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Case Report

GENERALIZED GINGIVAL ENLARGEMENT AS A MAJOR ORAL MANIFESTATION IN AML PATIENT: A RARE CASE REPORT

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ABSTRACT:
Oral cavity works as an early indicator for variety of underlying systemic diseases. Thorough dental examination of the oral mucosa, teeth, gingiva and all other hard and soft tissues of the oral cavity by the periodontist leads to early, accurate and timely diagnosis of these underlying systemic diseases. Although, gingival enlargement may occur due to local factors like plaque in oral cavity, this gingival enlargement as oral manifestation also expressed as in systemic conditions such as endocrinal imbalance, blood dyscrasias, hereditary and cancerous conditions. Acute myeloid leukemia (AML) is a malignancy of bone marrow, a cancerous disease that may lead to significant fatality rate if not diagnosed timely. A 36 years old female reported with chief complaint of generalized gingival enlargement associated with spontaneous bleeding and ulceration of the gingiva. So, the aim of this case report was to report the generalized gingival enlargement in an rare case of AML patient, emphasizes the importance of proper and thorough examination of oral cavity, proper dental management, health education, motivation and timely referral of the patient to the oncology department for further needful treatment to avoid the dreadful condition.

Keywords: Acute myeloid leukemia, bone marrow, generalized gingival enlargement, systemic disease.

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INTRODUCTION

"Gingival enlargement" or gingival overgrowth means increase in size of the gingiva,Various periodontal diseases leads to this gingival enlargement. On the basis of etiological factors and pathological changes, gingival enlargement can be classified as- On the basis of etiology:(1) Inflammatory enlargement: Acute and chronic; (2) Drug induced gingival enlargement:Anti- hpertensive Calcium channel blockers: e.g. amlodipine, nifidipine ,verapamil etc.Anticonvulsants drugs –phenytoin, immunosuppressant's - cyclosporine**;(3)** Enlargement due to various systemic diseases: Conditioned overgrowth – due to puberty, pregnancy, deficiency of vitamin C , plasma cell gingivitis, granuloma pyogenicum(non-specific conditioned overgrowth) and gingival overgrowth due to systemic diseases-leukemias, granulomatous diseases (sarcoidosis, Crohn's disease, Wegeners granulomatosis); (4) neoplastic overgrowth (gingival tumors): Benign tumors, malignant tumors; (5) false enlargements.[1]
The clinical manifestation of gingival enlargement differs based on its etiology. Genetically induced gingival enlargement appears pink in color with minimal signs of inflammation, has a slow growth rate, and is firm in consistency. Soft, edematous, tender gingiva with ease to bleeding is a sign in blood disorders.[2] Gingival overgrowth in leukemic patients occur due to infiltration of premature leukocyte cells. Gingival enlargement is a common symptom that alerts the patient to take dental consultation for the

diagnosis of leukemia. Many of the life-threatening diseases may present with oral lesions as the initial manifestation, thus, necessitating the familiarization of dental professionals with the manifestations of systemic diseases.[3]

Among leukemias , AML (Acute Myeloid Leukemia) is a malignant tumor of bone marrow that triggers the cells to develop into various types of premature blood cells. Commonly, AML disease affects old age people and rarely affects individuals below the age of 45.years. The average age of AML patients is approximately 67 years, with more prevalence in male than female patients, but the average life time risk for both the sexes are less than half of one percent. The AML disease occur in bone marrow where new blood cells are formed and it usually circulates quickly into the blood. Therefore, these immature blood cells sometimes spread to other parts of the body, including CNS (brain and spinal cord), lymph nodes, liver, spleen and testicle. In case of acute leukemia, the immature cancerous blood cells are called blast cells. These immature blast cells divide very fast leading to the quick spread of leukemia. In leukemic patients these immature blast cells do not stop dividing when normal blast cell would.[4] This condition correlates with bone marrow failure and lead to the reduction in number of mature blood cells like red blood cells and platelets causing cytopenia. Patient experiences various symptoms like fever ,lethargy, pallor of oral mucosa, mucosal bleeding, petechiae ,general weakness and local infections.[5]

