การรักษาที่ไม่เหมาะสมอาจทำให้เสียชีวิตได้ ผู้แต่งได้แสดงถึงความท้าทายในการวินิจฉัยแยกโรคระหว่างมะเร็งบริเวณฐานสมอง และกระดูกฐานสมองอักเสบ สัณญาณเตือนว่าผู้ป่วยมีกระดูกฐานสมองอักเสบคือ มีน้ำหรือหนองไหลออกจากช่องหู คอ หรือจมูกตลอดเวลาและมีอาการปวดอย่างรุนแรง ร่วมกับหลักฐานของกระดูกกร่อนในภาพถ่ายรังสี ในรายที่สงสัยกระดูกฐานสมองอักเสบ แนะนำว่าควรให้ยาปฏิชีวนะทันทีเพื่อป้องกันความพิการหรือเสียชีวิต
