Oral manifestations of leukemia

Marija Nakova,1 Kenan Ferati,1 Arbresha Ferati,1 Marija Stojanova,2 Borče Stojanov,3 Andreja Todorović4

1. Department of Oral Pathology, Faculty of Dental Medicine, Tetova, FYR Macedonia
2. Private Dental Office „Dental Care“, Skopje, FYR Macedonia
3. Private Dental Office „Dr Borče Stojanov“, Radoviš, FYR Macedonia
4. Cardiology Department, General Hospital, Ćuprija, Serbia

ABSTRACT

Leukemia is a neoplastic disorder of the blood forming tissues, primarily affecting leukocytes. This is a heterogeneous group of diseases, which occurs from a neoplastic proliferation in the bone marrow. The replacement of normal bone marrow elements by leukemic cells causes decreased production of erythrocytes, normal white blood cells and platelets. The clinical result is anemia with weakness, fatigue, pallor of skin and mucosal membranes; thrombocytopenia with associated bleeding tendencies and leucopenia resulting in increased susceptibility to infection. Leukemia is of special interest to the dentists because he is frequently the first person to whom the patient turns for treatment. Dental procedures such as oral surgery, periodontal treatment, or even prophylaxis that produced trauma to the tissue may aggravate the situation and give rise to exacerbations of acute symptoms, which can result in death. Primarily, oral clinical manifestations may be consisting of gingivitis, gingival hyperplasia, hemorrhage, petechiae, erosion ulceration and necrosis of the gingiva and mucosa. The aim of this article is to evaluate the oral signs and symptoms of leukemia and present a clinical case, 59-old female with oral and extra-oral manifestation, as an initial signs of the disease.

Key words: leukemia; mouth; oral ulcer; oral medicine; dentistry.

KORESPONDENCIJA / CORRESPONDENCE

Andreja Todorovic, MD, General Hospital Ćuprija, Miodraga Novakovića 78, 35230 Ćuprija, Serbia, Phone: +381 35 8470 775, E-mail: andrejatodorovic@hotmail.com; marijanakova@yahoo.com
Dr Andreja Todorović, Opšta bolnica Ćuprija, Miodraga Novakovica 78, 35230 Ćuprija, Tel: 035 8470 775, E-mail: andrejatodorovic@hotmail.com; marijanakova@yahoo.com

DOI: 10.5937/pomc15-17307
UDK: 616.155.392-07
616.31
COBISS.SR-ID 267549452
INTRODUCTION

Leukemia is a serious neoplastic disease characterized by the progressive overproduction of any of the white blood cells and their precursors, generally with the appearance of these white blood cells in the circulating blood, especially in their immature forms. The replacement of normal bone marrow elements by leukemic cells causes decreased production of erythrocytes, normal white blood cells and platelets. This results in clinical anemia with weakness, fatigue, pallor of skin and mucosal membranes, thrombocytopenia with associated bleeding tendencies, and leucopenia resulting in increased susceptibility to infection. The leukemias are classified as either acute or chronic, depending on the presentation of the disease. They are further classified relative to the predominant cell affected as either lymphocytic or myelocytic.1,2

Clinical picture is characterized by the appearance of symptoms and signs arising from the insufficiency of normal hematopoiesis, the infiltration of tissue and organs by malignant cells and the metabolic disorders.3 The symptoms usually appear a few weeks before turning to a doctor for help, and they may significantly differ from patient to patient. Due to the insufficient hematopoiesis, three clinical syndromes are present: anemia, bleeding and infection. The development of acute leukemia is sudden, characterized by weakness, fever, headache, generalized swelling of lymph node, petechial or ecchymotic hemorrhage in the skin and mucosal membranes and evidence of anemia. The lymphadenopathy is rarely the first sign of the disease, although many cases are recorded in which the oral lesions were the initial manifestation. Numerous organs, such as the spleen and liver, become enlarged, owing to leukemic infiltration. Hemorrhages are commonly due to decrease in platelets, involvement of the bone marrow and decrease in megakaryocytes. Terminal infection is frequent of myeloid tissue, which ordinarily produces granulocytes.4

