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## CASE STUDY

# CHRONIC MYELOID LEUKEMIA MANIFESTING ON PALATE: A RARE CASE REPORT WITH A BRIEF REVIEW OF LITERATURE

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**ABSTRACT**

Leukemias represent a varied group of malignancies of hematopoietic stem cell origin. A subgroup of thesemalignancies is represented by the myeloid leukemias which generally affect adults.Chronic myeloid leukaemia (CML) is a myeloproliferative disorder of pluripotent haemopoietic stem cells, affecting mature myeloid white blood cells. More than 90% of cases of CML result from a cytogenetic aberration known as the Philadelphia chromosome. CML accounts for 15% of all leukemias and males are more commonly affected than females. Most patients with CML are older than 60 years of age. It is a rare case as its annual incidence is one to two cases per 100000. A case of CML having all the characteristic features of the disease is presented. Due to its high morbidity rate, early diagnosis and appropriate medical therapy are essential andthe oral signs and symptoms may reflect an undetected serious systemic disease.



## INTRODUCTION

Leukemia is cancer of white blood cells (WBCs) that affects the bone marrow and circulating blood. It involves exponential proliferation of a clonal myeloid or lymphoid cell and occurs in both acute and chronic forms. Acute leukemia is a rapidly progressive disease that results from accumulation of immature, functionless WBCs in the marrow and blood. Chronic leukemias have a slower onset, which allows production of large numbers of more mature (terminally differentiated), functional cells. There are four types of leukemia: acute lymphocytic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL) and chronic myeloid leukemia (CML). Acute leukemias are more common than chronic leukemias, accounting for 55% of all leukemias (Little *et al.,* 2008). Chronic myeloid leukemia (CML) is a myeloproliferative disorder of pluripotent haemopoietic stem cells, affecting one or all cell lines (erythroid, platelet and myeloid). Over the time, the leukemic cells proliferate due to stepped-up production and failed apoptosis. More than 90% of cases of CML result from a cytogenetic aberration known as the Philadelphia chromosome. (Besa *et al* 2011) The annual incidence of CML is between one to two cases per 100,000, (Chronic myeloid leukemia 2010).

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It accounts for 15% of all leukemias and is less common than CLL. Most patients with CML are older than 60 years of age. Men are more commonly affected (2:1) than women. CML causes 3% of childhood leukemias, (Little *et al.,* 2008**).** The etiology is unknown, but radiation exposure increases risk for the disease. The genetic defect consists of translocation of the cellular oncogene ABL from chromosome 9 to the BCR gene of chromosome 22 and a reciprocal translocation of part of BCR from chromosome 22 to the ABL gene in chromosome 9. A shortened chromosome 22, the Philadelphia (Ph) chromosome, results from the translocations and is evident in more than 90% of cases of CML (Aster *et al.,* 2005). The Philadelphia chromosome is also present in ALL. Translocation contributes to increased tyrosine kinase activity and myeloid proliferation, (Keating *et al.,* 2000). CML typically progresses through three phases: I. Chronic phase The immune system is competent and patients are asymptomatic for prolonged periods - typically, about 4-5 years. More than 90% of patients are diagnosed in the initial chronic phase. (Chronic myeloid leukemia 2010) II. Accelerated phase - Defined by 15-29% blasts in blood or bone marrow, >20% basophils in blood, thrombocytosis, thrombocytopenia unrelated to therapy or clonal chromosome abnormalities in the Ph+ (Philadelphia chromosome) clone (CCA/Ph+). (Chronic myeloid leukemia 2010) III. Blast crisis or Blastic phase - Is characterized by ≥30% blasts in blood or bone marrow or extramedullary blastic

infiltration. This is an aggressive acute leukemia with marrow exhaustion, highly refractory to chemotherapy and usually rapidly fatal. The clinical features of CML include fatigue, weakness, night sweats due to anaemia, weight loss, abdominal fullness, left upper quadrant pain due to splenic infarction, splenomegaly and altered hematopoiesis. Hyperviscosity of blood may cause a stroke. (1) Chronic forms of leukemia are less likely to demonstrate oral manifestations than are acute forms of leukemia. Oral manifestations like pigmented mucosa,gingival involvement Generalized lymphadenopathy, pallor of the oral mucosa and soft tissue infection may be present. (Little *et al.,* 2008)

## Case Report

**Case History:** A 62 year old male patient reported to the department of Periodontics and Oral Implantology, Government Dental College and Hospital, Srinagar (J&K) with the chief complaint of swelling on the right side of the palate for the last nine months. It was a slow growing, painless swelling, nonpitting, round in shape, hard in consistency, with well-defined borders and no history of discharge of pus or blood. The patient also gave history of fatigue, weakness, night sweats and weight loss. The patient also revealed frequent episodes of fever in the past. There was no significant past medical history and no significant family history. Past dental history revealed extraction of two teeth in the right maxillary posterior region.

