

# Mandibular Osteomyelitis Associated with *Candida Albicans* in Marijuana and Heroin Abusers

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## Abstract

Osteomyelitis of the mandible is most commonly caused by bacterial infections and is rarely linked to fungal infections. In 2003, Friedman *et al.* studied the relationship of multiple drugs including marijuana, opioids, nicotine, and alcohol and its effect on the immune system. It is important to consider potential risks and complications of patients who are immunocompromised and present a history of substance abuse. These complications include infections and osteomyelitis which can be associated with multiple microorganisms; some of the most common microorganisms isolated in mandibular osteomyelitis include *Streptococcus*, *Eikenella*, and *Candida*. *Candida albicans* is commonly found in the skin and mucosa of healthy individuals; however, it has been proven to cause disease in individuals who are immunocompromised. Two cases of mandibular osteomyelitis after routine dental extractions and a history of drug abuse, including heroin and marijuana, are presented in this case series. These specific infections were resistant to multiple antibiotic therapy and grew *C. albicans* species in cultures collected. These cases were treated with irrigation and debridement or mandibular resection in combination with antimicrobial treatment and fluconazole with complete resolution. Although osteomyelitis is most commonly caused by bacterial infections, special attention must be given to patients with medical histories of immunosuppression and intravenous drug use. Patients who do not respond to broad-spectrum antibiotics might benefit from bacterial and fungal cultures and sensitivity. Antifungal treatment with an antifungal agent, such as oral fluconazole, is indicated if fungal organisms are yielded in the culture.

**Keywords:** *Candida*, fungus, osteomyelitis

## INTRODUCTION

Osteomyelitis of the mandible is an inflammatory disease of the bone marrow. It has been associated with chronic infections, trauma, vascular insufficiency, and surgery.<sup>[1]</sup> In the preantibiotic era, osteomyelitis was a common entity; however, with the advent and administration of antibiotic therapy, osteomyelitis has become very rare.<sup>[2]</sup> In recent times, there has been an increased incidence of osteomyelitis. This could be related to the expanded use of antibiotics and the appearance of multidrug-resistant microorganisms. Thus, increased antibiotic resistance further challenges the treatment and management of osteomyelitis.<sup>[2]</sup>

Certain illegal drugs such as marijuana, cocaine, heroin, and opioids, in addition to tobacco and alcohol, have been shown to significantly impact the immune response to infection.<sup>[3]</sup> Osteomyelitis is most commonly caused by bacterial infections; however, rare cases of *C. albicans*-associated osteomyelitis have been reported in the literature.<sup>[4]</sup> *Candida* osteomyelitis

can affect multiple bones including vertebrae, sternum, femur, hips, facial bones, foot, ankle, and tibia.<sup>[4]</sup>

We report two cases of mandibular osteomyelitis after routine dental extraction. In both cases, the patients had a history of heroin and marijuana abuse.

## CASE REPORTS

### Case 1

A 40-year-old male presented for medical consultation with a medical history contributory for chronic use of heroin and

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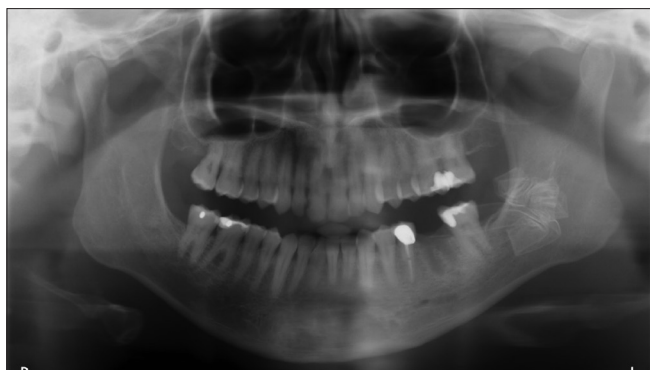
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**Figure 1:** Patient A. Initial presentation after extraction of #19. (Note Penrose drain in the left mandible)



**Figure 3:** Patient B. Nonhealing extraction site #32, with radiolucent area affecting inferior border and tooth #31

marijuana. At the time of the consultation, patient A was undergoing rehabilitation for substance abuse. Due to recurrent infections and a nonhealing extraction site on #19, patient A was referred to the Department of Oral and Maxillofacial Surgery at Nova Southeastern University. The patient was referred from a private oral surgeon in the community after extraction of tooth #19 [Figure 1]. His chief complaint included pain in the surgical site, failure of the extraction site to heal, and chronic infection. At this point, the patient underwent incision and drainage under general anesthesia. The cultures taken in the operating room yielded *C. albicans* and *Klebsiella pneumoniae*. The patient was commenced on antifungal treatment with fluconazole (Diflucan) 150 mg for 3 days with no signs of resolution of infection or swelling. The 2<sup>nd</sup> procedure of debridement of the surgical site #19 was recommended. During this procedure, bone specimens were obtained and submitted for final pathology [Figure 2]. Histopathological results were consistent with osteomyelitis of the mandible demonstrating sections of uninflamed sclerotic bone and reactive bone with associated fibrosis. No photographs were taken of the pathology.