Various oral manifestations which represent a number of diagnostic indicators for AML disease.The oral manifestations of AML include generalized gingival enlargement, spontaneous gingival bleeding, pale oral mucosa, petechiae, oral mucosal ulceration, candida infections and herpetic infection.[6] Generalized gingival enlargement along with spontaneous gingival bleeding are the major oral manifestations seen clinically after thorough dental examination of the oral cavity that leads to the first diagnosis of AML disease.[7] From the (SEER) surveillance, epidemiology and end results data in the year 2011 for AML patients were estimated to be 17.5 per 1,00,000 (n=7,245) among the ≥ 65 years old population and 1.8 per 1,00,000 (n =4,864) for those < 65 years old. In acute myeloid leukemia the generalized gingival enlargement is the common oral manifestation than in chronic leukemia. But,the progress of gingival infiltration is unpredictable in any individual leukemia patient.[8] The role of dentist's in identifying the oral manifestation of AML patient is central. Firstly, a diagnosis of AML disease is rarely made after a dental examination..The dentist main role is to identify leukemic disease by means of thorough oral examination and refer the patient to an Oncology Department for further investigations. Secondly ,a dentist plays an important role in patient education and motivation regarding the importance of maintaining the oral hygiene and advising them about the oral manifestations that may affect their quality of life.[9]

A female patient age 36 years visited for dental consultation and check up with a chief complaint of generalized gingival enlargement which restricted her nutritional intake. The purpose of this case report was to locate the cause of infection and gum infiltration which leads to the generalized gingival enlargement along with spontaneous bleeding in AML patients by thorough examination of oral cavity Through this case report we tried to diagnose the AML patient on the basis of generalized gingival enlargement as a oral manifestation, dental management of this condition by doing phase-1 periodontal therapy and considerations related with treating this AML patient in the Department of Periodontics.

CASE REPORT

A female patient of 36 years age reported on 13thMarch 2020, in the Department of Periodontics of Himachal Dental College Sundernagar for dental consultation with a chief complaint of generalized gingival enlargement which restricted her nutritional intake. Medical history taken from the patient elaborated that three months back, she started noticing fever, general weakness, lethargy, gingival swelling, difficulty in swallowing, loss of appetite and mild weight loss, previous to this period she was normal .On extra-oral examination patient showed palpable ,slightly tender submandibular lymph node adenopathy .On intraoral examination ,there was generalized marginal, papillary and attached gingival enlargement which cover almost all of the crowns of all the teeth in both the dental arches buccally, labially, palatally and lingually (Gingival Enlargemnt as shown in figure 1 : I-Buccal Aspect .II-Labial aspect ,III-Palatal aspect, IV-Lingual aspect respectivally). The color of gingiva vary from glazed, shiny to bluish red .The gingiva was inflamed with heavy deposits of dental plaque and calculus with generalized spontaneous bleeding on probing. Generalized gingival enlargement with continuous pain in gums leads to restricted nutritional intake of the patient due to difficulty in swallowing. On physical examination ,the patients was in good general condition, good communication with mild weakness. On the basis of careful clinical oral examination generalized gingival enlargement as a major oral manifestation, we found that the patient may suffer from AML disease. We took the blood sample from the patient for hematological findings and preparing peripheral blood smear film for confirming the final diagnosis of AML disease. Hematological findings of the patient illustrated, Hb-10.5, RBC count-1.47 million/cub mm, platelets count (PLT)-49000, Neutrophils-9%, Lymphocytes-4%,Eosinophils-5%,Basophils-1.4% ,TLC-7010, BM(F-3088/19) ,Monoblast cells 47%, ESR-90 mm/hour (as shown in table-I).Numerous monoblast with large indented nucleus (as shown in fig.2: I) and

immature white blood cells of moderate to severe basophilic cytoplasm with large, round nuclei (as shown in fig.2 : II) and lacy chromatin. Less number of platelets can be seen with the nucleated RBC in the background . Based on the haematological findings and peripheral blood smear film, the final diagnosis of generalized gingival enlargement due to Acute Myeloid Leukemia of Acute myelo-monocytic type was made.

CASE MANAGEMENT:

The phase-1 non surgical periodontal therapy like supragingival scaling was done in the patient and advised her to use soft bristle tooth brush and 0.2% chlorhexidine oral rinses for maintaining proper oral hygiene. Dental health education and motivation to the patient was given. The patient was then referred to Oncology Department (specialist consultation) I.G.M.C.Shimla for needful treatment. From Oncology Department we got the report of the patient which illustrate hematological and peripheral blood smear film findings. Hematological findings of the patient illustrated, Hb-10.5, RBC count-1.47 million/cub mm, platelets count (PLT)-49000, Neutrophils-9%, Lymphocytes-4%,Eosinophils-5%,Basophils-1.4% ,TLC-7010, BM(F-3088/19) ,Monoblast cells 47%, ESR-90 mm/hour (as shown in table-I).Numerous monoblast with large indented nucleus (as shown in fig.2: I) and immature white blood cells of moderate to severe basophilic cytoplasm with large, round nuclei (as shown in fig.2 : II) and lacy chromatin. Less number of platelets can be seen with the nucleated RBC in the background . Based on the haematological findings and peripheral blood smear film, the final diagnosis of generalized gingival enlargement due to Acute Myeloid Leukemia of Acute myelo-monocytic type was made.

