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Mandibular Osteomyelitis Caused by *Candida glabrata*: A Case Report

Candida glabrata'nın Neden Olduğu Mandibular Osteomiyelit: Bir Olgu Sunumu

Bilge Çağlar[1], Esra Zerdali[1], İclal Nur Bulut[2], Filiz Pehlivanoğlu[1]

[1]Haseki Training and Research Hospital, Clinic of Infectious Diseases, İstanbul, Türkiye
[2]Medipol University Pendik Hospital, Department of Radiology, İstanbul, Türkiye

Abstract

Osteomyelitis is an infection involving the bone and bone marrow, most commonly caused by bacterial pathogens, though it can rarely occur due to fungal organisms. *Candida glabrata* is a *Candida* species that is challenging to treat because of its inherent resistance to azoles. Fungal osteomyelitis of the mandible is exceedingly uncommon, and infection with *C. glabrata* at this site has not been previously reported.

This report describes an unusual case of mandibular osteomyelitis that developed following a dental procedure, with *C. glabrata* identified as the pathogen. A 36-year-old man with diabetes mellitus presented with painful swelling extending to the face and neck after undergoing root canal treatment on his right lower molar. Despite receiving antibiotics, his symptoms persisted, and contrast-enhanced magnetic resonance imaging confirmed mandibular osteomyelitis with abscess formation. *C. glabrata* was isolated from tissue obtained during surgical debridement, and antifungal susceptibility testing was performed. The patient received intravenous caspofungin for 6 weeks, followed by oral fluconazole to complete a 6-month total treatment course once clinical improvement was noted.

The patient demonstrated clear clinical and radiological improvement. This case highlights that fungal pathogens should be included in the differential diagnosis of infections occurring after dental procedures that do not respond to antibiotics. Selecting an appropriate antifungal agent and performing timely surgical management are essential for successful treatment.

Keywords: Antifungal agents, *Candida glabrata*, mandible, osteomyelitis

Öz

Osteomiyelit, genellikle bakteriyel patojenlerle ilişkili olmakla birlikte, nadiren mantar enfeksiyonlarına bağlı olarak gelişebilen bir kemik ve kemik iliği enfeksiyonudur. *Candida glabrata*, intrinsik azol direnci nedeniyle tedavi yönetimi zor olan *Candida* türlerinden biridir. Mandibula yerleşimli fungal osteomiyelit oldukça nadirdir ve bu lokalizasyonda *C. glabrata* enfeksiyonu daha önce hiç bildirilmemiştir.

Bu vaka raporunda, dental müdahale sonrası mandibular osteomiyelit gelişen ve etken olarak *C. glabrata* izole edilen nadir bir olgu sunulmaktadır. Diyabet mellitus tanılı 36 yaşındaki erkek hasta, sağ alt molar dişine uygulanan kanal tedavisi sonrası yüz ve boyun bölgesine yayılan ağrılı şişlik ile başvurmuştur. Antibiyotik tedavisine rağmen semptomlarda gerileme olmamış, kontrastlı manyetik rezonans görüntüleme ile mandibular osteomiyelit ve apse saptanmıştır. Cerrahi debridmanla elde edilen örnekte *C. glabrata* üremesi saptanmış ve antifungal duyarlılık testleri yapılmıştır. Hastaya 6 hafta boyunca intravenöz kaspofungin tedavisi uygulanmış; klinik stabilite sağlanmasının ardından tedaviye, toplamda 6 aya tamamlanacak şekilde oral flukonazol ile devam edilmiştir.

Hastada, uygulanan tedaviye belirgin klinik ve radyolojik yanıt alınmıştır. Bu olgu, dental girişim sonrasında gelişen ve antibiyotik tedavisine yanıtsız seyreden enfeksiyonlarda fungal etkenlerin ayırıcı tanıda mutlaka göz önünde bulundurulması gerektiğini ortaya koymaktadır. Uygun antifungal ajan seçimi ve zamanında gerçekleştirilen cerrahi müdahale, tedavi başarısının sağlanmasında kritik öneme sahiptir.

