

A rare maxillofacial manifestation of acute lymphoblastic leukemia in a 9-year-old child

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Acute lymphoblastic leukemia (ALL) is considered as the most common malignant neoplasm of childhood and the frequent cause of death from cancer before 20-years of age. The facial swelling mimicking a maxillofacial tumor is rarely associated with ALL. Clinicians should be aware of such rare manifestation of ALL. We present a case with an atypical mass in the facial region secondary to ALL, which resulted in diagnostic dilemma. Reports of such atypical swelling in patients with ALL are occasional. The swelling was aggressive and the disease had a fulminant course.

Keywords: Children, Maxillary swelling, Acute lymphoblastic leukemia, B-Cell lymphoblastic lymphoma

INTRODUCTION

Acute lymphoblastic leukemia (ALL) is one of the most common malignancies in children. The B-cell type consists of 85% of all ALL. In contrast to T-cell ALL, the B-cell ALL is rarely described with extra nodal manifestation^{1,2}. Moreover, the oral and maxillofacial manifestations of ALL are very rare. In addition to the general signs and symptoms, common oral manifestations include lymph node involvement (71.4%), gingival bleeding (28.6%) and oral ulcerations (27.5%); which are not sufficient to suspect the disease^{3,4}. There are few case reports mentioning the oral (predominantly intra-oral) and maxillofacial manifestations in primary^{2,5-7} and relapsed^{8,9} cases of ALL. This case report highlights an extra-oral involvement of a large painless swelling mimicking a maxillofacial tumor in a 9-year child with B-cell acute lymphoblastic leukemia.

CASE REPORT

A 9-year-old child reported to Pediatric Outpatient Department (OPD) with chief complaint of swelling on the left side face. With the impression of a maxillofacial tumor, the child was referred from Pediatric OPD to Dental OPD for further management. Parents revealed the incidence of trauma to the same site by a cricket ball two months prior to the development of facial swelling. Patient was apparently alright four weeks before and developed a rapidly growing painless swelling on the left side of the face. There was no fever but had severe fatigue, anorexia, and weight loss. The weight and height of the patient were 19 kg (<2 standard deviation) and 130 cm respectively.

On physical examination, an isolated nodular/oval swelling was noted on the left side of the middle face, 5 × 5 cm size,

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extending supero-inferiorly from the floor of the orbit to corner of the mouth and antero-posteriorly from the lateral border of the nose to tragus of the ear (Fig. 1).



Figure 1: Extra-oral front view of face showing an isolated nodular/oval swelling on the left side of the middle face.

There was mild obliteration of nasolabial fold. The swelling was non-tender, hard in consistency with no change in color and temperature of the overlying skin. Intraoral examination revealed obliteration of the left upper vestibule. There was no mucosal ulceration and any carious tooth. There was also no mobility in any tooth adjacent to the swelling. The submandibular and cervical lymph nodes were non-palpable. A provisional diagnosis of secondary metastatic tumor of unknown origin was made, and routine blood investigations with comments on peripheral smear and computed tomography (CT) scan of the face were advised. The patient was also referred to Medical Oncology/Hematology OPD for a consultation.

Complete hemogram with peripheral smear revealed microcytic hypochromic anemia with a presence of 6% atypical cells. Total leukocyte counts were within normal limit ($5.25 \times 10^3/\text{mm}^3$) with relative lymphoid predominance in reference to age (Neutrophils, 57.1%; lymphocytes, 29.5%; eosinophils, 0%; monocytes, 6.8%; and basophils, 0.6% with 6% atypical cells). The blast/atypical cells were of 22 to 24-micron in size with a high nuclear:cytoplasm (N:C) ratio, scant agranu-

lar basophilic cytoplasm, round nucleus with loose open chromatin and 2–3 prominent nucleolus. Morphologically the lymphoblasts were differentiated from myeloblasts as they are smaller in size, have scanty agranular cytoplasm, rounded nucleus, coarse chromatin, few nucleoli and no auer rods. The platelet count was within normal range. Peripheral blood flow cytometry remained inconclusive in view of inadequate blast population.

The CT scan images showed infiltrating soft tissue mass in the left maxilla, causing erosion and destruction of the anterior, posterior, and lateral wall of the maxillary sinus with extension into a subcutaneous plane (Fig. 2). There was pathological fracture of maxillary bone. Based on the CT scan features, the differential diagnosis of sarcomatous lesion or sinonasal lymphoma or leukemic deposit were made.

