

Chronic osteomyelitis of the zygomatic bone: Back to Benzathine penicillin

Shilpi Karmakar¹, Arun K. Singh^{2,3,4}, Saurabh Karmakar⁵

¹ Department of Burns and Plastic Surgery, All India Institute of Medical Sciences, Jodhpur, India

² Vice Chancellor, Atal Bihari Vajpayee Medical University, Lucknow, India

³ Director, Ram Monohar Lohia Institute of Medical Sciences, Lucknow, India.

⁴ Ex- Head of Department, Post Graduate Department of Plastic Surgery, King George's Medical University, Lucknow, India

⁵ Department of Pulmonary Medicine, All India Institute of Medical Sciences, Phulwarisharif, Patna, India

ORCID ID of the author(s)

SK: 0000-0001-7423-9186

AKS: 0000-0002-6513-1007

SK: 0000-0002-8135-4864

Abstract

Osteomyelitis (OM) of zygomatic bone (zyb) is a rare disease, characterized by relapses. We present two patients presenting with chronic discharging sinus over zyb, who had been treated in previous centers, with multiple culture-directed antibiotics, over many months, without cure. We administered intramuscular Benzathine Penicillin 1.2 million IU with oral Vitamin C 1000 mg/day, for a total of six months and achieved successful healing. In chronic OM (cOM), most bacteria are sessile, embedded in biofilm. Sessile bacteria are not picked by a swab; therefore, the bone must be biopsied. Sessile bacteria also do not grow well in culture media. Thus, the conventional cultures do not reflect the true organisms causing cOM. The Minimum Biofilm Eradication Concentration of antibiotics cause toxicity. To eradicate the biofilm bacteria in patients whose computed tomography showed absence of a sequestrum, we administer this regimen. Judicious case selection is necessary. This regimen adds to the clinician's armamentarium.

Keywords: Osteomyelitis, Zygomatic bone, Benzathine penicillin, Chronic osteomyelitis, Facial aesthetics

Introduction

Osteomyelitis (OM) is the infection of the bone and bone marrow. OM of the facial bones is a rare disease, but associated with high morbidity. OM of zygomatic bone (zyb) has a low incidence (1.42%). Chronic OM (cOM) is characterized by alternating periods of quiescence and sinus tract drainage [1].

We present two patients of cOM of zyb, who had been treated with various culture-directed antibiotics, over many months, without cure. We administered intramuscular (im) Benzathine Penicillin (BPn) with oral Vitamin C (oVitC) and achieved successful healing of the sinus.

Corresponding Author

Shilpi Karmakar

Department of Burns and Plastic Surgery, All India Institute of Medical Sciences, Jodhpur, India- 342005

E-mail: drshilpikarmakar@rediffmail.com

Informed Consent

The authors stated that the written consent was obtained from the patients and the parents of patients presented with images in the study.

Conflict of Interest

No conflict of interest was declared by the authors.

Financial Disclosure

The authors declared that this study has received no financial support.

Published

2021 November 15

Copyright © 2021 The Author(s)

Published by JOSAM

This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-NoDerivatives License 4.0 (CC BY-NC-ND 4.0) where it is permissible to download, share, remix, transform, and build upon the work provided it is properly cited. The work cannot be used commercially without permission from the journal.



Case presentation

Case 1

A 12-year-old male presented with history of mild fever and a spontaneous onset diffuse swelling in the left malar region 9 months ago. The lesion was slowly growing in size, painless, and not associated with any dental complaints or swellings in body. Suspecting it to be an abscess, a physician in a previous center had incised the swelling and sent the drained fluid for culture, which revealed a growth of Streptococci. Guided by the sensitivity reports, he was prescribed Amoxicillin–Clavulanic acid 625 mg thrice daily. There was a reduction in the discharge, followed by an increase of foul-smelling discharge. The patient consulted another doctor, and was prescribed intravenous Vancomycin, and over next six months was treated with Linezolid, Clindamycin, Levofloxacin and Metronidazole, in appropriate doses, with no sustained relief. He came to us with a discharging sinus over left malar eminence (Figure 1). A consent was obtained for scientific presentation. Total and differential leucocyte counts were normal, C-reactive protein was elevated, and biochemical tests were normal. We ordered a computed tomography (CT) of the face and did a bone biopsy. The CT revealed a cavitation of the left zyb (Figure 2). Bone culture was negative.

