Burkitt Lymphoma: Classification, Pathology and Treatment

Burkitt lymphoma (BL) is an aggressive, high-grade B-cell non-Hodgkin lymphoma (NHL) marked by rapid proliferation and characterized by chromosomal translocations involving the **C-MYC proto-oncogene** on chromosome 8. The most common translocation is **t(8;14)(q24;q32)**, leading to overexpression of the MYC oncogene and uncontrolled cell proliferation.

C-MYC Proto-oncogene

- Located on chromosome 8q24.
- Regulates cell cycle progression, apoptosis, and metabolism.
- When dysregulated (as in BL), promotes oncogenesis by driving rapid cell division and inhibiting differentiation.

Epidemiology

- Burkitt lymphoma accounts for **30–50% of pediatric NHLs**.
- More common in **males (M:F = 3:1)**.
- Three clinical variants:
    1. **Endemic (African)** – most common in equatorial Africa; strongly associated with **EBV**.
    2. **Sporadic (non-endemic)** – seen worldwide, especially in the U.S. and Europe.
    3. **Immunodeficiency-associated** – occurs in individuals with **HIV/AIDS**, post-transplantation, or congenital immunodeficiencies.

Pathophysiology

- BL is a **monoclonal B-cell tumor** arising from germinal center B lymphocytes.
- Characterized by:
    - High mitotic index.
    - **“Starry-sky” appearance** on histology: tangible body macrophages with apoptotic debris scattered among uniform tumor cells.
- Common genetic abnormalities:
    - **t(8;14)** – C-MYC and IgH (heavy chain).
    - **t(8;22)** – C-MYC and Ig? (light chain).
    - **t(8;2)** – C-MYC and Ig? (light chain).
- **Epstein-Barr Virus (EBV)** is implicated in >95% of endemic cases and ~20–30% of sporadic cases.
    - In endemic regions, co-infections (e.g., **malaria**) impair immune control over EBV.

Clinical Manifestations

Presentation varies by subtype:

Endemic Form

- Jaw or facial bone tumors (mandible or maxilla).
- Tooth loosening or facial asymmetry.

Sporadic Form

- Abdominal masses (commonly **ileocecal region**).
- Symptoms of **bowel obstruction** or **intussusception**.
- Hepatosplenomegaly, ascites.

Immunodeficiency-associated Form

- Generalized lymphadenopathy.
- CNS and bone marrow involvement more frequent.

Other Signs and Symptoms

- **B-symptoms**: fever, night sweats, weight loss.
- Painless lymphadenopathy.
- CNS symptoms: headaches, seizures, altered mental status.
- Bone marrow failure: anemia, thrombocytopenia, leukopenia.
- **Tumor lysis syndrome (TLS)**: electrolyte abnormalities, acute kidney injury.

Staging

Ann Arbor Staging (Adults)

- **Stage I**: Single lymph node region or a single extralymphatic organ.
- **Stage II**: ?2 lymph node regions on the same side of the diaphragm ± nearby extralymphatic involvement.
- **Stage III**: Lymph node regions on both sides of the diaphragm ± spleen or extralymphatic organ.
- **Stage IV**: Diffuse involvement of ?1 extralymphatic organs ± lymph nodes.

Suffixes:

- A: No systemic symptoms.
- B: Presence of B-symptoms.
- E: Extranodal involvement.
- H: Hepatic involvement.
- D: Cutaneous involvement.

St. Jude/Murphy Staging (Pediatric)

- **Stage I**: Single tumor or lymph node group outside the abdomen or mediastinum.
- **Stage II**: Multiple tumors or nodes on one side of the diaphragm.
- **Stage III**: Involvement on both sides of the diaphragm or large abdominal/chest tumors.

- **Stage IV**: CNS and/or bone marrow involvement.

Diagnostic Workup

Laboratory Investigations

- Complete blood count (CBC) with differential.
- Serum **LDH** – marker of tumor burden.
- Uric acid, creatinine, BUN – assess for tumor lysis syndrome.
- Liver function tests (LFTs).
- HIV serology.
- CSF analysis (cytology, flow cytometry).
- **Bone marrow biopsy**.

Imaging Studies

- Chest X-ray and CT.
- Abdominal ultrasound or CT scan.
- MRI or CT of the brain/spinal cord if CNS symptoms are present.
- **PET-CT scan** for staging and treatment monitoring.

Tissue Diagnosis

- **Excisional lymph node biopsy** is gold standard.
- Fine needle aspiration (FNA) may be adjunctive.
- Immunophenotyping: CD20+, CD10+, BCL6+, Ki-67 >95%.
- Cytogenetics/FISH: confirms MYC translocation.

Treatment

Supportive Management

- **Tumor Lysis Syndrome Prophylaxis**:
  - IV hydration, **allopurinol** or **rasburicase**.
  - Monitor electrolytes, renal function.
- Transfusions for anemia or thrombocytopenia.
- Antibiotics for infection.
- Antipyretics, antiemetics during chemotherapy.

Definitive Treatment

- **High-intensity, short-duration chemotherapy regimens** (CODOX-M/IVAC, HyperCVAD).
- Agents include:
  - Cyclophosphamide, Vincristine, Doxorubicin, Methotrexate.
  - Cytarabine, Ifosfamide, Etoposide.
  - Rituximab (anti-CD20 monoclonal antibody).
- CNS prophylaxis with intrathecal methotrexate and/or cytarabine is essential.

Note: Surgery is typically not indicated except for diagnostic biopsy or management of complications like obstruction.

Prognosis

- **High cure rate (>85%)** in children with early-stage disease.
- Prognosis depends on:
    - Disease stage.
    - Age and performance status.
    - CNS or bone marrow involvement.
    - LDH level at diagnosis.

Key Points for NCLEX & USMLE

- Burkitt lymphoma = **fast-growing B-cell lymphoma with MYC translocation**.
- Classic histologic finding = **“starry sky”** appearance.
- Endemic variant = **jaw mass, EBV-associated**.
- Sporadic variant = **abdominal mass**, often ileocecal.
- Evaluate and prevent **tumor lysis syndrome**.
- CNS prophylaxis is **critical** due to high risk of CNS dissemination.
- Treatment = **aggressive combination chemotherapy + Rituximab**.