### Case 2

A 45-year-old male presented with a medical history positive for heroin, opioid, and marijuana abuse. He presented to our institution after surgical extraction of tooth #32 carried out by an oral surgeon in the community. The extraction was done 2 months before his initial presentation to Nova Southeastern University for evaluation due to nonhealing surgical site and chronic infection [Figure 3]. At this point, biopsy of exposed



**Figure 2:** Patient A. Two-month follow-up, nonhealing extraction site of #19



**Figure 4:** Patient B. Right mandibular resection due to chronic osteomyelitis, 2-month follow-up with hardware in place, disease free

bone was done which showed fragments in vital and necrotic bone consistent with chronic osteomyelitis. On evaluation, the decision was made to take the patient to the operating room for a debridement and a formal resection of the affected area. With the patient under general anesthesia, a right submandibular approach was utilized to reach the affected area of the right mandible, areas of affected bone were delineated, and partial mandibular resection [Figure 4] was performed until bleeding and healthy bone was identified. Final pathology confirmed diagnosis of chronic osteomyelitis of the mandible and microbiology cultures of the surgical site were positive for *C. albicans* species. No Micro. An infectious disease consult was obtained, and antimicrobial treatment with fluconazole was commenced.

### DISCUSSION

Osteomyelitis is defined as a progressive inflammatory condition of the bone and bone marrow.<sup>[5]</sup> This rare condition can affect any bone but is commonly seen in teeth-bearing bones of the facial skeleton; this is due to direct access of microorganisms through infected teeth.<sup>[5]</sup> In 2012, Slenker et al.<sup>[4]</sup> studied 212 cases of *Candida* osteomyelitis, of which only six of them affected the facial skeleton.<sup>[4]</sup>

Infections of dental origin have been historically associated with bacterial microorganisms;<sup>[6,7]</sup> however, in recent years, there has been a trend in increasing infections associated with fungal pathogens.<sup>[8,9]</sup> There are a few studies in the literature reporting instances of *C. albicans* found in infected root canals. Baumgartner et al. identified *C. albicans* in 5 of 24 infected

root canal samples.<sup>[10]</sup> This increase in the prevalence of *Candida* infections may be attributed to contributing factors such as growth in the population of immunosuppressed patients, invasive surgeries, and overuse of broad-spectrum antibiotics.<sup>[11]</sup>

We report two cases of mandibular osteomyelitis after routine dental extraction in patients with a history of marijuana and heroin abuse as their only significant comorbidity. Friedman *et al.* demonstrated a correlation between marijuana and heroin abuse and a susceptibility to infections; this is due to the direct effect of these drugs over the immune response against pathogens.<sup>[3]</sup> Marijuana is the common name given to *Cannabis sativa*; this plant has been widely used for recreational and medicinal purposes.<sup>[3]</sup> An important factor to consider with marijuana use is the increased susceptibility to infections. Due to its effect on immune cells, macrophages, lymphocytes, and cytokines, there is a decrease in host defenses to infection.<sup>[12-14]</sup> On the other hand, heroin and other opioids have been linked to increase susceptibility to infection by direct exposure of pathogens through injections.<sup>[15]</sup> Moreover, opioids have also been linked to host resistance to microorganisms through direct actions in immune cells.<sup>[16]</sup>

Both cases presented were treated with a combination of surgical debridement and fluconazole. The management of *Candida* osteomyelitis has not been well established due to the uncommon nature of this condition. Treatment recommendations for *Candida* osteomyelitis are based on case reports and case series. Amphotericin B has widely been used in the past;<sup>[17]</sup> however, more recent literature supports the use of fluconazole or echinocandin over amphotericin B due to high toxicity rate.<sup>[4,18,19]</sup> Recommendations of the Infectious Diseases Society of America<sup>[20]</sup> include the following:

1. Fluconazole, 400 mg (6 mg/kg) daily, for 6–12 months or an echinocandin (caspofungin 50–70 mg daily, micafungin 100 mg daily, or anidulafungin 100 mg daily) for at least 2 weeks followed by fluconazole, 400 mg (6 mg/kg) daily, for 6–12 months is recommended (strong recommendation; low-quality evidence)
2. Lipid formulation amphotericin B, 3–5 mg/kg daily, for at least 2 weeks followed by fluconazole, 400 mg (6 mg/kg) daily, for 6–12 months is a less attractive alternative (weak recommendation; low-quality evidence)
3. Surgical debridement is recommended in selected cases (strong recommendation; low-quality evidence).

## CONCLUSION

Although mandibular osteomyelitis is most commonly caused by bacterial microorganisms, special attention must be given to patients with medical histories of immunosuppression and illicit drug use of cannabis and opiates. Patients who do not respond to broad-spectrum antibiotics might benefit from bacterial cultures, fungal cultures, and sensitivity. In cases of positive fungal microorganisms, antifungal treatment with an antifungal agent such as oral fluconazole is indicated if fungal organisms are yielded in the culture.

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## Conflicts of interest

There are no conflicts of interest.

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