HODGKIN LYMPHOMA

Classical Hodgkin lymphoma (CHL)

- Large atypical mononuclear or multinucleated cells (minority) surrounded by variable mixture of non-neoplastic inflammatory cells (majority)
- Accounts for 90% of all Hodgkin lymphoma
- Bimodal age distribution: Peaks at 20-30 years old and 40-50 years old
- Clinical presentation: B symptoms including fever, night sweat, weight loss
- Localized lymphadenopathy spreads in continuous fashion, most commonly neck, mediastinum, abdominal

**Morphology:** Hodgkin and Reed-Sternberg cells (HRS cells): Substantially larger than other cells, one or multiple large nuclear lobes, each with a prominent eosinophilic nucleolus often surrounded by a halo, abundant basophilic cytoplasm

**Background:** Mixed inflammatory background with variable numbers of eosinophils, small lymphocytes, neutrophils, plasma cells, histiocytes

**Phenotype:** HRS cells: CD30+, CD15+ (~75%, variable number and intensity), CD45-, CD20- (rarely dim positive), Pax-5+ (dimmer than B-lymphocytes), BOB1 dim+ or neg, OCT2 dim+ or neg, CD3-, EBV+ (~40% cases)

**Background lymphocytes:** Mostly T cells

**Genetics:** Unknown

**Prognosis:** Curable >85% with combination therapy. New therapy includes check point inhibitors, anti-CD30 therapy

**Morphologic subtypes:**

- **Nodular sclerosis:** Most common subtype (70%). Mediastinum involvement. Male: female 1:1. Large fibrotic bands surround neoplastic nodules. Often with Lacunar cells (retraction artifact) and mummified cells (dying cells). 10-25% associated with EBV

- **Synctial variant:** HRS cells form sheets

- **Mixed cellularity:** Second most common subtype (25%). Frequently associated with EBV (75%). Peripheral lymphadenopathy most common. Diffuse pattern, no fibrosis

- **Lymphocyte rich:** Uncommon subtype (5%). Nodular or vaguely nodular pattern without fibrotic bands. Background has more B lymphocytes (in contrast to other subtypes). No eosinophils or neutrophils. Clinical behavior more indolent than other subtypes (similar to nodular lymphocyte predominant HL)

- **Lymphocyte depleted:** Uncommon subtype (2%). Frequently associated with HIV. 75% EBV positive. Rich in HRS cells, depleted background lymphocytes. Often with diffuse background fibrosis. Worse prognosis than other subtypes

**Subtypes of classical Hodgkin lymphoma**

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**Nodular Lymphocyte Predominant Hodgkin lymphoma (NLPHL)**

- B-cell neoplasm with typical nodular pattern containing scattered large neoplastic cells and numerous reactive lymphocytes in the background
- Accounts for 10% of all Hodgkin lymphoma
- Male > female, affects mostly 30-50 years old adults
- Peripheral lymphadenopathy, localized disease (stage I or II) most common

**Morphology:** Nodular or nodular and diffuse pattern. No fibrosis

**Neoplastic cells (LP cells or popcorn cells):** Substantially larger than other cells, highly folded or lobated nucleus, one to several small nucleoli, abundant pale cytoplasm

**Background:** Small B-lymphocytes predominant. Eosinophils and neutrophils absent

**Phenotype:**
- **LP cells:** CD20+ (strong), Pax-5+ (strong), CD45+, CD30 negative or variably dim+, CD15-, EBV-
- **Background lymphocytes:** Mixed B and T lymphocytes, often more B cells. Increased CD57+ lymphocytes. PD-1+ T cells form rosette around popcorn cells

**Genetics:** Unknown

**Prognosis:** Good. Behaves like low grade non-Hodgkin lymphoma, slow growing but with frequently relapse. 10 year survival >80% for low stage disease

**Differential diagnosis:**
- **Progressive transformation of germinal centers (PTGC):** Similar types of nodules as NLPHL, but are usually in smaller number and mixed with other regular hyperplastic follicles. Typical popcorn cells are absent or rare
- **T-cell/histiocyte rich large B-cell lymphoma:** Similar type of cell composition but in diffuse pattern (not nodular). The phenotype of large cells are identical to NLPHL. Background T lymphocytes predominant