## A 9-year old boy with leukemia and oral manifestation

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**Summary:**

Childhood leukemia is not a common disease. We report a case of precursor B-cell Acute Lymphoblastic Leukemia (ALL), initially presented by unusual manifestations such as; teeth ache, loose teeth and gum swelling, knee pain and a normal Cell Blood Count (CBC). It was first considered to be Histiocytosis. Several laboratory work-ups have been performed to rule out the immunologic, infectious and rheumatologic diseases. A bone marrow aspiration revealed the diagnosis of leukemia. However, Acute Myeloid Leukemia is more famous for being accompanied with oral presentation, our patient was afflicted by ALL. The patient was first referred to a dentist for the oral manifestations.

**Key words**: Childhood Acute Lymphoblastic Leukemia, Oral manifestation, loose teeth

**Introduction:**

The most prevalent malignant neoplasms in children are the leukemias and 77% of these cases are ALL. In leukemias, the genetic abnormalities in a hematopoietic cell leads to uncontrolled proliferation of cells. ALL is more prevalent in boys and its peak incidence is at 2-3 year of age. The initial manifestations of ALL are often nonspecific, such as; anorexia, malaise, irritability, fatigue and low grade fever. Bone and joint pain especially in the lower limbs and joint swelling may be present.

**Case presentation:**

A 9-year old boy of Kurdish origin was brought to our hospital with teeth and jaw ache, gingival swelling, loose teeth and left knee pain.

The problems had started from about 40 days ago with pain and swelling of the left knee. He couldn’t bear weight on his left lower limb. The pain of the left knee got worse by activity. The swelling of gum and pain of the chin had started from 3 weeks earlier, and he had toothache since the previous 2 weeks. The jaw and toothache radiated toward the head. He felt that all of his teeth had become loose; therefore he could just eat watery foods.

On examination, both sides of the left knee were found to be tender on examination. The range of motion of the left knee had reduced and it was painful on active and passive motions, but it was not warm or red. The other joints were not painful and were normal on examination. He didn’t have weight loss, loss of appetite or skin rashes. The vital signs were stable and he didn’t have fever, nausea or vomiting. On examination of the left eye, he had lateral gaze palsy and it was deviated to right (Which is suggestive of the involvement of the left sixth cranial nerve). He reported having double vision. Funduscopic retinal exam of both eyes and other neurologic examinations were also unremarkable. On oral exam, he had poor oral hygiene, several teeth decays, and swollen gum without bleeding, swollen upper lip and chin (more prominent at left side) and a subcutaneous mass was palpated on the left maxilla beneath the eye. At both sides of the neck, several small size, mobile and non-tender lymph nodes were palpated. The 1st and 2nd teeth of upper and lower jaws were examined gently and were found to be loose. The rest of the teeth were also felt to be loose and these were the reasons for which he was, in the first place, referred to a dentist for the oral complaints. Abdominal exam wasn’t remarkable and no hepatosplenomegaly was detected.

His past medical history had a history of varicella infection about 4 months ago which was cured without complications. Twenty days before coming to our clinic, he had travelled to mountainous rural areas and contracted Herpes Labialis on the lower lip that caused numbness and tingling on the lip and chin, which lasted about 3 days and then chin scaling, pain of the gum and teeth, inflammation of the gum, and loosing of the teeth started in a few days afterwards. The laboratory work-ups at our hospital were as follows:

White blood cells: 12650/microliter, neutrophils: 43.2%, lymphocytes: 43.3%, monocytes: 11.5%, eosinophils: 1.2%, basophils: 0.8%, Red blood cells: 4950000/microliter, hemoglobin: 13.4 gram/deciliter, MCH: 27.1 pg, MCHC: 35.2 gram/deciliter, MCV: 77 FL, Platelet: 214000/microliter, MPV: 9.3 FL, Erythrocyte sediment rate: 27 millimeter/hour, Uric acid: 3.4 milligram/deciliter, calcium: 10.2 milligram/deciliter, phosphorous: 6 milligram/deciliter AST: 36 U/L, ALT: 5 U/L, C-reactive protein: 2.7

Considering an unremarkable cell blood count (CBC), and the oral signs and symptoms, the doctors considered Histiocytosis as the first diagnosis, then malignancies and immunologic disorders as the second possibilities. A radiography of the left knee revealed ‘’lytic lesion with periosteal reaction’’ (Figure 1). A three phase bone scintigraphy was performed and reported as follows: *Fusiform uptake in the lateral aspect of the distal physis of the left femur which could be tumoral involvement. No other abnormal bone lesion was seen.*



Figure 1. A lytic lesion with the periosteal reaction on the distal epiphysis of the left femur.

