Lymphoma

Lymphomas are a group of diseases caused by malignant lymphocytes (T, B, or NK) that accumulate in lymph nodes and cause the characteristic clinical features of lymphadenopathy

- Although having different characteristics from their normal counterparts, the neoplastic cells of many lymphomas have the features of lymphoid cells at a particular stage of differentiation.

- Lymphomas arise as a result of a series of mutations in a single lymphoid cell.

The major subdivisions of lymphomas are:

- **Hodgkin's lymphoma (HL)** and
- **non-Hodgkin's lymphoma (NHL)**

This is based on the histological presence of ***Reed-Sternberg (RS) cells in Hodgkin's lymphoma***

The biologic behavior and treatment of Hodgkin lymphoma differ from those of most NHLs, thus making the distinction between the two is of practical importance.

- B- and T-cell tumors are composed of cells derived from specific stage of normal lymphocyte differentiation.
- All lymphomas are derived from a single transformed cell and thus are by definition monoclonal.

➢ ***Hodgkin's lymphoma***

Hodgkin lymphoma (HL) include distinctive group of neoplasms that arise almost invariably in a single lymph node or chain of lymph nodes and spread characteristically in a stepwise fashion to the anatomically contiguous nodes.

■ HL accounts for 30% of all lymphomas

■ Molecular studies have shown that it is a tumor ***of B-cell origin***

■ It is characterized morphologically by the presence of distinctive neoplastic giant cells called **Reed-Sternberg (RS) cells**, and large mononuclear cells called Hodgkin's cells in a reactive background composed of lymphocytes, histiocytes (macrophages), and granulocytes.

■ The neoplastic Reed-Sternberg cells typically make up a minor fraction (1 - 5%) of the total tumor cell mass, making HL more difficult to study than typical NHLs.

■ The neoplastic RS-cells are derived from **germinal center or post-germinal center B cells** in the vast majority of cases,

■ The EBV genome is present in the RS cells in up to 70% of cases of the mixed-cellularity type and a smaller fraction of the nodular sclerosis type. Thus, EBV infection is likely to be a contributing step to the development of Hodgkin lymphoma, particularly the mixed-cellularity type.

■ The disease can present at any age but is rare in children and has a peak incidence in young adults. There is an almost 2 : 1 male predominance

■The usual clinical presentation is with painless asymmetrical lymphadenopathy–most commonly in the neck. Typically the disease is localized initially to **a single** peripheral lymph node region and its subsequent **progression is by contiguity** within the lymphatic system.

■ Constitutional symptoms of fever, weight loss & sweating are prominent in patients with widespread disease. Alcohol-induced pain in the areas where disease is present occurs in some patients.

Diagnosis and histological classification:

❖ The diagnosis is made by histological examination of an excised lymph node.

❖ **The histologic diagnosis of Hodgkin lymphoma rests on the definitive identification of Reed-Sterberg cells or their variants in the appropriate background of reactive cells.**

Morphology of Reed –Sternberg cells:

The **Reed-Sternberg (RS) cell** is a large cell with an enlarged multilobated nucleus, prominent nucleoli, and abundant, usually slightly eosinophilic, cytoplasm. **Particularly characteristic are cells with two mirror-image nuclei or nuclear lobes, each containing a large (inclusion-like) acidophilic nucleolus surrounded by a distinctive clear zone; together they give an owl-eye appearance. The nuclear membrane is distinct.**

Such "classic" RS cells are common in the mixed-cellularity subtype, uncommon in the nodular sclerosis subtype, and rare in the lymphocyte-predominance subtype.

❖ Blood tests may show anaemia, neutrophilia, eosinophilia & raised erythrocyte sedimentation rate (ESR) or lactate dehydrogenase (LDH).

Classification:

Five subtypes of Hodgkin lymphoma are recognized:

(1) Nodular sclerosis.

(2) Mixed cellularity.

(3) Lymphocyte predominance.

(4) Lymphocyte rich.

(5) Lymphocyte depletion.

} **Uncommon**

WHO classification of Hodgkin lymphoma.

- ***Nodular lymphocyte - predominant Hodgkin lymphoma***

-***Classical Hodgkin lymphoma***

are subclassified into 4 pathologic subtypes based upon Reed-Sternberg cell morphology and the composition of the reactive cell infiltrate seen in the lymph node biopsy specimen.

Nodular sclerosis classical Hodgkin lymphoma

Mixed- cellularity classical Hodgkin lymphoma

Lymphocyte- rich classical Hodgkin lymphoma (rare)

Lymphocyte- depleted classical Hodgkin lymphoma (rare)

- **Nodular Sclerosis Hodgkin Lymphoma:**

- The most common form**.**

- It is equally frequent in men and women**.**

- Most of the patients are adolescents or young adults**.**

- has a striking tendency to involve the lower cervical, supraclavicular, and mediastinal lymph nodes**.**

- The overall prognosis is excellent**.**

Morphology:

A variant of the RS cell, the **lacunar cell**. This cell is large and has a single multilobate nucleus with multiple small nucleoli and an abundant, pale-staining cytoplasm.

-In formalin-fixed tissue, the cytoplasm often retracts, giving rise to the appearance of cells lying in empty spaces, or lacunae**.**

There are varying proportions of lymphocytes, eosinophils, histiocytes.

- Classic RS cells are infrequent**.**

-There are collagen bands that divide the lymphoid tissue into circumscribed nodules.

- **Mixed-Cellularity Hodgkin Lymphoma:**

- Patients older than the age of 50 year.

-Male predominance.

- **Classic RS cells are plentiful** within a distinctive mixed cellular infiltrate of small lymphocytes, eosinophils, plasma cells, and benign histiocytes.

- Compared with the other subtypes, more patients with mixed cellularity have disseminated disease and systemic manifestations**.**

- **Lymphocyte-depleted HL**

- (< 1% of cases)

- Characterized by the presence of large numbers of RS cells that are often bizarre morphologically.

- It is associated with older age and HIV positive status.

- Patients usually present with advanced-stage disease.

- **Lymphocyte-rich HL**

- (5%) of cases.

- RS cells of the classic or lacunar type are observed, with a background infiltrate of lymphocytes.

- Clinically, the presentation and survival patterns are similar to mixed cellularity HL.

- **Nodular Lymphocyte-Predominance Hodgkin Lymphoma:**

- This subgroup, comprising about 5% of Hodgkin lymphoma.

- Affected LN in a nodular appearance.

-It is characterized by a large number of small resting lymphocytes admixed with a variable number of benign histiocytes**.**

-Eosinophils, neutrophils, and plasma cells, are scanty or absent, and classic RS cells are extremely difficult to find.

- Lymphohistiocytic (L&H) variant RS cells that have a delicate multilobed, puffy nucleus that has been likened in appearance to popcorn (**"popcorn cell"**), in a lympho-histiocytic background.

- Unlike classic RS cells, L&H cells are positive for B-cell antigens (CD19 & 20), and are negative for CD15 & 30).

- It presents mostly as isolated cervical or axillary lymphadenopathy and have excellent prognosis.

■ **In all subtypes, involvement of the spleen, liver, bone marrow, and other organs may appear in the course of the disease.**