**General and Extraoral Examination:** The patient had overall normal mental development but physically he was appearing to beaesthetic. Extraoral examination revealed the presence of pallor and anemia. The submandibular lymph nodes of both sides were enlarged, non-tender and freely movable.

**Intraoral Examination:** The intraoral examination revealed presence of soft tissue swelling on the right side of the palate extending from canine region upto distal aspect of the third molar and also crossing the midline of the palate. The swelling was blue-grey in color, round, non-pedunculated, non-pitting, non-tender, non-ulcerated and firm in consistency.Rest of the oral mucosa was normal (Fig. 1).

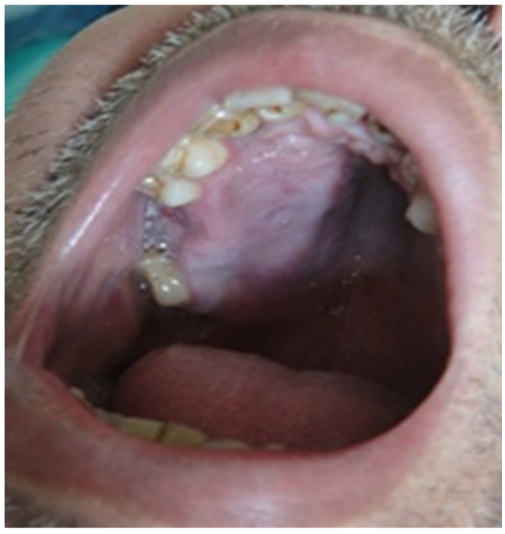

**Fig. 1. Pre-operative view of the palate**

## Radiographic Examination

Orthopantamogramic view (Fig. 2) revealed no significant findings but the occlusal view (Fig. 3) revealed palatal bone loss in the area underlying the soft tissue swelling.