Anahtar Kelimeler: Antifungal ajanlar, *Candida glabrata*, mandibula, osteomiyelit

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Address for Correspondence/Yazışma Adresi: Bilge Çağlar, MD. Haseki Training and Research Hospital, Clinic of Infectious Diseases, İstanbul, Türkiye
E-mail: bilgecaglaar1@gmail.com **ORCID ID:** orcid.org/0000-0002-7970-1795

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Introduction

Osteomyelitis is an inflammatory disease that arises in the bone and bone marrow due to a persistent infection[1]. Although it most commonly occurs as a result of bacterial pathogens, fungal, parasitic, and viral infections can also cause osteomyelitis[1]. The primary route of spread for *Candida* osteomyelitis is hematogenous dissemination, and in adults, the vertebrae, ribs, and sternum are the sites most frequently involved[2]. Osteomyelitis of the mandible due to *Candida* is very rare, and there are no established guidelines for diagnosis, treatment, or prognosis at this site. *Candida* species normally exist as commensals in the oral cavity; however, under certain local or systemic conditions, they may occasionally lead to invasive infections such as osteomyelitis[3].

Candida osteomyelitis typically has a chronic course, may persist for months from symptom onset, and can cause significant morbidity if not recognized early or managed properly[4]. These infections often show a mild or moderate inflammatory response, and inflammatory markers may not rise noticeably[4]. In this report, we describe a rare case of mandibular osteomyelitis due to *Candida glabrata* following a dental procedure. The patient was successfully managed with surgical debridement and prolonged antifungal therapy.

Case Report

A 36-year-old man with a known history of diabetes mellitus visited a dentist about 1 month earlier with a complaint of tooth pain. He underwent root canal treatment on his right lower molar. However, he developed swelling and pain on the right side of his face after the procedure, leading to extraction of the tooth. The patient was prescribed oral amoxicillin–clavulanate and clindamycin, but his symptoms did not improve, and the resulting dental abscess required surgical drainage.

He was then referred to our infectious diseases clinic due to persistent swelling on the right side of the face, which had extended to the neck. At the time of admission, he was afebrile and his vital signs were stable. Physical examination revealed swelling and warmth on the right side of the face. A fistula was observed extending from the right mandibular area to the skin surface. Laboratory tests showed a leukocyte count of 7400/mm^3, neutrophil count of 3800/mm^3, C-reactive protein of 4 mg/L and erythrocyte sedimentation rate of 18 mm/h. Contrast-enhanced neck magnetic resonance imaging (MRI) demonstrated a focal diffusion restriction indicating an abscess near the tooth root in the posterior right mandible, along with infectious-inflammatory T1A hypointense signal changes (focal osteomyelitis) within the bone marrow. There was also evidence of increased inflammatory signal in the adjacent masseter and pterygoid muscles and soft tissue enhancement. Additionally, a collection consistent with an abscess was identified within the superficial fascia, measuring 4 cm anteroposteriorly, with a maximum thickness of 4 mm and peripheral enhancement following IV contrast administration (Figure 1).

Based on these findings, the patient was empirically started on ampicillin-sulbactam. Abscess drainage and surgical debridement were carried out by the Ear, Nose, Throat and Maxillofacial Surgery teams. *C. glabrata* was identified in the abscess specimen collected during the procedure. Susceptibility testing showed that micafungin [minimum inhibitory concentration MIC <0.06 mg/L caspofungin MIC < 0.12 mg/L and amphotericin B (MIC<0.25) were effective. Given these results, the patient was treated with piperacillin-tazobactam, teicoplanin, and caspofungin. The antibiotic course was planned for a total of 6 weeks (piperacillin-tazobactam and teicoplanin for 2 weeks, followed by oral amoxicillin-clavulanate and ciprofloxacin for an additional 4 weeks). Caspofungin was administered intravenously for 6 weeks, and therapy was then continued with oral fluconazole (400 mg daily) to complete a 6-month total treatment duration.