Oral lesions could occur in the both acute and chronic forms of all types of leukemia, myeloid, lymphoid and monocytic. The exact data in published literature differ depending on particular methodological approach and, particularly, patients’ population and the time of study reporting. For example, majority of modern authors consider that oral manifestation of either acute or chronic leukemia are not so common and that they are, at least in some disease types (e.g. acute lymphoblastic leukemia), mostly caused by chemotherapy used in the treatment of the disease. On the other side, historical studies, mostly based on case-series analyses, described somewhat higher incidence in some circumstances. For example, there were old suggestion that oral manifestations had been more common in acute, monocytic leukemia in comparison with other types of leukemias.5 Similarly, in a case series analyzed and literature review performed some decades ago, researchers reported relatively high incidence of oral manifestation in monocytic leukemia, with predominant gingival hyperplasia in affected patients exhibited.6 Other investigators in these times also found high incidence of positive oral findings in the series of adult and pediatric patients with leukemia.7,8

The papers published in the recent time re-affirmed the importance of recognizing oral manifestation in hematological malignancies because they might represent the important signs of the disease in the substantial portion of the patients. For example, some investigators suggested that about 65% of patients with leukemia during their disease could experience oral signs or symptoms.9 Oral petechiae or bleeding, mucosal erosion, necrosis, vesicles, ulceration and gingival enlargement are the most common signs.9,10 When such or similar clinical features emerge during initial course of hematological disease the dental professionals have high responsibility of recognizing the primary illness, with early referring to the hematologist for comprehensive diagnostic approaches.

Taking into account above-mentioned facts, the aim of our paper was to describe a clinical case of 59-year old female who had the oral disorders as an initial signs of the acute myeloid leukemia (AML).

CASE REPORT

A 59-year old female visited our Dental Clinic in Radešev, with the complaint of pain and swelling of the right part of face and mouth, over the last two weeks. The extra-oral dental examination showed swelling and limited infiltrative hyperemic nodular lesion on the right side of face and mentum. The skin of the face was covered with many ecchymoses, papules, pustules, vesicles and hyperkeratosis. On the low and upper lips, we noticed some erosion and ulceration with brown, yellow and white cover. There were also swelling and tenderness to palpation of the cervical lymph nodes (Figure 1). On the both of the lips, we saw noticeable swelling, more exceptional on the lower lip with numerous erosions and ulcerations covered with different colored crusts (Figure 2). Several ulcerations were also present on the buccal mucosa, retromolar area, the floor of the mouth and the right half surface of the tongue and gingival bleeding. The ulceration where covered with fibrin. On the tongue, there was an evident dental impression (Figure 3).
General physical examination revealed that the patient had pallor and fatigue. There was a history of intermittent fever, which started 9 days ago. The blood count and differential were as following: hemoglobin 64 g/L, hematocrit 0.13, mean corpuscular volume (MCV) 103 fL, mean corpuscular hemoglobin (MCH) 34.8 pg/cell, platelets 33.0x10^9/L, neutrophils <0.1x10^9/L, lymphocytes 0.4x10^9/L, monocytes 0.1x10^9/L, eosinophils <0.01x10^9/L, and basophils <0.01x10^9/L. C-reactive protein (CRP) was 220 mg/L. High decrease of haemoglobin level and increased MCV and MCH suggested diagnosis of macrocytic hyperchromic anemia. Neutrophil count was almost undetectable with profound thrombocytopenia and highly elevated CRP concentrations. Therefore, the patient was in high risk for developing life-threatening infection and spontaneous bleeding. She was immediately referred to Hematology Clinic, Medical Faculty, Skopje, for further treatment. Final diagnosis was acute myeloid leukemia and the patient was treated in the hospital according to the hematological protocols for that disease. The outcomes of the treatment were unknown at the time of paper preparation as she had been lost for subsequent follow-up dental visits for unknown reasons.