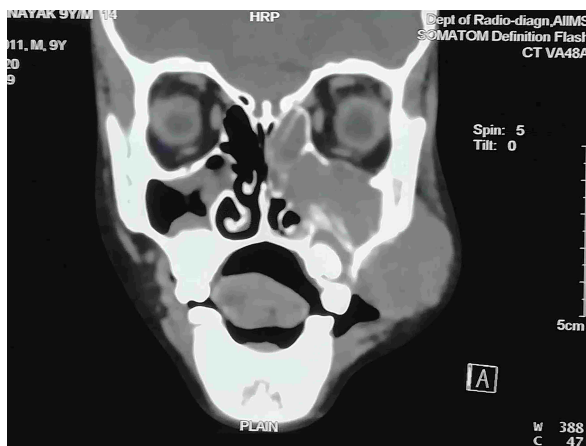


Figure 2: CT scan images showing infiltrating soft tissue mass in the left maxilla.

The bone marrow biopsy came as a dry tap, but biopsy confirmed >50% blast cells among all nucleated cells and the immunohistochemistry (IHC) features were consistent with the acute lymphoblastic leukemia (Fig. 3). The tumor biopsy revealed features of lymphoblastic lymphoma (Fig. 4). The cytogenetic report sent from peripheral blood came as 46, XY (Fig. 5). Immunohistochemically, it was diagnosed as cluster of differentiation (CD) 20+ B-cell type ALL (Fig. 6).

Based on the histopathology and IHC reports, treatment was initiated as per BFM 2002 (Berlin-Frankfurt-Munster) chemotherapy protocol. On day one, the cerebrospinal fluid (CSF) sample came positive for leukemic cells (CNS3), further intra-thecal chemotherapy with methotrexate was continued as per the protocol. The patient improved clinically after initiation of chemotherapy for initial few days, but his clinical condition deteriorated rapidly after 16th day. He became irritable with gradual drop in sensorium. The metabolic panel along with sepsis screen came normal. The magnetic resonance imaging (MRI) of brain revealed bilateral smooth pachymeningeal enhancement overlying the bilateral cerebral hemisphere (left > right), anterior flax and tentorium cerebelli secondary to leukemic infiltrates. There was minimal subacute subdural hematoma overlying the left parietal lobe. The left maxillary sinus was opacified with an ill-defined le-

sion causing erosion and destruction of its walls and extending anteriorly into the subcutaneous plane suggesting likely leukemic deposits. Further, he went into septic shock and could not be salvaged despite the best supportive care possible. The cause of his fulminant course and death could not be identified.

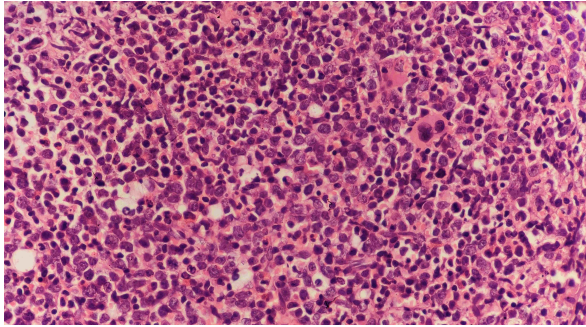


Figure 3: H & E section of bone marrow biopsy tissue showing hypercellular marrow space with more than 50% space diffusely infiltrated by large atypical cells, blasts.

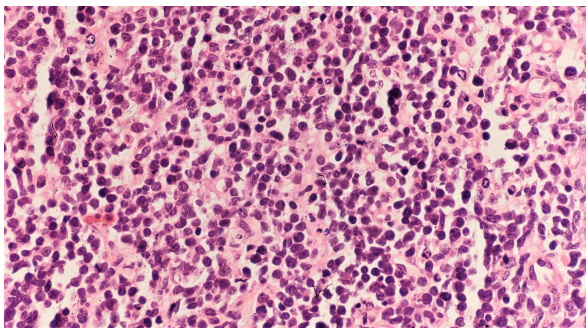


Figure 4: H & E section of biopsy from maxillary mass showing tumor tissue comprising of medium to large size atypical lymphoid cells diffusely spread showing neoplastic cells.



Figure 5: Photographic evidence of cytogenetic report.

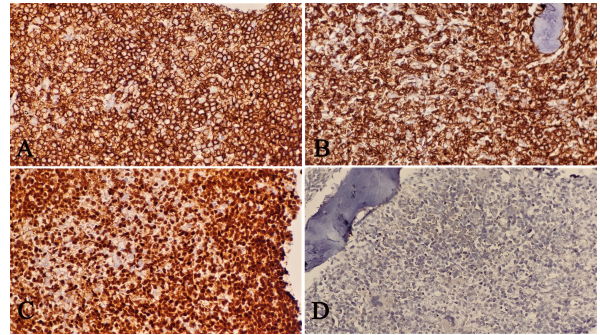


Figure 6: Immunohistochemistry report for (A) CD 20+, (B) CD 99+, (C) TdT+ and (D) Desmin-, suggestive of B-cell ALL.