A contrast-enhanced neck Magnetic resonance imaging (MRI) obtained at the sixth month of treatment showed complete resolution of the osteomyelitis and abscesses previously seen in the right mandibular ramus (Figure 2). In addition, the swelling in the patient's right facial and neck region had fully subsided.

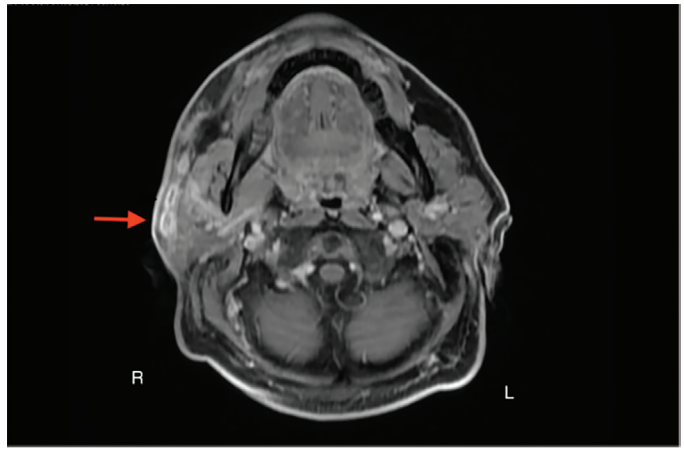

Figure 1. Peripheral enhancing abscess formation in the posterior region of the right mandible shown on a fat-suppressed contrast-enhanced T1-weighted axial MRI image

MRI: Magnetic resonance imaging

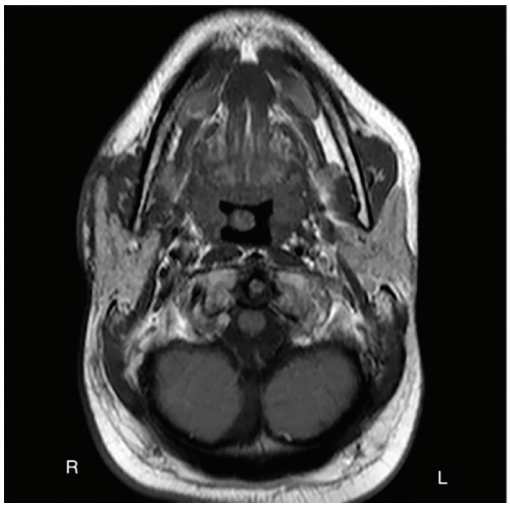

Figure 2. Contrast-enhanced T1-weighted MRI (T1W TSE) image demonstrating resolution of infectious and inflammatory findings

MRI: Magnetic resonance imaging

Discussion

The pathways of infection in *Candida* osteomyelitis are categorized as hematogenous spread (67%), direct inoculation (25%), and contiguous spread from nearby tissues (9%)[2]. The most frequent causative species are *Candida albicans* (65%), *Candida tropicalis* (16%), and *C. glabrata* (8%), while the vertebrae, sternum, and ribs are the bone sites most commonly affected in adults[2,4]. Mandibular osteomyelitis caused by *Candida* is very uncommon.

Most patients who develop *Candida* osteomyelitis are not receiving immunosuppressive medications. Reported risk factors include surgical procedures, intravenous drug use, orthopedic implants, trauma, and open wounds. In addition, factors related to candidemia, such as the presence of a central venous catheter and total parenteral nutrition, are also important predisposing conditions. However, *Candida* osteomyelitis can also occur in conditions that suppress the immune system, such as leukemia, lymphoma, or kidney and liver transplants[5].

