

Esra GÜZELDEMİR¹
Hilal USLU TOYGAR¹
Nebil BAL²
Can BOGA³

İletişim (Correspondance)

Esra GÜZELDEMİR
Başkent Üniversitesi Diş Hekimliği Fakültesi
Periodontoloji Anabilim Dalı ADANA
Tlf: 0322 322 82 82
e-posta: esragd@yahoo.com

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- 1 Başkent Üniversitesi Diş Hekimliği Fakültesi
Periodontoloji Anabilim Dalı ANKARA
- 2 Başkent Üniversitesi Tıp Fakültesi Patoloji
Anabilim Dalı ANKARA
- 3 Başkent Üniversitesi Tıp Fakültesi Hematoloji
Anabilim Dalı ANKARA



CASE REPORT

CHRONIC MYELOGENOUS LEUKEMIA PRESENTING WITH OSTEOMYELITIS: A CASE REPORT AND REVIEW OF LITERATURE

ABSTRACT

Chronic myelogenous leukemia (CML), osteomyelitis, and chronic periodontal diseases affect elderly people in common. These disorders also have direct/indirect associations between them. CML is a pluripotential stem cell disease and usually presents as an increased incidence of infections, generalized gingival hypertrophy, and gingival bleeding. These may be the initial presenting features of the disease. Osteomyelitis is an inflammation of the bone and bone marrow in which reduced vascularity and osteocyte destruction occur. The clinical presentation and course depend on the virulence of the micro-organism involved and the patient's resistance. The reason that osteomyelitis varies in elderly is chronically impaired immune host response. We report an 83-year-old man with severe gingival bleeding who was referred to periodontology clinic for consultation. He had uncontrolled gingival bleeding from buccal side of lower right second molar. We extracted involved tooth and removed granulation tissues from cavity. Healing was satisfactory. Our preliminary diagnosis of osteomyelitis was confirmed by CT, and on pathological examination, he was also diagnosed as having CML. Treatment procedures must be individually designed, especially for elderly patients. To avoid secondary infections and complications, it is imperative that elderly patients have regular examinations and not wait for problems to occur.

Key words: Chronic myelogenous leukemia; Osteomyelitis; Ageing (aging); Abscess.



OLGU SUNUMU

KRONİK MYELOİD LÖSEMİLİ BİR HASTADA GELİŞEN OSTEOMYELITİS: VAKA RAPORU VE LİTERATÜR DEĞERLENDİRMESİ

Öz

Kronik myeloid lösemi (KML), osteomyelit ve kronik periodontal hastalıklar, ileri yaştaki bireyleri daha fazla etkilemektedir. Bu hastalıkların, birbirlerini üzerine de olumsuz yönde, dolaylı ve dolaysız etkileri vardır. KML, bir kök hücre hastalığıdır ve genellikle enfeksiyon sıklığında artış, genelleşmiş dişeti büyümesi ve dişeti kanaması ile seyretmektedir. Bu bulgular hastalığın erken dönem belirtileri olabilir. Kemik ve kemik iliğinin inflamasyonu olan osteomyelitis, vasküleritede azalmaya ve osteosit yıkımına neden olmaktadır. Hastalığın klinik görüntüsü ve ilerlemesi, etken mikroorganizmaya ve hastanın bu mikroorganizmaya karşı direncine bağlıdır. Yaşlı hastalarda osteomyelitisin farklı formlarının görülmesinin nedeni, sürekli olarak bozuk olan konak savunma sistemidir. Bu olgu sunumunda, şiddetli dişeti kanaması nedeni ile kliniğimize konsültasyon amacıyla yönlendirilen 83 yaşındaki erkek anlatılmaktadır. Yapılan muayenede, hastanın sağ alt ikinci molar dişinin, bukkal yüzeyinde kontrol edilemeyen dişeti kanaması mevcuttu. Söz konusu diş çekilerek, enfekte bölge kürete edildi. Klinik bulgular ışığında konulan osteomyelit teşhisi, BT ve patolojik değerlendirmelerle doğrulanırken, aynı örneklerde yapılan laboratuvar tetkiklerle hastaya KML teşhisi konuldu. Yaşlı bireylerde, tedavi prosedürleri, ikincil enfeksiyonları ve komplikasyonları en aza indirmek amacıyla bireysel olarak oluşturulmalıdır. Hastalar, herhangi bir şikayetlerinin tedavisi için hastanelere başvurduklarında, hekimleri tarafından uzman diş hekimlerine yönlendirilmeli ve kümülatif olarak ortaya çıkabilecek dental ve periodontal sorunları erken teşhis ve müdahale ile önlenmelidir.