DISCUSSION

The ALL is primarily a disease of children, and approximately 75% of affected are children aged <6 years. The B-cell lymphoblastic leukemia (B-ALL) is a neoplasm of lymphoblast committed to the B-cell lineage, with primary involvement of bone marrow and lymph nodes, rarely extranodal sites¹⁰. If a patient present with a mass lesion, and lymphoblasts in the bone marrow, then the distinction between leukemia (ALL) and lymphoblastic lymphoma (LBL) become arbitrary. However, in many treatment protocols, a value of >25% of bone marrow blasts defines leukemia¹¹.

The common extra-medullary sites of involvement in B-LBL are the skin, soft tissue, bone, and lymph nodes¹². Patients presenting with B-LBL are usually asymptomatic, and mostly have the limited-stage disease^{2,10}. Extra-medullary development of a solid tumor in ALL is occasional, having high predilection for the central nervous system, lymph nodes, spleen, liver, and testes¹².

There are few cases reported in the literature mentioning the maxillary involvement in ALL. However, most of the cases, the swelling was typically restricted intraorally without any gross facial asymmetry. Whereas, our patient presented with a unilateral, well defined, firm, extra-oral swelling, mimicking maxillary neoplasm. In contrast to our patient, Sánchez-Romero *et al.*² reported an erythematous asymptomatic swelling in the maxilla of a 38-year male patient with B-cell ALL. Dalirsani *et al.*⁵ in 2015 reported bilateral painless diffuse swelling in maxilla and mandible in T-cell ALL. Brito *et al.*⁸ reported swelling, pain and tooth mobility in the maxilla and palate involving maxillary sinus on right side associated in the T-cell type of lineage. Fallahinejad-Ghajari *et al.*⁹ reported pain, swelling and associated teeth mobility in the palate and maxilla, but did not report the nature of cell lineage. Cavalcante *et al.*⁶ found painful swelling on the maxilla on the right side in B-cell type of lineage. Karimi *et al.*⁷ reported enlargement of maxilla and mandible with mild pain in T-cell type ALL.

The biopsy from solid mass and IHC remain as gold standard for diagnosis. However further staging workup with whole-body CT scan, and the bone marrow becomes essential. Microscopic feature of the growth in our patient revealed the typical characteristics of B-cell lymphoblastic lymphoma.

There was an infiltration of small to moderate sized immature cells, with finely dispersed chromatin and inconspicuous nucleoli. The immunohistochemistry of bone marrow biopsy revealed acute lymphoblastic leukemia and helped in differentiating it from Burkitt lymphoma and Ewing sarcoma.

Burkitt lymphoma can be easily differentiated from LBL using immunohistochemistry, particularly with immunostaining for Bcl-2, Bcl-6 and TdT. Tumor cells are negative for Bcl-6 in LBL, whereas they are positive for Bcl-6 in Burkitt lymphoma; Bcl-2 and TdT are negative in Burkitt lymphoma. It is noteworthy that B-LBL cells often express CD99. As this feature can cause confusion with Ewing sarcoma/primitive neuroectodermal tumor, extensive immunohistochemistry is always necessary. However, complete blood profile, histopathology and positivity for TdT, CD 34, CD 99, CD 3, and CD 79a in a small to medium-sized neoplasm is a reliable profile to confirm the diagnosis and to differentiate ALL/LBL from other pathology.

Data on the prognostic significance of facial mass in ALL are limited. According to the St Jude classification^{12,13}, for LBL the stage of disease has a prognostic impact on both event free survival (EFS) and overall survival (OS), with a statistically significant difference between Stages I to III and Stage IV.

The EFS and OS for ALL are related to gender, age, leucocyte count at diagnosis, molecular profile and response to therapy at days 8 and 35 and the end of consolidation¹³. Although the prognosis and survival rate (SR) of ALL or B-LBL is more than 90%, but in our case, the prognosis was poor.

The ALL presenting as mass is in the oral and maxillofacial region is rarely encountered. The clinician might face difficulties while differentiating it from any other frequently occurred maxillofacial pathology. It is crucial for a clinician like, pediatrician or dental surgeon to be aware of the atypical presentation of this neoplasm.

CONCLUSION

The extra-oral maxillo-facial representation in the present case was unusual, which preceded the diagnosis of acute lymphoblastic leukemia. Early diagnosis with tumor biopsy, peripheral blood smear to look for any atypical cells, immunophenotype, molecular and cytogenetic analysis are critical factors for the outcome and prognosis of the disease. A clinician must be aware of such atypical presentations of an ALL for its early diagnosis and treatment.

CONFLICT OF INTERESTS

None.

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CONSENT TO PARTICIPATE

Consent from the patient was obtained for treatment and photo release.

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