**DISCUSSION**

AML is an aggressive disease that predominantly occurs in older adults, it has a variable presentation and leukemic infiltration in vital organs can cause splenomegaly, hepatomegaly and lymphadenopathy. Replacement of normal bone marrow hematopoietic stem cells results in neutropenia, thrombocytopenia and anemia. This is the reason why AML patients commonly have signs and symptoms related to pancytopenia, such as fever, fatigue, pallor, bleeding and purpura and recurrent infections.

Substantial portion of patients with leukemia develop symptoms such as fatigue, weakness, loss of appetite and decreased weight within few months before disease emergence. If acute leukemia is left untreated or misdiagnosed, the serious consequences develop. It is therefore very important to find out the reasons of possible underlying cause of gingival enlargement in some patients, since early detection can increases the probability of survival. Therefore, early, less common or atypical signs and symptoms of the disease could be important clues for timely diagnosis.

Oral manifestations may occur in any types of the leukemia’s, but they are most common in AML and they might represent the first sign of the disease. Oral examination may show mucosal pallor due to anemia, spontaneous bleeding and petechial hemorrhages on the gingiva and palate as a result of thrombocytopenia, and gingival hyperplasia due to leukemic infiltration. Oral ulcerations are results of either neutropenia or direct infiltration by the leukemic cells. Patients may also have serious, recurrent viral, bacterial and fungal oral infection due to underlying immunosuppression. Therefore, all oral health practitioners should be aware of the significance of these oral manifestations in relation to AML. For example, leukemic gingival enlargement may be misdiagnosed because as it is rarely seen in everyday dental practice. In addition, the majority of oral lesion, in general, are benign and often self-limiting and therefore, the art of a physician is to diagnose those lesions that can be life-threatening. For example, while genetically induced gingival overgrowth is normal colored and firm, gingival overgrowth due to AML are edematous, soft, tender to touch and show ten-
dency to bleed.\textsuperscript{20,21} Further, patients having specific types of leukemia could be particularly susceptible to the gingival infiltration of leukemic cells.\textsuperscript{22,23}

Dentists may face a dilemma regarding whether any dental treatment will aggravate the leukemic situation and alter the patient’s systemic condition. Some found that periodontal status depends on plaque accumulation and that there were no direct correlation with hematological parameters taking into account various types of leukemia type.\textsuperscript{24} On the other side, gingival enlargement in leukemic patients is known to disappear without any specific periodontal treatment. However, enlarged gingiva facilitates plaque accumulation and food impaction, and complicates oral hygiene practice. This may lead to gingival inflammation with secondary gingival swelling. Patients in these cases are also concerned about bleeding during routine oral hygiene practice.\textsuperscript{23}

In conclusion, oral manifestations, when occur, could have clinical consequences for the patients suffering from acute myeloid leukemia (AML). Firstly, they could represent diagnostic challenge because, due to different oral problems, many patients could first contact a doctor of dental medicine, who can suspect acute leukemia through carefully and through examination and thus enable early diagnosis.\textsuperscript{2} Secondly, oral manifestation of acute myeloid leukemia (AML) may cause complication which necessitate additional treatments such as petechiae, hemorrhages of the of the tongue, lips, posterior hard and soft palate, gingival hyperplasia and spontaneous gingival bleeding as well as oral erosion and ulceration.\textsuperscript{15,16} All this clinical changes (erosion, vesicle papule, pustule, bleeding gums) we founded in our case report.

Systemic diseases may present with abnormalities in the oral cavity and leukemia is one of them. This case presented in our paper illustrates the importance of including systemic disease in the differential diagnosis of gingival pain, bleeding, and hyperplasia, and highlights the significance of a systematic approach to diagnosis. Dental professionals should be aware of clinical manifestation and complications associated with this neoplastic disease to aid in diagnosis and subsequent treatment and management.
REFERENCES