Anahtar sözcükler: Kronik myeloid lösemi, Osteomyelitis, Yaşlanma, Abse.



INTRODUCTION

Periodontal infection together with a systemic disease, impaired immune response, and aging could be a trigger for osteomyelitis. These diseases act synergistically with each other. Osteomyelitis, chronic myelogenous leukemia (CML), and periodontal diseases are common diseases among elderly persons (1).

Osteomyelitis is an inflammation of the bone and bone marrow that tends to spread. It is a sclerosing intramedullary bone infection caused by the actinomyces species. Older adults are at risk for osteomyelitis either because of an increased incidence of associated disorders such as CML, acute myeloblastic anemia, and leukemia that predispose them to osteomyelitis, or as the result of surgery. Mandibular osteomyelitis may occur secondarily to a periapical or periodontal abscess. Lymphadenopathy, fever, and malaise might be seen in severe cases of osteomyelitis (2).

While the hallmark of osteomyelitis is persistent and intense pain, there are periods of more intense pain, mild expansion of the mandible, and even soft tissue swelling (ie, active exacerbations). The mandible is involved mostly in the body, angle, and ramus areas. Although not as many, similar cases have been seen in the maxilla. The mandible may be tender to palpation, particularly at the buccal cortex. No suppuration or drainage is noted. Radiographic imaging may show an indistinct trabeculation or disappearance of the lamina dura. Sclerosis of the bone typically occurs with time. The clinical presentation and course depend on the virulence of the microorganism involved and the host's immune defenses.

Leukemias are characterized by diffuse replacement of bone marrow with proliferating leukemic cells; abnormal numbers and forms of immature white blood cells in the blood; and widespread infiltrates in the liver, spleen, lymph nodes, and other sites throughout the body. Leukemias are classified as lymphocytic or myelocytic, according to the type of white blood cells involved (3).

CML is a pluripotential stem cell disease characterized by anemia, extreme blood granulocytosis, granulocytic immaturity, basophilia, often thrombocytosis, and splenomegaly (4). CML is a disease of adults and accounts for about 15% of all cases of leukemia. Patients may fatigue easily, lose their sense of well-being, and have a decreased tolerance to exertion, anorexia, abdominal discomfort, early satiety (related to splenic enlargement), weight loss, fever, and excessive sweating (5). The presumptive diagnosis of CML may be made from the results of blood cell counts and examination of the blood film.

The disease is refractory to treatment, and even with current maximal therapy and stem cell rescue, cures are rare.

A common oral finding of CML is gingival hemorrhage. This may be the initial presenting feature of CML. Oral and periodontal manifestations of leukemia consist of leukemic infiltration, gingival bleeding, oral ulcerations, and infection. In CML, the gingiva simply may present with inflammation with no suggestion of a hematologic disturbance.

To the best of our knowledge, this is the first report of an elderly patient with CML with bleeding secondary to osteomyelitis of the mandible. In addition, we review the literature on the subject.

CASE REPORT

An 83-year-old man with severe gingival bleeding was referred for consultation to the periodontology clinic at Baskent University Hospital. Before referring the patient to a periodontist, according to his physician, systemic haemostatic agents had been administered. The patient had been hospitalized with uncontrolled gingival bleeding before he had been sent to our clinic. He appeared tired and had difficulty breathing and standing by himself. After cleaning the oral cavity, the origin of the bleeding was localized at the mid-buccal region of the lower right second molar. The alveolar bone was exposed. Owing to the presence of infected bone fragments without a blood supply, the alveolar bone was yellowish and glassy. After a consultation with the patient's physician, the diseased tooth was extracted (Figures 1), and granulation tis-

