Osteomyelitis Of The Jaw: A Retrospective Analysis

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Citation

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Abstract

There is a paucity of recent data regarding osteomyelitis of the jaw (OMJ).Patients with inflammation of the jaw from Jan. 2000-Dec. 2005 at TJUH underwent retrospective chart review. Forty-two patients met the criteria for OMJ (37 definite, 5 probable). Mean age was 58 years. 78% were Caucasian. Most common risk factors associated with OMJ were tooth extraction, orofacial malignancy and radiotherapy, and bisphosphonates use. Most common symptoms were pain, exposed bone/plate and cheek swelling. Aerobic (GP 84%, GN 42%) and anaerobic (GP 53%, GN 27%) bacteria were identified. 34% of patients received > 4 weeks of IV antibiotics. Five patients achieved full recovery. Limited recovery was associated with orofacial malignancy and radiotherapy (p= 0.06). Bisphosphonates use and radiotherapy for orofacial malignancy have emerged as major risk factors associated with OMJ. Only orofacial malignancy and radiotherapy predicted limited recovery. Length of antibiotic therapy or HBOT did not predict treatment outcome.

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INTRODUCTION

Osteomyelitis in the maxillofacial region has been a topic of discussion for many centuries. The unique environment of the oral cavity and dentition in conjunction with a constantly changing intraoral environment has led to several classification schemes for mandibular and maxillofacial osteomyelitis. Newer challenges have declared themselves with the emergence of osteoradionecrosis of the jaw secondary to radiation to the head and neck as well as osteonecrosis of the jaw as seen with bisphosphonates. These new clinical entities may be different than traditional osteomyelitis in terms of pathogenesis but are managed alike in many respects. The presence of microorganisms in osteoradionecrosis and osteonecrosis are thought to be secondary in their pathogenesis.

Numerous classification systems for osteomyelitis of the jaw exists [Hudson 1993], but regardless of the classification, the goals of treatment always remain the same. The goals of therapy are to remove dead bone and eliminate or at least attenuate the proliferating pathogenic microorganisms through a combination of surgery and antibiotics, and then give supportive care for healing. It is important to identify the causative or associated pathogens [Hudson 1993, Marx 1991, Bernier et al 1995, Aitasalo et al 1998, Kushner et al 2004, Ruggiero et al 2004]. Risk factors associated with osteomyelitis of the jaw must be identified and modified if possible. Known risk factors associate with osteomyelitis of the jaw include diabetes mellitus, autoimmune diseases, malignancy, malnutrition, systemic steroids, chemotherapy, radiotherapy, bisphosphonates use, trauma, osteopetrosis, acquired immunodeficiency disease, dental implant, sickle cell anemia, alcoholism, intravenous drug abuse, renal or hepatic failure, chronic hypoxia, extremes of age and tobacco abuse [Hudson 1993, Marx 1991, Bernier et al 1995, Aitasalo et al 1998, Kushner et al 2004, Ruggiero et al 2004, Lew et al 2004, Lew et al 1997].

There has been, however, a paucity of studies on osteomyelitis of the jaw taking into account new risk factors. Hence a comprehensive review of the management of osteomyelitis of the jaw as seen in an academic medical center was undertaken. The objectives of the study were as follows: to determine and update the risk factors associated with osteomyelitis of the jaw, to determine the clinical presentation and

microbiological etiology associated with osteomyelitis of the jaw, to determine treatment outcomes and which variables might impact the management of osteomyelitis of the jaw and to determine the morbidity and mortality associated with osteomyelitis of the jaw.

METHODS

A retrospective chart review was performed at Thomas Jefferson University Hospital, Philadelphia, PA. Subjects included patients seen between January 1, 2000 and December 31, 2005 in the Department of Oral and Maxillofacial Surgery. The International Classification of Diseases, Revision 9 (ICD-9) codes 526.4, 526.8 and 526.9 were used to initially select patients with possible osteomyelitis. ICD-9 code 526.4 describes inflammatory jaw conditions. This category includes the diagnoses of abscess, osteitis, acute and chronic osteomyelitis, suppurative osteomyelitis and periostitis. ICD-9 codes 526.8 and 526.9 describe other and unspecified diseases of the jaw. Individual patient charts were then reviewed for study eligibility.

A definite diagnosis of osteomyelitis was given for biopsy proven osteomyelitis and as probable when one of the following three conditions was present: (i) positive cultures isolated from jaw during surgical debridement (deep bone cultures), (ii) presence of exposed bone during examination, or (iii) surgeon's clinical impression of osteomyelitis. The University institutional review board (IRB) approved the study prior to chart review.

Data collection was performed by reviewing patient charts and computer records. Data collected included demographics, risk factors associated with osteomyelitis, clinical presentation (subjective complaints and physical examination findings), treatment (type of surgery and details of antibiotics), operating room cultures, imaging findings (MRI, CT and Xray findings), surgical pathology results and outcomes including complications.