The Bone Marrow aspiration exam performed and was reported as: *Hypocellular marrow, with decreased myelopoiesis, erythropoiesis, and megakaryopoiesis, with more than 90% large lymphoblasts* *with cytoplasmic vacuole were seen suggestive of acute lymphoblastic leukemia (ALL) (FIGURE 2).*

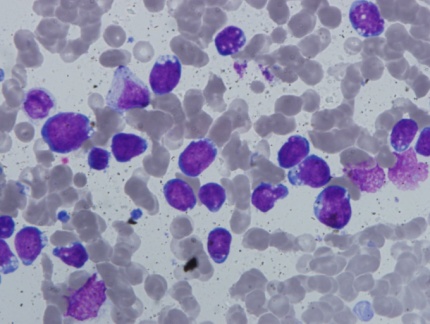
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FIGURE 2. More than 90% large lymphoblasts with cytoplasmic vacuole were seen, suggestive of acute lymphoblastic leukemia

Immunophenotyping marker analysis requested, which confirmed the diagnosis of ALL.

The flow cytometry analysis reported as follows:

Flow cytometry analysis and morphology showed: about 60% blast population with positive CD45/CD10/CD19/CD20/CD22 and HLA-DR which is consistent with a common precursor B-cell ALL(common ALL).

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| --- | --- | --- | --- | --- | --- |
| **HLA-DR 89%** | CD5 10% | CD13 3% | **CD19 51%** | CD33 8% | CD64 10% |
| CD2 2.1% | CD7 2% | CD14 4% | **CD20 82%** | CD34 2% | CD117 0.3% |
| CD3 2 | **CD10 33%** | CD15 3% | CD22 23% | **CD45 96%** |  |

Chemotherapy for high risk ALL started. The oral presentation (gingival hyperplasia and loose teeth) resolved in a few weeks after the initiation of the treatment.

**Discussion:**

In Langerhans cell histiocytosis (LCH), oral involvement could be the first and sometimes the only affected site. Oral manifestation of LCH may include gingival ulceration and inflammation and floating teeth. Maxilla and mandible are the commonly affected bones and solitary intra-bony lesions may cause facial swelling [[1](#_ENREF_1)]. LCH in all children with jaw pain or swelling and/or loose teeth should be considered [[2](#_ENREF_2)].

Gingival hyperplasia is commonly seen in acute leukemia which can be localized or generalized and caused by inflammation or leukemic infiltration. It mainly affects the interdental papillae and the marginal gingiva. It is less frequent in chronic leukemia [[3](#_ENREF_3)]. Calcium channel blockers, cyclosporine, anticonvulsants, hereditary gingival fibromatosis, chronic inflammation and leukemic infiltration, may lead to gingival hypertrophy [[4](#_ENREF_4)].

Throughout the course of leukemia, periodontal lesions are common. The most common signs and symptoms of oral cavity in leukemia include; gingival hemorrhage, petechiae, echymoses, infections, mucosal ulcers and gingival enlargement. Poor oral hygiene, neoplasia and systemic diseases may cause gingival hyperplasia [[5](#_ENREF_5)]. Gingival enlargement has been reported as an early sign of AML [[6](#_ENREF_6)]. Gingival hyperplasia is mostly seen in AML, commonly in acute monocytic leukemia (M5) and acute myelocytic leukemia (M1, M2) [[7](#_ENREF_7)]. In AML, gingival hyperplasia and leukemic infiltration could be aggravated with pre-existing periodontal disease [[8](#_ENREF_8)]. Manifestations of bone marrow failure such as pallor, fatigability, bruising and epistaxis will occur in the course of the illness. Lymphadenopathy, cranial nerve neuropathy, hepatosplenomegaly, headache, seizure, testicular enlargement are caused by organ infiltration. Enlarged mediastinal node may compress the airways and lead to respiratory distress. AML causes secondary bone marrow failure and may present with manifestations that are not common in ALL such as distinct masses (chloroma or granulocytic sarcomas), infiltration of gingiva, subcutaneous nodules or disseminated intravascular coagulation [[9](#_ENREF_9)]. Leukemic treatment in ALL may commonly lead to dental problems which need close follow-up and care [[10](#_ENREF_10)].

Because of the initial oral presentation in our patient, such as teeth ache, loose teeth and gum erythema and swelling he was first referred to the dentist office. He had also knee pain, which has not initially grabbed the appropriate attention. Later he was referred to the pediatric department and hematology assessment performed and a normal Cell Blood Count (CBC) provoked the doctors to consider Histiocytosis as one of the probable diagnoses. A bone marrow exam proved the diagnosis of leukemia. However Acute Myeloid Leukemia is more famous for being accompanied with oral presentation, our patient was afflicted by ALL, which is an unusual presentation in ALL.

The chemotherapy regimen with prednisolone, vincristine, daunorubicin, and L-asparginase started as the induction phase. In about one month (until the end of the induction phase of the chemotherapy), the loose teeth improved and he started to eat and chew the solid food. After two months, the oral manifestations improved completely. In the seventh day of the induction phase, the conducted bone marrow aspiration indicated less than 10 percent of blast cells; therefore, the patient was considered eligible to be treated on the Rapid Early Response protocol. During the 2-year follow-up, he was completely well and in complete remission.

**Conclusion:**

This case reminds the importance of systemic evaluation of a localized signs and symptoms in children and detailed history taking, follow-ups and physical examination. The first clue of the diagnosis in this patient was the presence of bone pain accompanied by the oral manifestations which with further investigation proved to be leukemia.

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