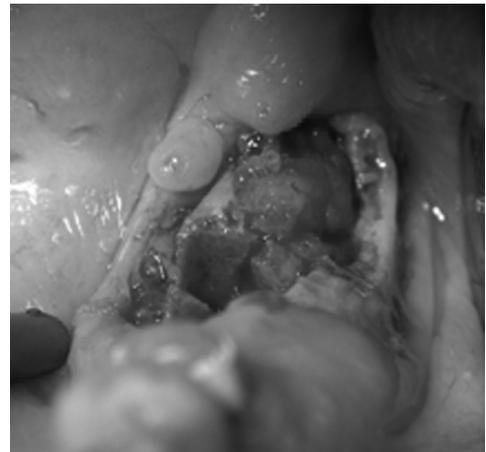


Figure 1— After the extraction of lower right 2. molar tooth. Alveolar socket with granulation tissue bordered with infected alveolar bone.

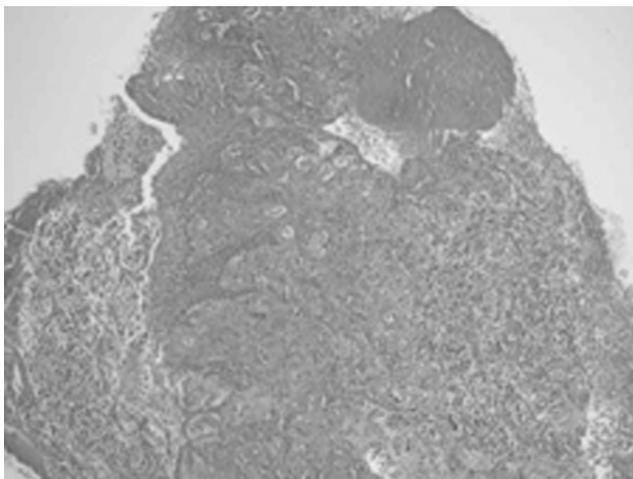


Figure 2— Active inflammatory cells.

sues and bone fragments were removed from the cavity. Bone spicules and granulation tissues were sent for pathology evaluation.

The clinical diagnosis was osteomyelitis. After the extraction, the patient was referred to the radiology department for computerized tomography (CT) scanning. The diagnosis of osteomyelitis was confirmed by pathological (Figures 2) and radiologic evaluation (Figure 3a).

The patient’s medical history was significant for a hospitalization owing to infection, swelling, and pain at lower

right second molar tooth and its posterior region 18 months earlier. The patient had had a combined abscess at the same tooth before. He had been diagnosed as having osteomyelitis, and combined antimicrobial therapy had been administered at that time. Osteomyelitis was confirmed by CT (Figure 3b). Because his relatives did not approve of dental treatment or extraction of the involved teeth, the patient was discharged without dental treatment rather than systemic antibiotic therapy.

Neither chemotherapy nor radiotherapy was administered because of the CML. The patient had prolonged acute kidney failure in the chronic base and osteoporosis.

Two months after the tooth extraction (Figure 4a and b), his medical and physical conditions improved. He gained weight, his blood count scores improved, and he began walking with a walking stick by himself.

DISCUSSION

The present case elucidates 3 common disorders, all of which are associated with the others, and negative synergistic disorders: an immune disorder (cancer-CML), severe infectious disease (osteomyelitis), and ongoing infectious disease (periodontitis and periodontal abscess).

Usually, priority is given to patient’ systemic diseases, and oral and periodontal diseases are neglected. Uncontrolled oral and periodontal diseases result in pain; periapical and periodontal abscesses; alveolar bone loss; pathological tooth mo-