Adequate follow-up for this study was defined as physician-patient contact for at least three months post-operatively. Targeted antibiotics were defined as antibiotic therapy based on culture and sensitivity data (when available). An outcome was classified as follows: "Full recovery" was defined as resolution of all signs and symptoms of active infection with no residual disability. "Limited recovery" was defined as resolution of all signs and symptoms of infection, but persistence of clinically significant residual disability, such as pain that limited activity or required analgesic therapy. Patients with limited recovery were compared with patients who fully recovered. A relapse was defined as recurrence of symptoms of infections after apparent resolution.

Descriptive analysis was used to present a set of data. Chi square, Fisher's exact test and t-test were used for analysis of compared data. Data compared included outcomes and other variables such as risk factors associated with osteomyelitis, antibiotic regimen, duration of symptoms, number of surgeries and demographic variables.

RESULTS

Demographics. Three hundred patients were identified with ICD-9 codes 526.4, 526.8 and 526.9. Forty two patients met the criteria for definite or probable osteomyelitis (37 definite, 5 probable). Forty one patients had one episode of osteomyelitis and one patient had 4 episodes. Twenty three patients (54.8%) were females. The mean age of the patients and standard deviation (SD) was 58.3 ± 17.5 years (95% CI 53.11-63.21). Thirty three patients (78.6%) were Caucasian, 8 (19.0%) were African-Americans and one was Asian.

Risk Factors. Risk factors associated with osteomyelitis are shown in table 1. The most frequent risk factors were tooth extraction, orofacial malignancy and radiotherapy, use of bisphosphonates and nicotine abuse. Twenty nine patients (69.0%) had more than one risk factor for osteomyelitis.

Clinical Presentation. Twenty nine patients (69%) reported pain. Other frequently encountered presentations were exposed bone/reconstruction plate and check swelling in 42.9% and 38.1% of patients respectively. A summary of the clinical presentation is shown in Table 2. The duration of symptoms ranged from 1 week to 29 years. The mean duration was 14.6 months. When the patient with the 29 years of symptoms was omitted, the longest duration was 3.5 years and the mean and standard deviation were 6.0 ± 8.1 months (95%CI 3.46-8.56). The location of lesions is presented in Table 3. The vast majority of lesions occurred in the mandibular body.

Microbiological Data. Microbiological samples were obtained during surgery in 45 culture specimens for 34 patients. The most common isolates were streptococci (46), Actinomyces species (12) and prevotella species (11) were the most common anaerobes. A summary of microorganisms is shown in table 4. Two surgical cultures were reported as normal flora (not included in table 4). The overwhelming majority (94.1%) of patients had polymicrobial cultures. Thirty eight cultures (84.4%) contained aerobic gram positive bacteria while aerobic gram negative bacteria were obtained in nineteen cultures (42.2%). Twenty four cultures (53.3%) included anaerobic gram positive bacteria while anaerobic gram negative bacteria was seen in twelve cultures (26.7%). Candida species were seen in fifteen cultures (33.3%).

Therapy. (a) Surgical Procedures. Every patient had a least one surgical procedure. A total of 114 surgical procedures in 97 surgeries were performed with a mean and SD of 2.3 ± 1.7 surgeries per patient. One patient with 29 years of symptoms had 11 surgeries during the time of our study. If she was omitted, the mean and SD would be 2.1 ± 1.0 surgeries. Almost half of the patients had debridement without continuity defect. See table 5 for types of surgery. (b) Antibiotic Therapy. A total of 67 courses of

antibiotics were ordered and received. The largest group of patients (34.3%) received ≥ 4 weeks of IV targeted antibiotics ± simultaneous or subsequent oral targeted antibiotics. See table 6 for the classification and distribution of antibiotic therapy. Peri-operative antibiotics are excluded from this table. (c) Hyperbaric Oxygen. Twenty five patients had hyperbaric oxygen therapy (HBOT). None of the patients that received HBOT fully recovered. Sixteen patients (88.9%) with a history of orofacial malignancy and radiotherapy received HBOT.

Outcomes. The mean length of follow up was 13.1 ± 11.3 months. Six patients had follow up for less than 3 months. There were no deaths in this study. Five patients (11.9%) experienced full recovery while 37 patients (88.1%) achieved limited recovery. There was no significant difference in outcomes when patients that received ≥ 4 weeks of antibiotics were compared with patients that received less than 4 weeks (P = 0.57). The only risk factor associated with osteomyelitis of the jaw that approached statistical significance for an adverse outcome (limited recovery) was orofacial malignancy and radiotherapy (P = 0.06). None of these patients (n = 18) achieved a full recovery. Outcome was not influenced by duration of symptoms (P = 0.78), number of surgeries (P = 0.33) or type of microorganism obtained during surgery. A good outcome was associated with the female sex (P = 0.04). Full recovery was more likely in a younger patient (mean age 40.8 ± 22.1 years) than an older patient (mean age 60.7 ± 15.7 years; P = 0.015). A total of 7 relapses and 8 complications (5 of which were fistulae) were recorded. None of the patients with good outcomes had a relapse or complication.

