CASE REPORT

Precursor B-cell lymphoblastic lymphoma of oral cavity: A case report with its diagnostic workup

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INTRODUCTION

Lymphoblastic lymphoma (LBL) is a neoplasm of immature lymphocytes committed to the B-cell (B-LBL) or T-cell lineage (T-LBL) and forms approximately 2% of all lymphomas.[1] Precursor B-LBL, forms 10% of LBL and is a rare subtype of non-Hodgkin's lymphoma (NHL).[2,3] It is a high-grade malignancy first described by Sternberg in 1916.[4,5] In 1975, Barcos and Lukes defined this pathological entity as LBL.[6] Both T- and B-LBL with oral cavity involvement are rare and cases reported to date include only one case of B-LBL presenting in oral soft tissues and two involving each of mandible and maxilla.[7,8]

CASE REPORT

A 10-year-old male child presented with a slowly enlarging painless left mandibular mass of 3 months duration with a history of trauma few months back. Extraorally, a firm swelling of 5 cm × 4 cm with diffuse borders involved the left body of mandible extending in the submandibular region [Figure 1a]. Intraorally, the swelling obliterated the left buccal vestibule from distal of canine to distal aspect of the first molar with Grade I mobility of associated teeth [Figure 1b]. Radiographically, orthopantomography and lateral cephalogram showed mixed radiolucent-radiopaque lesion in premolar-molar region of left mandible with periosteal reaction along the lower border of mandible giving sunburst appearance [Figure 2a and b]. Computed tomography (CT) scan showed large well-defined iso-to hypo-dense peripherally enhancing soft tissue density mass surrounding the left half of body and angle of mandible. The lesion caused cortical erosion and destruction of mandibular body along with irregular periosteal reaction [Figure 2c]. Due to patient's unresponsiveness, 2 months later, a repeat CT scan showed ill-defined soft tissue density mass that had increased in size, extending up to zygomatic arch with bony destruction extending into ramus and coronoid process of left mandible. Ultrasonography of the neck showed enlargement of bilateral level I, II and III neck (largest measuring 1 cm × 0.6 cm) and para-aortic lymph nodes. Chest X-ray, complete blood count, liver function test and kidney function test were normal.

Fine needle aspiration cytology of the lesion showed small round blue cells with scant cytoplasm, hyperchromatic and pleomorphic nuclei with dispersed chromatin which suggested a round blue cell neoplasm [Figure 3a]. Incisional biopsy of the mass showed parakeratinized stratified squamous epithelium

ABSTRACT

Lymphoblastic lymphoma (LBL), seen primarily in children or young adults, is a malignant neoplasia that originates from B or T lymphocyte precursors and rarely occurs in the oral cavity. In this localization, neither the clinical features nor the radiologic appearances are pathognomonic and can pose significant diagnostic problems. Histopathologically, it presents as a round blue cell tumor. An early and accurate diagnosis of this entity is very important due to its high cure rate. We report a case of B-cell LBL involving oral cavity in a 10-year-old child. The purpose of this report is to explore the diagnostic workup.

Key words: Lymphoblastic lymphoma, mandibular lytic bone lesion, periosteal reaction, round blue cell tumor, sunburst appearance

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and deeper connective tissue was infiltrated by small round blue cells with scant cytoplasm and hyperchromatic pleomorphic nuclei. The nuclei showed dispersed chromatin and inconspicuous nucleoli. The connective tissue was moderate to densely vascularized. This indicated a small round blue cell neoplasm [Figure 3b and c]. Bone marrow aspiration revealed its normoblastic nature. The first panel of immunohistochemical markers included epithelial membrane antigen, myogenin, pancytokeratin, leukocyte common antigen (LCA), terminal deoxynucleotidyl transferase (TdT) and CD99, of which TdT and CD99 were immunopositive and rest negative. Though CD99 was positive, strong nuclear staining with TdT classified it as an LBL and helped to differentiate it from Ewing’s Sarcoma. CD99 is positive in 75% of LBL. The second panel of markers to differentiate between T- and B-LBL included CD2, CD3, CD5, CD7 (T-cell markers) and CD10, CD20, PAX5 (B-cell markers) of which CD10, CD20 and PAX5 were immunopositive. Positivity for B-cell markers (CD10, CD20) and PAX5 which is a protein encoded by the gene required for B-cell development, confirmed the B-cell origin of the lymphoblasts. Thus, based on these results, a diagnosis of precursor B-LBL was made [Figures 4a-h, 5a-f and Table 1]. The patient was managed with (cyclophosphamide, hydroxydaunorubicin, oncovin and prednisone (CHOP) regimen followed by radiotherapy. Considerable reduction in the size of the lesion was evident after chemotherapy and radiotherapy [Figure 2d]. Currently, the patient is on maintenance chemotherapy.