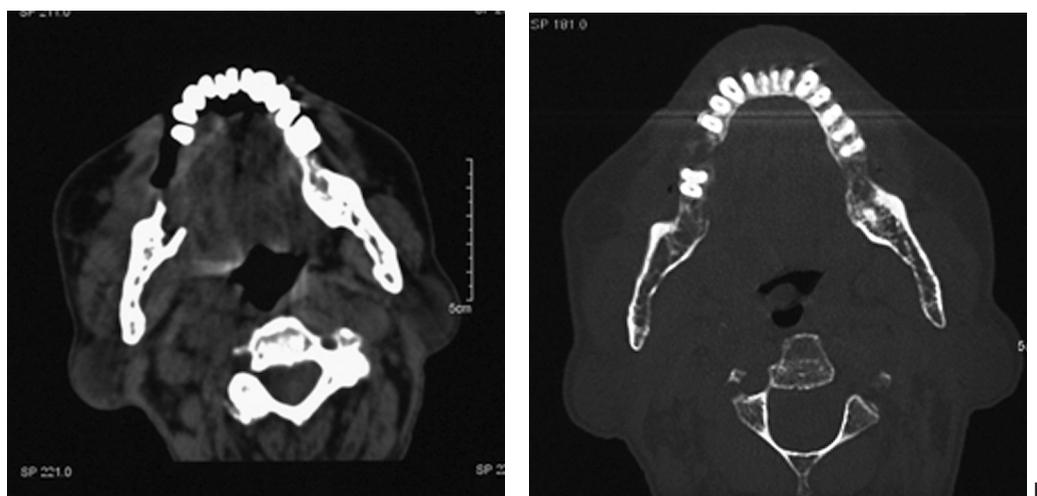


Figure 3— a. CT scan image after the extraction of lower right 2. molar (December 2005) and b. Previous CT scan image (August, 2004)

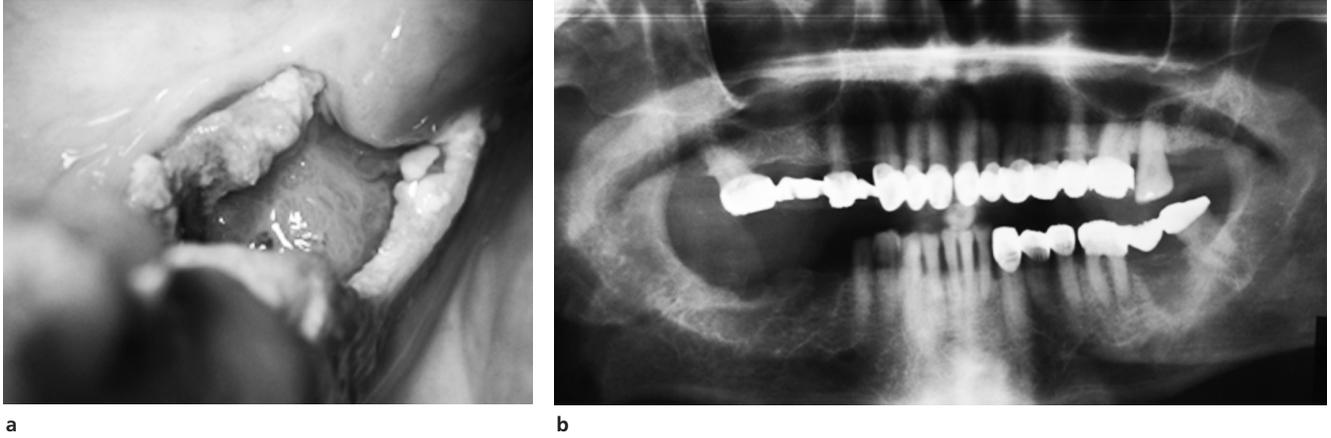


Figure 4— a-b. Two months after the extraction, intraoral and radiographic view.

bility; tooth loss; caries; and secondary infectious diseases such as osteomyelitis, mucositis, candidiasis. Also, periodontal diseases may be manifestations of systemic diseases. Systemic factors have effects on the host response and alter the response to plaque and infectious lesions.

Medically compromised and hospitalized patients usually die of secondary infections. Physicians should be aware of the dental condition of their patients, and patients should receive oral and periodontal care. Potential and focal infection sources must be eliminated before they become systemic problems. A poor dental condition could result in malnutrition, poor quality of life, or an uncontrolled medical condition. Evidence shows that following proper dental and periodontal treatment can improve systemic medical conditions.