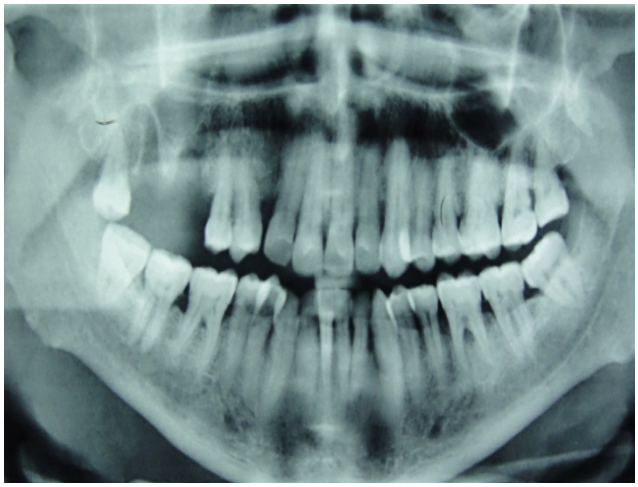

**Fig. 2. OPG of the palate**

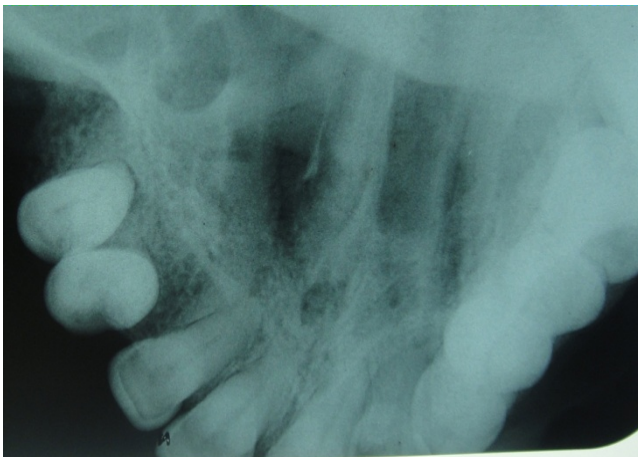

**Fig. 3. Occlusal view of the palate**

## Laboratory Investigations

Routine blood examination revealed marked elevation of WBC count. WBC count was 32,000/$mm^3$ and basophilia and eosinophilia were also present. RBC count was also reduced to 3.5 million/$mm^3$ and haemomoglobin was 8 gm. % being evident of anemia. Platelet count was also decreased to 1,06,000/$mm^3$. Cytogenetic analysis, a part of the standard diagnostic workup, revealed the presence of Philadelphia chromosome. Serum chemistry revealed elevated levels of lactate dehydrogenase and low levels of leukocyte alkaline phosphatase. The bone marrow was markedly hypercellular.

**Histopathologic Examination:** An incisional biopsy was performed by taking an elliptical section of representative lesional mucosa, 10 x 4 mm with a variable depth measuring 2-4 mm from the right hard palate and was sent for histopathology examination. Biopsy report revealed sections of normal lining squamous epithelium with underlying dermis showing infiltration by myeloid series cells (Fig. 4).

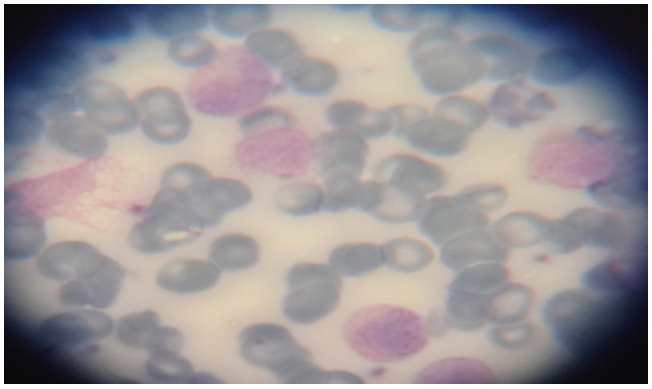

**Fig. 4. Histopatholgical view**

**Diagnosis:** In view of the above findings, the patient was diagnosed to be suffering from chronic myeloid leukemia. The patient was referred to the oncosurgeon for the management. The patient was treated by multiple doses of radiotherapy over a period of one month.the patient was recalled after the treatment for follow up and evalvation (Fig. 5).

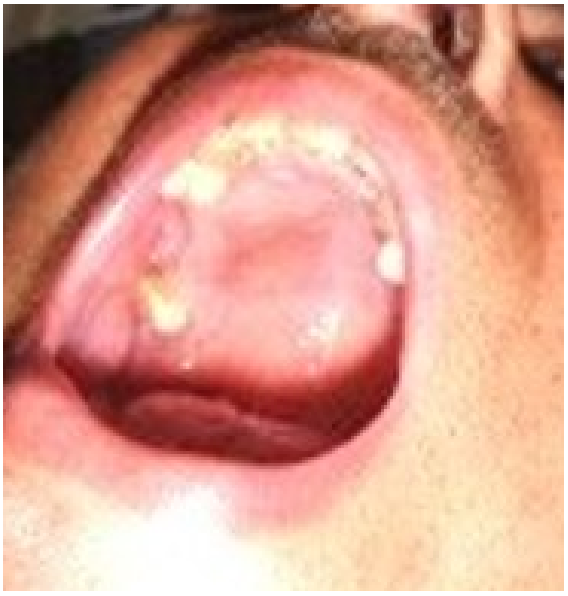

**Fig. 5. Post-operative view of the palate**

**Discussion:** There are three main groups of hematologic malignancies: leukemia, lymphoma and plasma cell tumors. Leukemia is a hematological disorder which is caused by proliferating white blood cell-forming tissues resulting in a marked increase in circulating immature or abnormal white blood cells. Leukemia arises from a hematopoietic stem cell characterized by a disordered differentiation and proliferation of neoplastic cells. Leukemia results from the proliferation of a clone of abnormal hematopoietic cells with impaired differentiation, regulation, and programmed cell death (apoptosis). Leukemic cell multiplication at the expense of normal hematopoietic cell lines causes marrow failure, depressed blood cell count (cytopenia), and death as a result of infection, bleeding, or both, (Franch *et al*., 2011), Demirer 2007. The cause of leukemia remains unknown. Increased risk is associated with large doses of ionizing radiation, certain chemicals (benzene), and infection with specific viruses (e.g. Epstein-Barr virus, human lymphotropic virus. Cigarette smoking and exposure to electromagnetic fields also have been proposed to be causative factors. (Greenberg *et al.,* 2008).

