Problem 10 – Unit 6 – Pathology: Non-Hodgkin lymphoma



- Note: classification of non-Hodgkin lymphoma:
 - B & T cell tumors are often composed of cells that are arrested at or derived from a specific stage of their normal differentiation.
 - The diagnosis and classification of these tumors rely on tests (IHC and/or flow cytometry) which detect lineage-specific antigens and markers of maturity.

SMALL LYMPHOCYTIC LYMPHOMA (SLL):

- It similar to Chronic Lymphocytic Leukemia (CLL) but here the lymph nodes are involved (instead of the bone marrow and blood in CLL).
- Both SLL and CLL occur in middle-aged and elderly (although SLL is more common in elderly).
- Both SLL and CLL are indolent (بطيء) slowly growing tumors.
- **Histology of SLL**: sheets of small lymphocytes (soccer-ball chromatin: figure) and scattered ill-defined foci of larger actively dividing cells (proliferation centers).
- Markers: CD5+ , CD20+ and CD23+
- SLL can transform to more aggressive tumors (ex: pro-lymphocytic leukemia or diffuse large B-cell lymphoma).

- FOLLICULAR LYMPHOMA:

- Most common form of non-Hodgkin lymphoma in US (45% of cases) but has a lower incidence among Asians.
- The median age is 55 years.
- Follicular lymphoma originated from germinal centers of B-cells.
- In more than 85% of patients with follicular lymphoma, there will be t(14;18) → resulting in over-expression of BCL-2 an anti-apoptotic (normally when a lymph node is stained for the presence of BCL-2 the result is negative) → BCL-2 will bind to IgH leading to the formation of (IgH-BCL-2) → therefore the cells will not die and continue proliferation.
- Histology: nodular proliferation with a mixture of small lymphocytes (centrocytes) + larger cells with vesicular (حُوَيْصَلِي) chromatin and several nucleoli (centroblasts: follicular lymphoma is graded from 1 to 3 depending on the number of these cells). Tangible-body macrophages are not found.
- Markers: CD10+ , CD20+, BCL-2+ and BCL-6+
- The bone marrow is almost always involved in follicular lymphoma.
- This lymphoma is not curable and the natural history is prolonged. 40% of cases will progress to diffuse large B-cell lymphoma (which is more aggressive) and only then we consider to treat the patient









with chemotherapy.

BURKITT LYMPHOMA:

- It is a high grade malignant lymphoma originating from the germinal centers of the B-cells.
- There are 3 clinical settings:
 - ✓ <u>Endemic</u>: occurring in Africa → African children will present with jaw and orbital lesions (figure).
 - ✓ <u>Sporadic</u>: throughout the world with more tendency to involve the abdominal cavity.
 - ✓ *Immunodeficiency-associated*: mostly with HIV.
- Causes include:
 - ✓ Translocation involving the MYC gene (present on chromosome 8) with: IgH, κ (light chain) or λ (light chain) loci.
 - ✓ Dysregulation and overexpression of MYC protein.
 - ✓ EBV (in most endemic cases).
- **Histology**: the tumor cells are intermediate in size and their cytoplasm contains small lipid-filled vacuoles. There are numerous tangible-body macrophages giving what is known as starry-sky pattern.
- Markers: CD10+ , CD20+ and BCL-6 +

DIFFUSE LARGE B-CELL LYMPHOMA:

- It is the most common type of lymphoma in adults (50% of non-Hodgkin lymphoma).
- It has an aggressive natural history and several subtypes.
- Causes include:
 - ✓ > $\frac{1}{3}$ of cases → BCL-6 rearrangement or point mutation (leading to increased levels of BCL-6 protein).
 - ✓ 30% of cases → t(14;18) leading to overexpression of BCL-2 protein.
 - ✓ Some cases → MYC translocation.
- Histology: variable from case to case.
- Markers: CD20+ (other antigens such as CD10, BCL-2...etc are variably expressed).
- Lymph node processing to diagnose lymphoma:







