Diagnosing acute lymphoid leukemia based on oral manifestations: A case report

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Leukemia represents malignancies of the haemopoietic stem cell. The disease begins with the malignant transformation of one of the stem cells, which initially proliferates in the bone marrow and eventually overflows into peripheral blood of affected patient. Leukemia may begin at anytime in the life and is many times fatal due to failure of timely diagnosis. Gingival enlargement is a clinical feature that is very commonly



Fig. 1. Showing generalised gingival enlargement covering the labial surfaces of anterior teeth & few petechiae on left malar region.

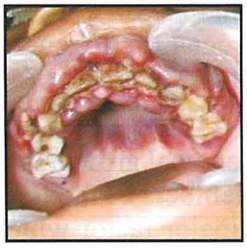


Fig. 2. Showing generalised gingival enlargement covering the entire labial and palatal surfaces of teeth along with congestion of the palate.



Fig. 3. Showing generalised gingival enlargement in the lower arch.

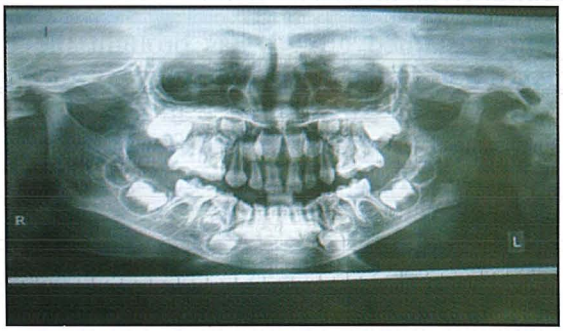


Fig. 4. OPG showing decrease in the density of bone.

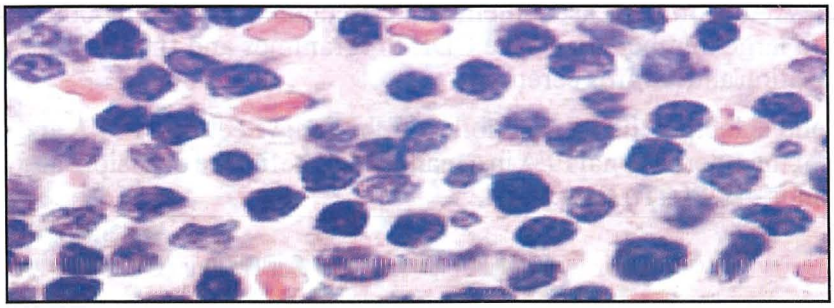


Fig. 5. H&E stain 100X Bone marrow biopsy showing deeply staining immature lymphocytes.

seen, but the underlying cause may many a times not be diagnosed, leading to recurrence of the lesion as well as worsening of the condition. This case report aims to make the dentist aware of the routine presentation of leukemia and increase the knowledge about the disease so as to prepare them to identify the disease early and thus prevent progression of the disease and improve prognosis of the patient.

Key words: leukemia, malignancy, gingival enlargement.

Leukemia is a type of cancer of blood or the bone marrow characterised by an abnormal increase in the number of white blood cells. The word *leukemia*, which means 'white blood', is derived from the pathological picture which shows a high white blood cell counts. Frequently, these extra white blood cells are immature or dysfunctional. The excessive number of cells can also interfere with the level of other cells, causing a harmful imbalance in the blood count. Clinically and pathologically, leukemia is subdivided into a variety of groups as shown in table 1.

Acute lymphoblastic leukemia (ALL) is the most common type of leukemia in young children. This disease also affects adults, especially those above the age of 65years. Standard treatments involve chemotherapy and radiotherapy. The survival rates vary among children and adults i.e. approximately 85% in children and 50% in adults. Subtypes of Acute lymphoblastic leukemia include precursor B cell lymphoblastic leukemia, precursor T cell lymphoblastic leukemia, Burkitt's leukemia, and acute biphenotypic leukemia.

Chronic lymphocytic leukemia (CLL) most often affects adults over the age of 55. It sometimes occurs in younger adults, but it almost never affects children. Two-thirds of affected people are men. The five-year survival rate is 75%. It is incurable, but there are many effective treatments that increase the survival rate. The subtype of Chronic lymphocytic leukemia is B-cell prolymphocytic leukemia, which is a more aggressive form of the disease[1].

Acute myelogenous leukemia (AML) occurs more commonly in adults than in children, and more commonly in men than women. AML is treated by chemotherapy. The five-year survival rate is 40%. Subtypes of AML include acute promyelocytic leukemia, acute myeloblastic leukemia, and acute megakaryoblastic leukemia.