We diagnosed cOM of the zyb and proceeded with BPn 1.2 million IU im, fortnightly and oVitC 500mg BD. The discharge reduced within a month and ceased in two months. The sinus healed in three months.

Figure 1: Left oblique view of patient 1 showing pus discharge from the sinus over the left zygomatic bone



Figure 2: Transverse section of CT scan of the face of patient 1, showing a cavitation of left zygomatic bone (arrow)



Case 2

A 24-year-old female was referred to us with a persistently discharging sinus over the right zyb. Four months ago, the patient had spontaneously developed a diffuse, painful swelling over right zyb, which had not resolved with oral Cefpodoxime and Metronidazole. The swelling spontaneously ruptured. She consulted a surgeon, who curetted the sinus and sent the tissue for culture, which revealed Staphylococcus sensitive to Vancomycin. Over three months, she was treated with multiple antibiotics, but relief was temporary. We diagnosed cOM of the zyb based on the CT of the face (Figure 3) and bone biopsy and started her on BPn 1.2million IU im, fortnightly and oVitC 500 mg BD. Photographic documentation was performed. The discharge ceased in two months and the sinus healed in four months. We continued the treatment for six months.

The patient has been followed up for two years now, without recurrence. There is a depressed scar over the zyb, for which fat grafting is planned (Figure 4).

Figure 3: Coronal section of CT scan of the face of patient 2, showing a cavitation of right zygomatic bone (arrow)

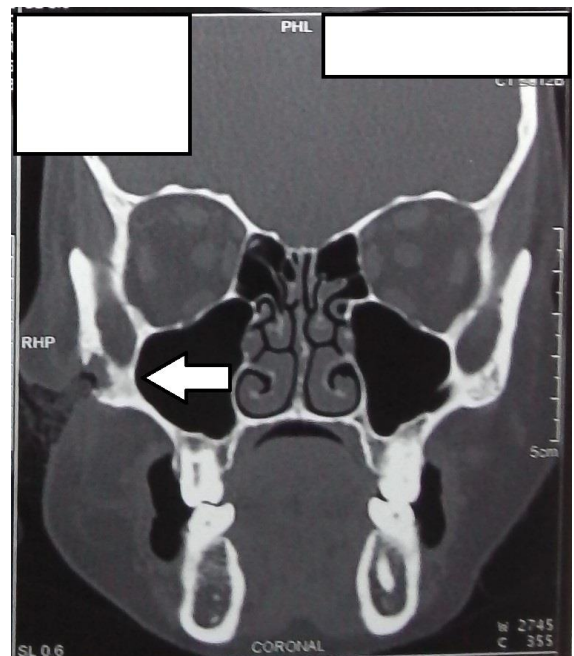


Figure 4: Healed sinus of patient 2, forming a depressed scar over the right zygomatic bone



Discussion

The underlying pathology, rather than the timescale, differentiates cOM from acute OM. Acute OM is a suppurative infection, with edema and small vessel thrombosis, while cOM is biofilm and sessile bacterial infection. In cOM, a small fraction of the microorganisms is free-floating (planktonic) and the rest are embedded within a hydrated polysaccharide matrix with nucleic acid and protein (biofilm) [2].

Culture is the best method to detect the viable bacteria [3]. The sessile bacteria within the glycocalyx-enclosed microcolonies are adherent to the bone and are not picked by swabs. The planktonic bacteria, however, are [2, 4]. The affected bone must be cultured. Also, the sessile bacteria are adapted to grow very slowly. The media used to culture bacteria in laboratory, thus, selects the planktonic bacteria [4].

The conventional method to determine the sensitivity towards antibiotics (Minimum Inhibitory Concentration, MIC) is measured against the planktonic flora. The Minimum Biofilm Eradication Concentration of various drugs is 50 to 1000 times higher than MIC. Such high plasma level of antibiotics cannot be achieved because of toxicity [2, 4].

Staphylococcus aureus is the most common organism causing OM, followed by coagulase-negative *Staphylococci*, *Streptococcus*, gram-negative bacilli, and anaerobic organisms [2, 5]. Other bacterial species that are unculturable are also present [2].

Penicillin is effective against *Staphylococcus*, *Streptococcus* and other gram-positive bacteria [6]. Penicillin with a biofilm dispersing agent, like oVitC, administered for long enough, has been used to treat psoriasis, rheumatic fever, and Alzheimer-like disease, which are notorious for relapses [6]. Both biofilm and planktonic forms of *S. dysgalactiae* and *S. suis* are shown to be sensitive to penicillin [4].

oVitC inhibits both preformed and new biofilm production. This effect might be due to the anti-quorum sensing activity [7].