DISCUSSION

In this retrospective study, we sought to undertake a comprehensive review of osteomyelitis of the jaw as seen in Thomas Jefferson University Hospital, Philadelphia, Pennsylvania in a six-year period. This study is timely because there has been a dearth of studies exploring the full range of this subject matter in recent years. We anticipate that this study will enhance knowledge in this clinical entity and assist clinicians in the management of osteomyelitis of the jaw.

Much earlier studies in two centers in Nigeria revealed that patients presented late in the natural history and the mean age of patients was usually in the second to forth decade. The major predisposing factor was advanced periodontal disease or odontogenic infection [Daramola et al 1982, Adekeye et al 1985]. More recent studies in the United States had predominantly Caucasian patients with mean ages of patients in the fifth and sixth decade like this study and recognized the emerging role of osteoradionecrosis [Calhoun et al 1988, Lobati et al 2001, Koorbusch et al 1992]. These previous studies were prior to the widespread use of bisphosphonates in the management of malignancies.

The three major risk factors in this study were tooth extraction, radiotherapy for orofacial malignancy and use of bisphosphonates for the management of malignancies. These risk factors were not mutually exclusive. This is in sharp contrast to the study by Calhoun et al which the top three risk factors were post-radiation therapy (46.7%), posttraumatic (25%) and odontogenic infection (21.7%) [Calhoun et al 1988]. Another study by Koorbusch et al showed odontogenic infections (36.1%), traumatic (fracture related) (36.1%) and radiation and neoplasm (16.7%) as the most common risk factors [Koorbusch et al 1992]. Finally, a Korean study in the late 1990s revealed that teeth-related (38.5%), postextraction complications (33.3%) and periodontal disease (12.8%) were the most risk factors [Kim et al 2001]. We can therefore conclude that osteonecrosis of the jaw which results from the use of bisphosphonates for the management of malignancies has emerged as a significant risk factor associated with the development of osteomyelitis of the jaw. Furthermore, we also conclude that osteoradionecrosis that results from radiotherapy for orofacial malignancy continues to play a significant role as a predisposing factor in the development of osteomyelitis of the jaw in the United States.

Bisphosphonates inhibit osteoclast activity which negatively impact bone resorption and bone remodeling. Bisphosphonates also have antiangiogenic properties which can delay wound healing [Ruggiero et al 2004, Migliorati et al 2006]. Bisphosphonate-associated osteonecrosis can develop spontaneously [Migliorati et al 2006]. Irradiation affects osteoblasts and consequently, decreases collagen formation. Irradiation also affects osteoclast activity initially

and causes vascular injury ultimately leading to sclerosis of bone marrow connective tissues [Ruggiero et al 2004, Teng et al 2005]. With the compromised bone micro-environment described above in osteonecrosis and osteoradionecrosis and the continued oral contamination, it is not surprising that even small insults such as dental extraction or ill-fitting dentures can result in such a protracted illness [Mortensen et al 2005, Teng et al 2005, Melo et al 2005]. However, a new hypothesis proposes that osteoradionecrosis arises from a fibroatrophic process and new considerations for treatment include antioxidants and antifibrotic drugs [Teng et al 2005].

The most common symptoms and signs in the study were pain, exposed bone or reconstruction plate, cheek swelling and discharge/drainage. Fever was seen in a minority of patients. We noted that five of the seven patients with maxillary lesions were on bisphosphonates. This was noted in previous studies [Mortensen et al 2007, Migliorati et al 2005, Dimitrakopoulos et al 2006]. The clinical presentation and site of osteomyelitis is essentially similar to other studies [Calhoun et al 1988, Koorbusch et al 1992, Kim et al 2001].

The polymicrobial nature of surgical specimens obtained from osteomyelitis of the jaw has been recognized, largely mimicking mouth flora. The spectrum of organisms in this study is as seen in earlier studies [Aitasalo et al 1998, Ruggiero et al 2004, Calhoun et al 1988, Koorbusch et al 1992, Kim et al 2001] These cultures are deep bone cultures obtained in the operating room. The most common bacteria encountered are the Streptococci, Actinomyces and Prevotella species. Candida species are also seen. It is important to note that while candida, corynbacteria, enterococci and anaerobic streptococci are common in the mouth, they may not be pathogens in the bone. Calhoun et al had noted that the presence of Candida in cultures did not affect outcome [Calhoun et al]. We found that patient outcome and type of microorganisms recovered during surgery were not statistically related.