**DISCUSSION**

Lymphomas, third most common group of malignant lesions in oral cavity, are of two distinct types, Hodgkin’s lymphoma and NHL. Most of the head and neck NHL including oral lesions are of B-cell origin while blastic type is mainly of T-cell origin. B-LBL, in contrast to T-LBL clinically presents as acute leukemia in 80% of cases, whereas only 20% occur as solid tumors primarily.[2,4] The median age for B-LBL is reported to be 20 years with 64% occurring below 18 years.[7,8] Out of the three cases of B-LBL in oral cavity reported in the literature, one of them occurred in an adult.[5] The occurrence of B-LBL in oral cavity without blood or bone marrow involvement is uncommon as seen in the present case.[2,5,7] Jaw lesions typically present with nonspecific signs and symptoms, particularly as painless swelling as in this case, with other symptoms such as paresthesia, loosening of teeth and lymphadenopathy.[8] However, lesions presenting as painful swellings are also reported in the literature.[5,7] The clinical presentation of B-LBL in oral cavity ranges from swelling covered with healthy mucosa as in the present case to a lobulated mass with red hue or fungating and friable mass.[5,7] There are no risk factors identified in LBL. However, a number of cases have been reported in studies assessing the carcinogenic activity of drugs, viruses, oncogenes, immunodeficiency, chemicals and radiations.
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Radiologic imaging studies show lytic or sclerotic bone changes mimicking benign or malignant primary bone lesions.[9] Histopathologically, B-LBL is composed of small to medium size round blue cells showing high mitotic rate. The cells have scant basophilic cytoplasm and characteristic nuclear features such as fine chromatin and inconspicuous nucleoli. Other features seen are focal or diffuse starry sky pattern, necrotic foci or karyorrhectic debris, in a background of mature small lymphocytes and plasma cells, linear arrangement of neoplastic cells and presence of sclerosis.

The diagnosis of a small round cell tumor of bone is difficult, particularly in children, because the clinical, radiographic, histological and immunophenotypic features overlap.[9] The differential diagnosis includes T-LBL, the blastoid variant of mantle cell lymphoma, small cell osteosarcoma, rhabdomyosarcoma, neuroblastoma, primitive neuroectodermal tumor, neuroendocrine carcinoma and Ewing’s Sarcoma when tumor occurs in bone [Table 1].[7]

The distinction of malignant lymphoma from Ewing’s sarcoma is important because treatment and outcome differ in these. The types of NHL most commonly found in children are Burkitt’s lymphoma, LBL and anaplastic large cell lymphoma.[7] Immunohistochemistry is potentially the most reliable diagnostic aid. In the present case among the first panel of Immunohistochemical markers applied, immunopositivity was found for only TdT and CD99. This excluded the epithelial and muscle origin of the tumor. Strong nuclear immunopositivity for TdT, a unique DNA polymerase in lymphoblasts indicated it to be LBL. For further B- and T-cell differentiation, second panel of markers were applied which showed immunopositivity for B-cell markers such as PAX5, CD10 and CD20. PAX5 is a protein encoding gene required for B-cell development which was positive in this case. Thus, a diagnosis of precursor B-LBL was made.

Cytogenetic and molecular-genetic studies also can be useful for diagnosing precursor B-LBL as 95% of cases exhibit clonal Ig rearrangement and may also rearrange TCR genes (predominant with precursor lymphoid neoplasms).[12] Several chromosomal abnormalities have been associated with LBL, but t (9;17)(q34;q23) has been associated with an aggressive clinical course in children.[1,10]

Table 1: Differential diagnosis of B-lymphoblastic lymphoma

| Lesions                  | Differentiating feature                                      |
|--------------------------|------------------------------------------------------------|
| Ewing’s sarcoma          | CD99 and CD45 - positive                                   |
|                          | TdT* and B-cell markers negative                           |
|                          | Cyogenetic studies ([11,22] with EWS/FLI-1 fusion)         |
| T-LBL                    | Mediastinal mass in 50-65% as compared to 4% in B-LBL      |
|                          | B-cell marker negative                                     |
|                          | At least one T-cell marker positive                        |
| Burkitt’s lymphoma       | TdT negative                                               |
| Blastoid variant of      | Older people - sixth or seventh decades                    |
| mantle cell lymphoma     | TdT negative                                               |
| Rhabdomyosarcoma         | Myogenin-positive                                          |
|                          | Lymphoid markers negative                                  |
| Neuroblastoma            | Common in abdomen, thorax, pelvis (rare in head and neck)  |
|                          | Negative lymphoid markers                                  |
| Follicular lymphoma      | TdT negative, t (14,18)                                    |

*TdT: Terminal deoxynucleotidyl transferase, LBL: Lymphoblastic lymphoma

Treatment of primary lymphoma typically consists of a combination of chemotherapy and radiotherapy. LBL seems to be curable in the pediatric population with aggressive chemotherapy. Current chemotherapeutic modalities for LBL are based on those used for acute lymphocytic leukemia (ALL) such as Hyper-CVAD and CHOP regimens.[5] Autologous stem cell transplant (SCT) has been shown to produce similar good results as chemotherapy alone and allogeneic SCT is likely to be a more appropriate option for patients who are beyond...
first remission or with more advanced disease.\textsuperscript{[1]} Intensive intrathecal chemotherapy prophylaxis is required to reduce the CNS relapse incidence.

Prognostic predictors are presumed to be similar to B-ALL, with negative indicators being advanced age, high leukocyte count, circulating blasts, elevated serum lactate dehydrogenase, increase in organ size, central nervous system involvement, relapsed cases and delayed response to chemotherapy.\textsuperscript{[8]} Low propensity for peripheral blood involvement, in essence, a nonleukemic state, imparts the greatest survival advantage.\textsuperscript{[5,9]} The prognosis in all age groups has improved with the use of intensive ALL-type chemotherapy regimens, with a disease-free survival of 73–90% in children and 45–72% in adults.

CONCLUSION

The diagnosis of small round cell tumors can be made precisely by applying clinicopathologic criteria as well as a panel of IHC markers or genetic studies so as to facilitate prompt and accurate therapy. This was a rare case of B-LBL presenting in oral cavity (fourth to be reported) and its early and accurate diagnosis along with a nonleukemic state warranted a high cure rate.

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Conflicts of interest

There are no conflicts of interest.

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