Periodontal diseases affect people throughout the world. While older age is associated with an increased incidence of cumulative periodontal disease and extent and severity of disease, (6-11) age is also a known risk factor for periodontal disease. In a study performed by Guzeldemir et al., panoramic radiographs of 546 individuals were evaluated. That study revealed that vertical bone loss increased from the age of 36 to 65 years (11). Periodontal disease tends to lead to greater alveolar bone destruction in older persons than in younger ones. This would explain the increased incidence of chronic periodontal diseases in older persons. The phrase “getting long in the tooth” expresses a widespread belief that age is inevitably associated with an increased loss of connective tissue attachment. This might be show a cumulative exposure to several potentially destructive processes (12). However, in the absen-

ce of genetic background, poor oral hygiene is still a primary reason for periodontal diseases (13). The increased incidence of periodontitis seen in older persons would indicate changes in quantity, species, and proportions of the bacteria. These alterations also result with changes in microflora. Older individuals are affected by these pathologic factors and changes until death. Individual factors such as genetic background, smoking, immune response, systemic disorders, and environmental factors determine the differences and the severity of disease between the individuals.

The question remains how age modifies the host response and the patient's response to the therapy. Most systemic diseases, such as hormonal and cardiovascular diseases, occur in elderly individuals. Systemic diseases, medical management, medications, and the adverse effects of medications (eg, dry mouth, vascular complications, bleeding time, and suppressed immune response) all alter systemic stability and the tolerance of the patient to disease. An oral cavity is considered highly reflective of changes in the whole system, while it also may be a focal source of infection for some diseases. Hematologic malignancies are often responsible for an increased risk of infections because of the bacteremia (14), and altered phagocytosis and defective cellular immune response because of leukemia treatment protocols (15).

Persons older than 65 years represent the fastest growing segment of the population in western countries (16). While life expectancy in the United States was 77 years in 2000 (17), estimates for the European Union suggest a 22% increase in persons older than 65 years and a 50% increase in those older



than 80 years by 2015, (16). Approximately 7 in 10 deaths among older adults are caused by heart disease, cancer, or stroke. In the United States and Europe, approximately 1 in 5 people die of cancer (18). However, cancer incidence is lower in certain relatively affluent populations in Africa. More than half of all new cancers occur in patients 65 years of age or older. The incidence of cancer in persons older than 65 years is more than 10 times higher than that of the population younger than 65 years, and more than half of all cancer-related deaths occur in elderly patients (16).

The majority of patients are diagnosed as having CML when they are aged 65 years or older; many of the diagnoses are due to age-related medical problems (16). For CMLs, no specific signs or symptoms are present (19). CML was the underlying reason for osteomyelitis in our patient. According to a weighted index of underlying disorders described by Charlson and associates, leukemias are assigned a score of 2 (20). Using an illness severity scoring system, patients are assigned high or low risk, essentially based on clinical judgment. A weighted index of underlying disorders shows that illness severity and reasons for admission (low or high risk) are all significant predictors of CML (15).

Accurate diagnosis and staging of malignant diseases are essential for proper treatment (19). Age should not be a barrier to treatment. The common consensus on CML prognosis before the introduction of the molecularly targeted therapy with imatinib mesylate was poor. Now, persons aged 60 years and older seem to benefit just as well as younger individuals from this treatment (16).

Our patient had a history of a periapical and periodontal abscesses. The organisms involved in mandibular osteomyelitis are those of the oropharyngeal anaerobic microflora. *Actinomyces*, *Eikenella*, and *Peptostreptococcus* species are commonly isolated from dental abscesses associated with mandibular osteomyelitis (1). Treatment of mandibular osteomyelitis involves removing the diseased tooth or teeth and débriding the involved mandibular bone (21). Mandibular resection was not an option in the present case. In our patient, the main goals were to control excessive bleeding and prevent bacterial infection by extracting the tooth and eliminating granulation tissue and infected bone. Inadequate clot formation is associated with impaired wound healing and an impaired immune host response. Inappropriate activation of inflammatory responses such as impaired wound healing is an underlying cause of many diseases.

Treatment must be individualized for each patient. We consider a patient's age, medical condition, secondary diseases (eg, kidney disorders, anemia, and osteoporosis), physical condition, and medication use. Physiological modifications of body function are known to occur with age and may interfere with cancer treatment (16).

CONCLUSION

In medically compromised elderly patients, it is essential that their medical conditions be managed early so that they might enjoy a good quality of life. When following-up these patients, it is advisable to assess their dental and periodontal condition with regular visits to the dentist.

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