Classification of Leukemia

Leukemia is classified based on clinical behavior (acute or chronic) and the primary hematopoietic cell line affected (myeloid or lymphoid). The four principal diagnostic categories are the following (Greenberg *et al.,* 2008; Wu *et al.,* 2002):

1. Acute myelogenous leukemia (AML)
2. Acute lymphocytic leukemia (ALL)
3. Chronic myelogenous leukemia (CML) and
4. Chronic lymphocytic leukemia (CLL).

Chronic myeloid leukaemia (CML) is a myeloproliferative disorder of pluripotent haemopoietic stem cells, affecting mature myeloid white blood cells.CML is characterized by a consistent cytogenetic abnormality - a reciprocal translocation between the long arms of chromosomes 22 and 9, t(9;22). The result is a shortened chromosome 22, known as the Philadelphia (Ph) chromosome. The translocation is significant because it places an oncogene (ABL) from the long arm of chromosome 9 to the long arm of chromosome 22 in the BCR region. (Little *et al.,* 2008) The BCR-ABL fusion gene encodes a chimeric protein with strong tyrosine kinase activity. This constitutively active BCR-ABL tyrosine kinase causes CML but how the presence of this oncoprotein leads to the CML phenotype is not fully understood. CML's hallmark is the presence of BCR-ABL rearrangement and is considered diagnostic when present in a patient with clinical manifestations of CML.

CML progresses slowly through a chronic phase for 3 to 5 years, then onto an accelerated phase followed by a blast phase (or crisis). During the indolent phase of CML, leukemic cells are functional; thus infection is not a major problem. However, once transformation to the blastic stage has occurred, the leukemic cells are immature and non-functional. As a result, anemia, thrombocytopenia and infection become problems. (Little *et al.,* 2008) About 25% of the patients with CML patients per year undergo transformation to the blast phase of the disease 6 to 12 months after diagnosis. The blast phase consists of 30% or more leukemic cells in the peripheral blood or marrow. [(10)] More than 85% of the patients with CML die in the blast phase and patients without the Philadelphia chromosome have a worse prognosis. Ph chromosome is evident in more than 90% cases of CML, (Aster *et al.,* 2002). The overall prognosis for CML is poor and survival from the time of diagnosis is about 3.5 years (Aster *et al.,* 2002; Adamson *et al.,* 1991).

Patients with CML were historically treated during the chronic phase with hydroxyurea or busulphan; this resulted in good symptom and blood count control, alongwith significant toxicity. Interferon-α or imatinib mesylate (Gleevec), an inhibitor of tyrosine kinase, is widely used today. (Druker *et al.,* 2004) Stem cell transplantation has resulted in remission in more than 55% of patients at 5 years when treatment is provided prior to transformation to the blastic stage (Adamson *et al.,* 1991; Druker *et al.,* 2004). Stem cell transplants are

generally recommended for younger patients who have an adequate human leukocyte antigen (HLA) match. Regarding the dental management, first of all it is very important to detect and diagnose the patient with leukemia. Before any dental care is rendered, thorough medical consultation is taken. If the routine dental care is to be provided, dentist has to take care that no treatment is given to the patient with acute symptoms of leukemia. Once disease is under control, patient may receive indicated dental care. Scaling and surgical procedures are performed only if the platelet count is normal on the day of procedure. If it is < 50,000/$mm^3$, avoid invasive procedures. Prophylactic antibiotic therapy is given to prevent postoperative infection. Instruct the patient to maintain proper oral hygiene. If pain and infection are present, palliative treatment is given and conservative management is done, (Little *et al.,* 2008).

**Conclusion:** Oral health care professionals should be aware of the importance of recognizing oral manifestations of systemic diseases. The dentist and mainly the periodontist plays a fundamental role in the early diagnosis of leukemia knowing that the first symptoms of the disease occur in the oral cavity. It is essential for the professional to be able to clearly recognize oral physiological characteristics, and, when identifying a change of normalcy, to fully investigate it requesting additional tests or referring the patient to specialized professional. The early interception of chronic myeloid leukemia is very much important in preventing the exaggerated symptoms and further complications.

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