Chronic myelogenous leukemia (CML) occurs mainly in adults. The five-year survival rate is 90%. One subtype of CML is chronic monocytic leukemia. Hairy cell leukemia (HCL) is sometimes considered a subset of CLL. About 80% of affected people are men. There are no reported cases in young children. HCL is incurable, but easily treatable. Survival is 96% to 100% at ten years. T-cell prolymphocytic leukemia (T-PLL) is a very rare and aggressive leukemia affecting adults; affecting men more than women.

Table 1

Classification of leukemias based on cell type and rate of development of disease

Cell type	Acute	Chronic
Lymphocytic leukemia (or "lymphoblastic")	Acute lymphoblastic leukemia (ALL)	Chronic lymphocytic leukemia (CLL)
Myelogenous leukemia (also "myeloid" or "nonlymphocytic")	Acute myelogenous leukemia (AML)	Chronic myelogenous leukemia (CML)

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Despite its overall rarity, it is also the most common type of mature T cell leukemia; nearly all other leukemias involve B cells. It is difficult to treat, and the median survival is measured in months. Large granular lymphocytic leukemia may involve either T-cells or NK cells; like hairy cell leukemia, which involves solely B cells, it is a rare and indolent (not aggressive) leukemia.[2]

Signs & symptoms

Damage to the bone marrow, by way of displacing the normal bone marrow cells with higher numbers of immature white blood cells, results in a lack of blood platelets, which are important in the blood clotting process. Hence leukemic patients show easy bruising, bleed excessively, or develop pinprick bleeds (petechiae).White blood cells, may be suppressed or dysfunctional thereby depressing the patient's immune system and producing frequent infections, ranging from infected tonsils, sores in the mouth, or diarrhoea to life threatening pneumonia or opportunistic infections. The red blood cell deficiency leads to anaemia, which may cause dyspnea and pallor. Other symptoms include fevers, chills, night sweats and flu-like symptoms. Unexplained weight loss is also seen. If the leukemic cells invade the central nervous system, then neurological symptoms like headaches can occur. Some leukemia patients do not have high white blood cell counts visible during a regular blood count this less-common condition is called Aleukemia. The bone marrow contains cancerous white blood cells which disrupt the normal production of blood cells, but they remain in the marrow instead of entering the bloodstream hence becoming invisible in a blood test. Aleukemia can occur in any of the four major types of leukemia, and is particularly common in hairy cell leukemia.[3]

Causes and Risk Factors

Leukemia, like other cancers, results from somatic mutations in the DNA. These mutations may occur spontaneously or as a result of exposure to radiation or carcinogenic substances, and are likely to be influenced by genetic factors.[1,5] Etiology is unknown but Epstein barr virus, human T cell leukemia virus-1are considered to be possible etiologic agents. Incidence of leukemia in mongoloids is 15-20 times more than in normal population. Philadelphia chromosome is translocation of chromosomal material from chromosome 22 to chromosome 9. This chromosomal abnormality is found in 85-90% of patients with chronic leukemia. This chromosome disappears from circulation during remission of disease but reappears when there is relapse. Leukemia in mongoloids is more of acute type as compared to chronic leukemia associated with Philadelphia chromosome[4].

Acute lymphoblastic leukemia (ALL)

Acute lymphoblastic leukemia (ALL) is a form of leukemia characterized by excess lymphoblasts. Other names of ALL are acute lymphoblastic leukemia and acute lymphoid leukemia. These leukemic cells are found in the blood, bone marrow, lymph nodes, spleen and other organs. Malignant, immature cells continuously multiply and are overproduced in the bone marrow. ALL causes damage and death by crowding out normal cells in the bone marrow and by spreading to other organs. It is the most common type of leukemia of childhood under the age of 15years. ALL makes up 80 %of childhood leukemias. Overall cure rate is 80% in children and 35-60% in adults[3].

Diagnosis is usually based on repeated complete blood counts and a bone marrow examination following observations of the symptoms, however, in rare cases blood tests may not show if a patient has leukemia, usually this is because the leukemia is in the early stages or has entered remission. A lymph node biopsy can be performed as well in order to diagnose certain types of leukemia in certain situations. Following diagnosis, blood chemistry tests can be used to determine the degree of liver and kidney damage or the effects of chemotherapy on the patient. When concerns arise about visible damage due to leukemia, doctors may use an X-ray, MRI, or ultrasound. These can potentially view leukemia's effects on such body parts as bones (X-

ray), the brain (MRI), or the kidneys, spleen, and liver (ultrasound). Finally, CT scans are rarely used to check lymph nodes in the chest. Despite the use of these methods to diagnose whether or not a patient has leukemia, many people have not been diagnosed because many of the symptoms are vague, unspecific, and can refer to other diseases. For this reason, the American Cancer Society predicts that at least one-fifth of the people with leukemia have not yet been diagnosed.[7]

This case report aims to make the dentist aware of the common presentation of patient with ALL so that diagnosis is made easy and prompt treatment is instituted to the patient thereby reducing the chances of metastasis and improving the prognosis.

