Burkitt lymphoma of bone: A single institutional experience

**Background:** Burkitt lymphoma (BL) of the bone is a rare entity. Very few reports about the entity are there in the literature until date. Here, we sought to describe the clinical characteristics of the patients with BL of the bone. **Materials and Methods:** A retrospective study was performed involving patients with BL of the bone. Data regarding patient demographics, clinical presentation, treatment, and outcome were analyzed using descriptive statistics. **Results:** Six patients were identified with a mean age being 24 years (range: 19-64 years). Four patients had localized disease. Five out of six patients received dose intense chemotherapy. All of them developed febrile neutropenic episodes during treatment. One progressed during chemotherapy. **Conclusions:** Burkitt lymphoma of the bone is an aggressive disease. Successful Treatment includes combination of dose intense chemotherapy along with supportive care.

**Key words:** Bone lymphoma, Burkitt lymphoma, chemotherapy

**INTRODUCTION**

Primary Non-Hodgkins lymphoma of bone (PNHLB) is a rare entity. It is defined as the presence of Non-Hodgkins lymphoma (NHL) in bone with no evidence of disease in lymph nodes or at other sites. PNHLB comprises less than 1% of all NHL. Most common histology of PNHLB is diffuse large B cell lymphoma. Rare histologies of small lymphocytic, anaplastic large cell and follicular lymphoma have been reported. Here, we are reporting a series of Burkitt lymphoma (BL) arising from bone.

**MATERIALS AND METHODS**

Our study sample included patients with BL of bone from January 2011 to December 2012. Patients were diagnosed to have BL of the bone when patients demonstrated bone lesion radiologically and the biopsy of the bone lesion revealed the histopathological and immunophenotyping characteristics associated with cytogenetic abnormalities suggestive of BL. Staging evaluation was done for all patients.

**RESULTS**

Six patients were diagnosed to have BL of the bone during the study period. Baselines characteristics are shown in Table 1. Five patients were treated with dose intense combination chemotherapy. One patient was put on 6-mercaptopurine and steroids in view of elderly age and poor performance status at presentation and was lost to follow-up. Four patients were demonstrated to be in clinical remission after completion of treatment. One patient progressed on treatment. All the patients had t (8;14) translocation characteristic of BL, which was diagnosed by fluorescence in situ hybridization (FISH).

**DISCUSSION**

Primary Non-Hodgkins lymphoma of bone comprises about 5% of primary bone tumors and less than 5% of extra nodal lymphoma. They originate from the medullary cavity and present as a solitary localized lesion. Coley's criteria are used to diagnose PNHLB as shown in Table 2. Regional lymph node involvement is not an exclusion criterion for the diagnosis of PNHLB. It can involve a single bone (mono-ostotic) or multiple bones (polyostotic). PNHLB has a slight male preponderance with peak

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**Table 1:** Baselines characteristics

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>Gender</th>
<th>Disease</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>24</td>
<td>M</td>
<td>Localized</td>
<td>Chemotherapy</td>
<td>Remission</td>
</tr>
<tr>
<td>2</td>
<td>19</td>
<td>F</td>
<td>Localized</td>
<td>Chemotherapy</td>
<td>Remission</td>
</tr>
<tr>
<td>3</td>
<td>26</td>
<td>M</td>
<td>Localized</td>
<td>Chemotherapy</td>
<td>Remission</td>
</tr>
<tr>
<td>4</td>
<td>34</td>
<td>F</td>
<td>Localized</td>
<td>Chemotherapy</td>
<td>Remission</td>
</tr>
<tr>
<td>5</td>
<td>42</td>
<td>M</td>
<td>Localized</td>
<td>Chemotherapy</td>
<td>Progress</td>
</tr>
<tr>
<td>6</td>
<td>64</td>
<td>M</td>
<td>Localized</td>
<td>Chemotherapy</td>
<td>Remission</td>
</tr>
</tbody>
</table>

**Table 2:** Coley's criteria

- Bone lesion
- Absence of lymph node involvement
- Non-aggressive clinical presentation
- Resolution on chemotherapy
incidence occurring in fifth decade. However, reports of PNHLB are there in all age groups. Patients present with bone pain or swelling of the involved bone or a combination of both. Neurological symptoms are common when there is involvement of vertebra. They can sometimes present with pathological fracture. Diagnostic study should include imaging of the local part. X-ray features of PNHLB are usually nonspecific. It can show predominantly lytic lesion with moth eaten appearance or a well-defined lytic lesion. Periosteal reaction if present is typically laminar. Magnetic resonance imaging (MRI) is the imaging investigation of choice. Region of bone marrow involvement can be seen as hypointense on T1-weighted and hyperintense on T2-weighted imaging. Hyperintensity can also be seen due to peritumoral reactive marrow and edema. Extent of adjoining soft tissue involvement is better determined by MRI. Treatment for PNHLB depends on whether the disease is mono-ostotic or polyostotic and also on the type of lymphoma. Combined modality therapy, including both chemotherapy and radiotherapy is superior to single modality of therapy in mono-ostotic variant and is the standard of treatment. In polyostotic cases, local therapy like radiotherapy and surgery are not feasible and systemic chemotherapy is the standard of care. Polyostotic variants carry a poor prognosis compared with mono-ostotic variants. Surgical management of PNHLB is included either for tissue diagnosis or in cases of pathological fracture.