Figure I: Clinical photograph of the patient on 13th March,2020,showing generalized gingival enlargement with localized necrosed and cyanotic area from Buccal aspect.

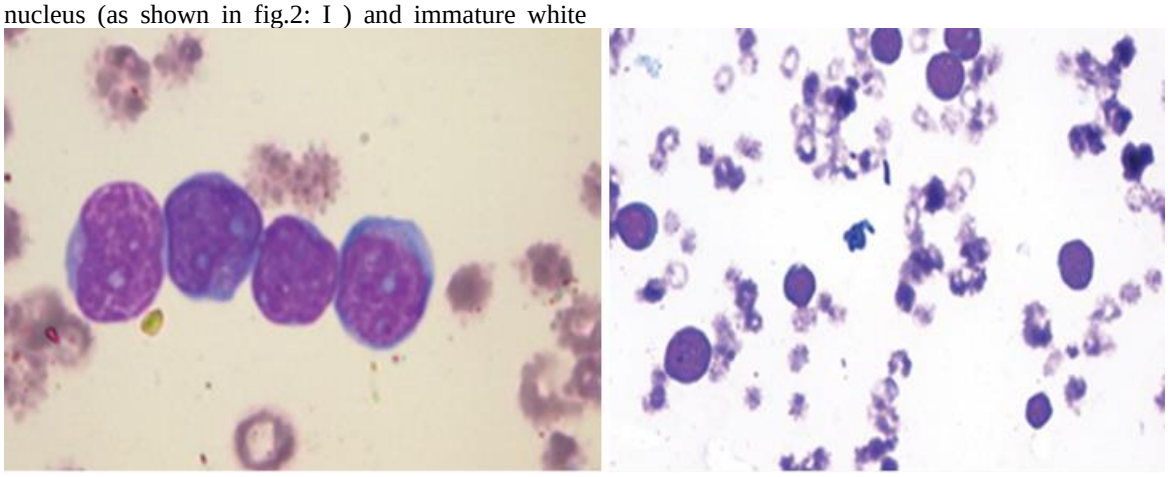

Figure II :. A. peripheral blood smear film showing numerous monoblasts with large indented nucleus , promonocytes and few platelets (Leishman's Stain; × 100) .B.. Photographs showing Immature,white blood cells with large nuclei with royal blue cytoplasm (Leishman's Stain; × 100)

Figure III: :Clinical photograph of the patient on 13th March,2020,showing generalized gingival enlargement with localized necrosed and cyanotic area of palatal aspect.

Figure IV : Clinical photograph of the patient on 13th March,2020,showing generalized gingival enlargement with localized necrosed and cyanotic area of lingual aspect.

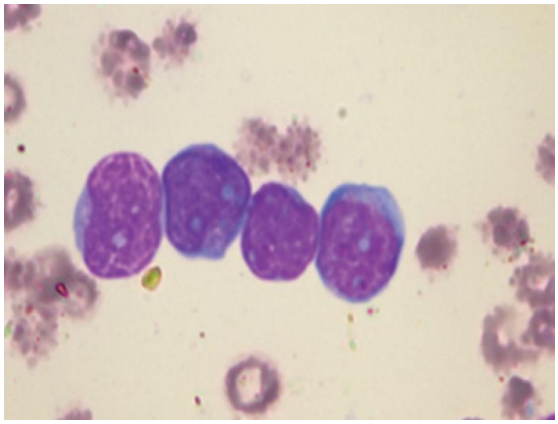

Figure V: A.Peripheral blood smear film showing numerous monoblasts with large indented nucleus, promonocytes and few platelets (Leishman's Stain; × 100)

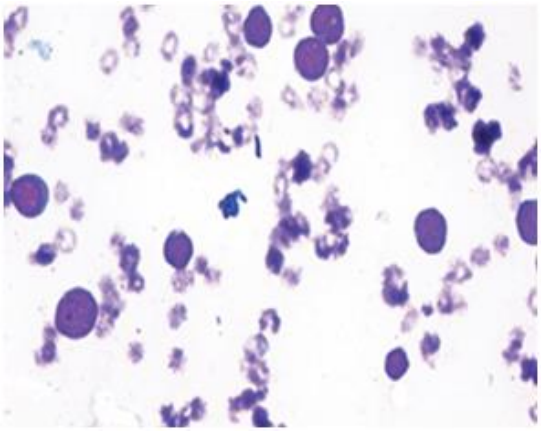

Figure VI : A.Peripheral blood smear film Photograph showing Immature,white blood cells with large nuclei with royal blue cytoplasm (Leishman's Stain; × 100)