Attie et al.[6] described two cases of mandibular osteomyelitis due to *C. albicans* following tooth extraction. These patients had a history of substance abuse and recovered after surgical debridement and fluconazole therapy. Choi et al.[3] reported a case of maxillary and mandibular osteomyelitis caused by *C. albicans* in an individual without any immune deficiency; complete resolution was achieved with debridement and antifungal therapy (micafungin followed by fluconazole). This shows that *Candida* osteomyelitis can also develop in immunocompetent individuals. To date, there has been no report in the literature of mandibular osteomyelitis due to *C. glabrata*. In this sense, our case adds to the existing literature.

Gagliano et al.[7] described a case of *C. glabrata* spondylodiscitis in a diabetic patient, diagnosed through surgical sampling after antibiotics failed, with successful treatment using antifungal agents. This highlights the importance of considering fungal pathogens and obtaining surgical samples for diagnosis in cases unresponsive to antibiotics. Similarly, in our patient, the diagnosis was made through culture obtained after surgical drainage.

Managing antifungal therapy in *Candida* osteomyelitis can be difficult, particularly with species like *C. glabrata* that have inherent resistance to azoles. The 2016 Infectious Diseases Society of America clinical practice guidelines for treating *Candida* osteomyelitis recommend oral fluconazole 400 mg daily for 6-12 months, or an echinocandin (e.g., caspofungin, micafungin, or anidulafungin) for at least 2 weeks, followed by a step-down to oral fluconazole 400 mg daily for 6-12 months, along with surgical debridement when appropriate[8]. In our patient, a treatment regimen aligned with these guidelines was implemented, resulting in clinical success.

Chesdachai et al.[9] analyzed 1,046 *C. glabrata* isolates collected at the Mayo Clinic from 2012 to 2022 and found that 17.9% were resistant to fluconazole based on CLSI standards and 24.5% according to European Committee on Antimicrobial Susceptibility Testing criteria. This study highlighted the limited effectiveness of fluconazole for *C. glabrata* and the need for antifungal susceptibility testing to guide therapy.

In a retrospective study by Eschenauer et al.[10] involving 224 patients with *C. glabrata* bloodstream infections, it was demonstrated that fluconazole MIC values play a key role in predicting treatment success. Outcomes were significantly better in patients with a fluconazole dose/MIC ratio above 12.5. These results suggest that fluconazole should be used only for isolates confirmed as susceptible and at appropriate doses. In our case, although fluconazole susceptibility was not specifically tested, the patient could not continue intravenous therapy, but after achieving clinical stability, treatment was successfully maintained with oral fluconazole.

The capacity of *Candida* species to form biofilms is another key factor that complicates treatment. Biofilm presence limits antifungal penetration and contributes to treatment resistance. Godart et al.[11] reported that prolonged antifungal therapy and surgical intervention were needed due to biofilm formation in a *C. albicans* infection that developed on the basis of mandibular osteoradionecrosis. Gamaletsou et al.[5] described biofilm formation in *Candida* species as involving adhesion, proliferation, maturation and dissemination stages and noted that echinocandins are more effective against these biofilms than triazoles.

In a meta-analysis including 1,072 patients, long-term antifungal therapy was found to improve survival, whereas short-term treatment was linked to higher mortality. Although not statistically significant, surgical intervention is also thought to potentially reduce mortality[12]. In our patient, caspofungin was started as antifungal therapy, and a favorable response was achieved with extended treatment, supporting the role of echinocandins in overcoming biofilm-related resistance. Additionally, timely surgical drainage was important in controlling the infection.

This case adds to the literature as a rare example of *C. glabrata* osteomyelitis that arose after dental treatment, was initially presumed bacterial, but was identified by abscess culture due to its persistent course. Fungal pathogens should be considered, especially when immunosuppressive conditions like diabetes are present and when dental infections do not respond to standard antibiotics.

Ethics

Informed Consent: Informed consent was obtained from the patient.

Footnotes

Authorship Contributions

Concept: E.Z., F.P., Design: B.Ç., E.Z., F.P., Data Collection or Processing: B.Ç., İ.N.B., Analysis or Interpretation: B.Ç., E.Z., İ.N.B., F.P., Literature Search: B.Ç., Writing: B.Ç.

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