Surgical treatment options are decided based upon the radiographic and clinical features of disease. At times a curative measure can be simply extraction of a tooth with local curettage while at other times a resection of the affected area may be needed. For purposes of clarification all marginal debridements are classified as, “debridement without continuity defect.” This was by far the most widely used surgical treatment both in this study and in the literature. This surgical technique was used when osteomyelitic changes extended through only one cortex of bone but not both, or if osteomyelitic changes did not advance to the inferior margin of bone. If pathologic fracture occurred or if clear clinical and radiographic evidence was seen of bicortical osteomyelitis than a resection with continuity defect was often used. Efforts were always made to maintain a continuity of native bone and this is why the vast majority of cases proved to have debridement without continuity defect.

Selecting antibiotics is based mostly on isolating bacteria from these cultures [Hudson 1993, Marx 1991]. Empiric antibiotics are started pending cultures providing adequate coverage for Streptococci and anaerobic bacteria such as Actinomyces and Prevotella. Penicillins remain the drug of choice [Hudson 1992]. Other alternatives which may be used as a combination regimen include clindamycin, fluoroquinolones, metronidazole, a variety of cephalosporins, carbapenems, vancomycin in combination with other antibiotics and tetracyclines. Methicillin resistant Staphylococcus aureus (MRSA) is noted in only three cultures and does not appear to play a dominant role in this condition. Candida species were largely ignored in the selection of antimicrobials.

HBOT is known to enhance collagen synthesis and angiogenesis leading to improved wound healing in osteoradionecrosis. Therefore, at least theoretically, HBOT was felt to play an adjunctive role in the management of osteoradionecrosis [Aitasalo et al 1998, Kushner et al 2004, Teng et al 2005]. However, Annane et al in a prospective, multicenter, randomized, double-blind, placebo-controlled trial showed potentially worse outcomes in the HBO arm and the study was stopped early [Annane et al 2004]. Patients with overt mandibular osteoradionecrosis did not benefit from hyperbaric oxygenation [Annane et al 2004]. This was confirmed in this study. None of the 25 patients who had HBOT had a full recovery.

Female patients were more likely to have a good outcome. The reason for this is unclear. Full recovery was also more likely in a younger patient as seen in an earlier study [Lobati et al 2001]. The relationship between a limited recovery and the risk factor of orofacial malignancy and radiotherapy approached statistical significance. In this study, no patient with a risk factor of orofacial malignancy and radiotherapy achieved a full recovery. Calhoun et al showed cure was more likely in the non-radiation group, although this difference disappeared when followed up for more than six months [Calhoun et al 1988]. There was no statistically significant relationship between the use of bisphosphonates

and patient outcome in our study. The other risk factors associated with osteomyelitis of the jaw did not predict patient outcome. The role of surgery in the management of osteomyelitis is largely established. The confusion lies in determining the length of antibiotic therapy. Most clinicians use antibiotics empirically for 4-6 weeks. Arguments for longer or shorter courses remain unresolved [Lew et al 2004, Lew et al 1997, Calhoun et al 1988, Mader et al 1999, McHenry et al 2002, Lazzarini et al 2005]. Patient outcome was not affected by length of appropriate antibiotic therapy. Our study did not show any benefit with the use of HBOT. Other studies showed similar results [Calhoun et al 1988, Teng et al 2005, Annane et al 2004].

One male patient was the only patient with more than one episode. He had 4 episodes during this study. He had a history of osteopetrosis. Osteopetrosis is a heterogeneous group of heritable conditions in which there is a defect in bone resorption by osteoclasts resulting in abnormal shape and structure of bone and making the bone very brittle. It also predisposes to osteomyelitis [Tolar et al 2004]. Another patient had symptoms dating back to a subperiosteal implant 29 years prior to presentation. The hardware ultimately was explanted.

In summary, the mean age of patients in this study is 58.3 years. The major risk factors associated with osteomyelitis of jaw are tooth extraction, radiotherapy for orofacial malignancy and use of bisphosphonates for the management of malignancies. Most cultures were polymicrobial and targeted antibiotics were employed. However, this study showed that there was no benefit to an antibiotic regimen longer than 4 weeks and patient outcome was not influenced by type of microorganism isolated from operating room cultures. This study also found that a history of orofacial malignancy and radiotherapy was associated with limited recovery despite HBOT.

Our study had some limitations. Firstly, the small number of patients may have failed to unmask potential variables that may have affected patient outcome. Secondly, this study was carried out at only one academic medical center. A prospective, multicenter study would be useful in confirming our findings and addressing the above points. Thirdly, the lack of adequate documentation of antibiotic therapy in more than a quarter of patients probably impacted the results of our study. Better documentation and a prospective study would address this issue.

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