DISCUSSION:

Leukemia is a group of malignant hematological disorders of multipotent stem cells i.e. mesenchymal cells (myeloid or lymphoid) found in bone marrow.It is the malignancy of white blood cells (WBCs) and occurs due to increased number of immature, abnormal , uncoordinated hematopoietic white blood cells (WBC) in respect to their differentiation, proliferation and apoptosis (programmed cell death).Based on the cell lineage and evolution of the disease, leukemia's are broadly classified as lymphoid or myeloid, and acute or chronic respectively.[10] Chronic leukemia's progresses slowly, remained inactive from months to years and effect relatively well differentiated leukocytes.

In acute leukemia's there is uncoordinated proliferation of immature undifferentiated blast cells. They have rapid onset, spread very fast and untreated cases may leads to very high mortality rate. Chronic and acute leukemia's Acute and chronic leukemia's are classified on the basis of type of WBC involved, i.e. myeloid and lymphoid series.French - American - British classification further subdivides acute lymphoid leukemia and AML, based on the degree of differentiation along cell lines and the extent of cell maturation.[11] Although many predisposing factors like exposure to ionizing rediations or electromagnetic field ,cytotoxic therapy ,and various viral infections have been considered ,but yet the exact etiology of leukemia remains unknown. [12]According to Stafford *et al*., oral manifestations are more commonly seen in patients with acute leukemia.[13] The above said oral manifestations may either be the result of direct infiltration of leukemic cells(primary or secondary) in the connective tissue of oral mucosa to underlying neutropenia, thrombocytopenia or impaired granulocytes functions. Gingival connective tissue infiltration illustrate a 5% frequency as the early presenting complications of AML.[14] Dreizen et al, reported that patient with acute monocytic leukemia had the greatest incidence of gingival connective tissue infiltration (M5) (66.7%) followed by acute myelomonocytic leukemia (M4) (18.5%) and acute myeloblastic leukemia (M1,M2) (3.7%).[15]Common oral manifestations of acute leukemia's include swollen gingiva, oral ulcers, spontaneous gingival bleeding, petechiae, pale mucosa,various fungal and viral infections (candidiasis and herpes).[16] Hemorrhagic bullae present on anterior part of dorsum of the tongue, buccal and labial mucosa, cracked lips, gum and tooth pain, tooth mobility and petechiae accounts for the uncommon oral signs.[17] Generalized gingival enlargement may vary in severity, from least to complete tooth coverage which restricted the functions and leads to poor aesthetics. In edentulous individuals there is no leukemic cells infiltration in gingival connective tissues, thus , Leukemic gingival infiltration is not seen in edentulous individuals, thus, signifying a potential role of tooth-associated local factors in its

pathogenesis. Caries, calculus, and poor oral hygiene may exacerbate gingival signs and symptoms and predisposes the patient for oral pain, bleeding, super infection, and tissue necrosis.[18] The final diagnosis of AML was suggested by a complete blood cell count showing pancytopenia and blast cells was confirmed by examination of the bone marrow. Investigation of the specific type of leukemia simplifies the best treatment and most accurate prognosis. Treatment options in acute leukemia's include aggressive multi drug chemotherapy and allogenic bone marrow transplantation. Periodontal and dental treatment for leukemic patients should always be planned after medical evaluation and physicians consent. In the present case for periodontal intervention (scaling and root planning) under prophylactic antibiotics. Patients are advised 0.2% chlorhexidine oral rinses, postoperative oral hygiene procedures. Dental health education and motivation was given to the patient to maintain their oral hygiene. However, periodontal surgeries are postponed until complete remission of the underlying disease occurs. We did supragingival scaling of the patient and advised her to maintain thorough oral hygiene status by the use of soft bristles tooth brush and 0.2% chlorhexidine oral rinses and the patient was referred to Oncology Department of IGMC Shimla for further treatment.

CONCLUSION

A periodontist or dentist could play a most significant role in the early diagnosis of AML disease via oral manifestations like generalized gingival enlargements. AML disease commonly diagnosed by the general physicians but dentists were also responsible for diagnosing 33% cases of acute myelomonocytic leukemia and 25% cases of acute myeloid leukemia. Dental management of AML patients by the dentist should be implicated at three different levels, first is pre-antineoplastic therapy, second is ongoing anti-neoplastic therapy and third one is post treatment care of the AML patient. The main motive of dental treatment in AML patient was to maintain good oral hygiene. The dentists should have enough knowledge about the signs and complications associated with AML disease to enable early diagnosis of the disease and in time referral to the concerned specialist for needful treatment to avoid the dreadful effects of this disease.

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