First described by Dennis Burkitt in 1958, BL is a highly aggressive NHL arising from the mature B cells. Three variants have been reported:

1. **Endemic form** which is diagnosed mainly in children and seen mainly in equatorial Africa. It involves the facial bones and is associated with Epstein-Barr virus (EBV) infection as well as malarial infection when coinfected with EBV infection.

2. **Sporadic form** which comprises about 1-2% of all NHL. The peak incidence is in children and young adults, with male predominance and a median age of about 30 years. Abdominal presentation is characteristic. Involvement of retroperitoneum, testes and ovary are seen.

3. **Last variant is associated with immunodeficiency.** It comprises about 35-40% of BL. This variant is primarily seen in immunocompromised patients, especially those with AIDS and patients on immunosuppressive therapy. It is commonly nodal though extranodal involvement is seen.

A characteristic feature of BL is the presence of translocation involving c-myc gene. In 80% of the cases, the translocation occurs between c-myc gene and the IgH gene (t (8;14)) while in the remaining cases the translocation occurs between c-myc and the gene for either kappa or lambda light chain (t (2;8) or t (8;22), respectively). The myc/Ig translocation may not be detected by routine cytogenetic, but by doing FISH or polymerase chain reaction may increase the chance of detecting the translocation. The variant of BL has a distinct translocation of its own. In endemic form, break point in c-myc is >100 kb upstream from first coding exon and break point in the IgH gene is in the joining segment. In cases of sporadic and immunosuppression associated Burkitt, the break point in myc is between exons 1 and 2, and the break point in IgH is in the switch region. However, these break points are not always uniform. Rearrangement of c-myc is the earliest event in lymphomagenesis leading to a perpetual proliferative state and over a period of time, there are additional genetic events like p53 mutation, which ultimately lead to phenotypic manifestation of the disease. Figures 1-3 shows the involvement of bone trabeculae by lymphomatous cells and positive for its characteristic immunohistochemical markers. BL is a rapidly proliferating neoplasm with a doubling time of 18-24 h. Hence, the diagnosis should be established quickly followed by rapid initiation of definitive treatment. Treatment consists of combination of high intensity chemotherapeutic agents along with measures to prevent tumor lysis syndrome. Unlike other NHLs, CHOP chemotherapeutic regime does not have much value in BL. Radiotherapy does not have any role in BL even if patients present with a localized disease or paraspinal involvement. Hence, neither CHOP chemotherapeutic regime nor radiotherapy has not been used for any of our patients. Initially, acute lymphoblastic leukemia regimes with induction, consolidation and maintenance were used. However, high-growth fraction of BL favors re-entry

### Table 1: Characteristics of the patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Site</th>
<th>Treatment given</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>16/male</td>
<td>Humerus</td>
<td>Hyper CVAD</td>
<td>In remission</td>
</tr>
<tr>
<td>22/female</td>
<td>Multifocal</td>
<td>Hyper CVAD</td>
<td>In remission</td>
</tr>
<tr>
<td>24/male</td>
<td>Humerus</td>
<td>Rituximab+hyper CVAD</td>
<td>In remission</td>
</tr>
<tr>
<td>67/male</td>
<td>Multifocal</td>
<td>6-MP+steroids</td>
<td>Lost for follow-up</td>
</tr>
<tr>
<td>17/female</td>
<td>Femur</td>
<td>Hyper CVAD</td>
<td>Progressed</td>
</tr>
<tr>
<td>16/male</td>
<td>Femur</td>
<td>Hyper CVAD</td>
<td>In remission</td>
</tr>
</tbody>
</table>

CVAD: Combination of chemotherapy consisting of Cyclophosphamide, vincristine, Adriamycin, dexamethasone and cytarabine and methotrexate, 6-MP: 6-mercaptopurine

### Table 2: Coley’s criteria

- Primary focus in a single bone
- Positive histological diagnosis
- No evidence of distant soft tissue or distant lymph node involvement
of remaining viable malignant cells into the cell cycle and rapid growth between chemotherapy cycles with subsequent development of resistance leading to lower cure rates.[14] Thus, combination of chemotherapeutic agents given repetitively at short duration is the ideal treatment. Central nervous system (CNS) prophylaxis consisting of intrathecal administration of cytabine, methotrexate is a must. Along with CNS prophylaxis, complete remission (CR) rates in adults reached more than 80%. The direct comparison of each treatment protocol is difficult to compare because of the heterogeneous age of the population, disease phenotype (BL) and the difference in staging system. Addition of rituximab to the regime has led to increased response rate with better prolonged disease free and overall survival.[3] However, these chemotherapeutic regimes are associated with increased toxicity. Recently, a newer chemotherapeutic regime R-EPOCH was tried in BL, which has shown 100% CR with no mortality.[16]

REFERENCES


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