Case History

6 year old female patient reported to the clinic with complaints of gingival overgrowth. This overgrowth was present since many years. According to the patient the gingival overgrowth was growing slowly but steadily. There was no pain associated with the enlargement but local discomfort was present. Gingivectomy had earlier been performed by a private practitioner one year ago, which had recurred in some time. On examination there was generalised gingival enlargement, with boggy gingiva covering almost all the erupted teeth.

The overgrowth was seen on both the labial as well as palatal surfaces, leaving only the incisal and occlusal surfaces visible. Gingiva was dusky red with an easy tendency to bleed. Palatal gingiva showed large areas of congestion giving a blue black appearance to the palate. Mandibular arch also showed generalised gingival enlargement which extended to involve all the teeth in the mandibular arch and covered the labial and lingual surfaces of all the erupted teeth. The extra oral skin showed numerous pin point bleeding areas (petechiae). Such petechiae were found to be present on the rest of the body also.

Radiograph

The orthopantomograph (OPG) Showed erupted deciduous dentition and developing permanent dentition. Bone density was found to be decreased. No other pathological findings were found.

Bone marrow biopsy

A bone marrow biopsy was taken using a 21 gauge needle. The aspirated material was stained using haematoxylin and eosin stain. Bone marrow aspiration cytology showed the presence of large number of deeply staining immature lymphoblasts and few mature lymphocytes. As bone marrow biopsy is diagnostic of ALL hence a further histopathology was not required.

Discussion

Leukemia is characterised by progressive overproduction of white blood corpuscles which appear in the circulating blood in an immature form. Any of the white blood cells may be involved hence it is classified into two types: lymphoid & myeloid leukemia. Leukemias are usually classified according to their histogenesis and clinical behaviour. Thus broad categories would be acute, subacute & chronic (referring to the clinical course) and myeloid and lymphocytic/lymphoblastic (referring to histogenetic origin). Acute form is one which has survival rate less than 6 months, chronic form has survival rate of over 1 year and subacute lies in between the two. It is interchangeably referred to as Lymphocytic or Lymphoblastic. This refers to the cells that are involved, which if they were normal would be referred to as lymphocytes but are seen in this disease in a relatively immature (also termed 'blast') state[8].

If all types of leukemia are considered, it occurs at a rate of 13 cases per 100,000 populations annually. Many of the clinical signs and symptoms of leukemia are related to the marked reduction in the number of normal white and red blood cells, which occurs due to crowding out of normal haemopoietic stem cells by the malignant proliferation. Because of the reduced red blood cell count and subsequent

reduction in oxygen carrying capacity of blood, patients complain of fatigue, easy tiring and dyspnea on mild exertion[9].

Leukemic patients also complain of easy bleeding and bruising, caused by depletion of platelets. Petecheial haemorrhages are also seen on posterior part of hard and soft palate accompanied by gingival haemorrhages. Ulceration of oral mucosa is often present as a result of impaired ability of the host to combat normal microbial flora.

Petecheial haemorrhages were seen in our patient on oral and extraoral skin. The soft and hard palate had a dusky red appearance and pin point Petecheial haemorrhages. Neutropenic ulcers produced are deep punched out lesions with greyish white necrotic base. Oral candidiasis & herpetic infections are the most common fungal and viral infections associated with leukemia.

Occasionally leukemic cells infiltrate the soft tissues and produce boggy, non tender swelling that may or may not be ulcerated. This may result in diffuse gingival enlargement or a prominent tumor like.[6]

The most common oral manifestations seen in patients with leukemia are gingival enlargement or hyperplasia. The clinical features exhibited by our patient were generalised gingival hyperplasia & petechiae. The gingiva was deep red, friable & boggy. It almost covered the entire tooth surface hiding the teeth from vision.

Bone marrow biopsy is gold standard for the diagnosis of leukemia. The bone marrow biopsy showed presence of multiple immature leukocytes which further confirm the diagnosis of acute lymphoid leukemia.

Conclusion

Thus, leukemia is a disease that usually fails early detection as the patient reports to the clinic early much prior to the onset of severe symptoms. If the dentist is aware of the signs and symptoms he should look for, then early detection of the disease is possible and it will facilitate faster treatment better follow up and better prognosis for the patient.

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