Our management is supported by Banham, who treated OM of the maxilla with Penicillin. [8] Merkesteyn treated cOM of the mandible with Penicillin [9].

BPn (depot form of Penicillin) is hydrolyzed to Penicillin G over 14 to 28 days from the intramuscular injection sites [10]. Hydrolysis and slow absorption results in prolonged serum levels [5]. Adults have detectable drug levels for 14 days [10]. Since short duration of treatment is associated with relapse [9], we recommend a treatment of at least six months.

Penicillin is a relatively less toxic antibiotic. Hypersensitivity reactions are the most serious concern, which may be averted by injecting a test dose [10]. Hyperbaric oxygen is another alternative to surgical reperfusion.

Intracellular persistence of *S.aureus* maybe another cause of cOM. In vivo studies show this to be insignificant [5].

Presence of sequestrum and necrotic tissue necessitate surgical debridement [2, 9]. In selected cases of cOM, without apparent necrotic tissue, we administer this regimen. Debridement of zyb obliterates an important aesthetic landmark of face. Reconstruction, too, has its pitfalls. A careful case selection is emphasized.

Conclusion

In judiciously selected cases of cOM of zyb, BPn 1.2 million IU administered intramuscularly, fortnightly with oVitC 1000 mg, daily, for at least six months, is effective. This regimen adds to the armamentarium of surgeons and is worthy of wider use. The need to sensitize surgeons to the role of BPn with oVitC in eradicating cOM led us to report these cases.

Acknowledgements

The authors acknowledge the patients' and their families for their faith in the treatment and their consent for obtaining and publishing photographs.

References

1. Mejia B, Bordoy A, Mendez B. Osteomyelitis of the zygomatic bone: a case report and literature review. *Internat J Oral maxillofac Surg.* 2017;46:308.
2. Calhoun JH, Manring MM, Shirliff M. Osteomyelitis of the long bones. *Semin Plast Surg.* 2009;23(2):59–72. doi: 10.1055/s-0029-1214158.
3. Barer MR, Harwood CR. Bacterial viability and culturability. *Adv Microb Physiol.* 1999;41:93–137. doi: 10.1016/s0065-2911(08)60166-6.
4. Olson ME, Ceri H, Morck DW, Buret AG, Read RR. Biofilm bacteria: formation and comparative susceptibility to antibiotics. *Can J Vet Res.* 2002;66(2):86-92.
5. Masters EA, Trombetta RP, Bentley KLM, Boyce BF, Gill AL, Gill SR, et al. Evolving concepts in bone infection: redefining "biofilm", "acute vs. chronic osteomyelitis", "the immune proteome" and "local antibiotic therapy". *Bone Res.* 2019;7:20. doi: 10.1038/s41413-019-0061-z. eCollection 2019.
6. Allen HB, Hossain C, Abidi N, Larjani M, Joshi SG. Penicillin: The old/new wonder drug. *Adv Tech Biol Med.* 2017;5:17.
7. El-Gebaly E, Essam T, Hashem S, El-Baky RA. Effect of Levofloxacin and Vitamin C on bacterial adherence and preformed biofilm on urethral catheter surfaces. *J Microb Biochem Technol.* 2012;4:131-6.
8. Banham TM. A case of Osteomyelitis of the Superior Maxilla treated with penicillin. *J Laryngol Otol.* 1949;63(4):233. doi: 10.1017/s0022215100046387.
9. Merkesteyn JPRV, Groot RH, Akker VD, Bakker DJ, Borgmeijer-Hoelen AMMJ. Treatment of chronic suppurative osteomyelitis of the mandible. *Int J Oral Maxillofac Surg.* 1997;26:450-4. doi: 10.1016/s0901-5027(97)80012-4.
10. Ball AP, Gray JA, Murdoch JMcC. The Natural Penicillins. In: Ball AP, Gray JA, Murdoch JMcC, eds. *Antibacterial Drugs Today*, 2nd ed. Lancaster: MTP Press Ltd; 1978. pp. 8-11.

This paper has been checked for language accuracy by JOSAM editors.

The National Library of Medicine (NLM) citation style guide has been used in this paper.