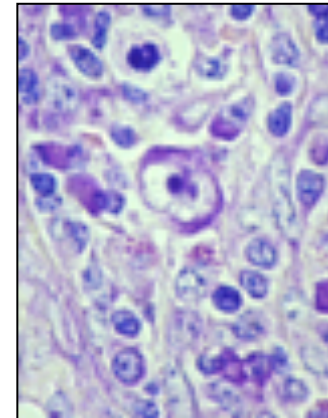
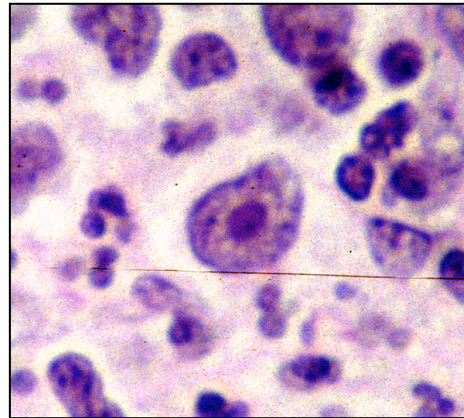


# HODGKIN LYMPHOMA



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# HODGKIN LYMPHOMA

**Thomas Hodgkin's first description in 1832 of  
"On some morbid appearances of the  
absorbent glands and spleen"**

**Hodgkin Lymphogranuloma**

**Initially interpreted a chronic inflammatory  
process**

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# HODGKIN LYMPHOMA

## Peculiar cell populations:

### *Neoplastic*

Hodgkin cells (mononucleated)  
Reed-Sternberg cells (bi-nucleated)

### *Reactive*

Lymphocytes  
Macrophages  
Eosinophils  
Plasma cells

# HODGKIN LYMPHOMA

**Both H and RS cells are germinal centre or post-germinal centre cells of B lineage, though they may may not express B-cell antigens (CD20, CD79a = classical) or CD30 (= activation antigen)**

## **Cytokines and chemokines (produced by H & RS cells):**

- **Attract reactive cells within the tumour**
- **Induce H & RS cells proliferation and survival**
- **Modulate the effects on endothelial cells, fibroblasts and macrophages**
- **Are responsible for the “pseuso-inflammatory” clinical presentation**

# HODGKIN LYMPHOMA

## Pathogenesis

***EBV infection*** (50% Classical HL, in H/RS cells)

|  
**LMP1 & LMP2** from infected cells

|  
**NFkB transcription factor activation**

|  
***NFkB intra-nuclear delocalization***

|  
***Target genes activation***

|  
***Apoptosis inhibition***

|  
***Prolonged cell survival & proliferation***

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# HODGKIN LYMPHOMA

**2 distinct clinico-pathological entities, based on presentation, prognosis and CD30 expression**

- **Lymphocyte predominant** HL (CD20/CD79a+, CD30-)
- **Classical** HL (CD20/CD79a-, CD30+)

# HODGKIN LYMPHOMA

## Clinico-pathological subtypes

**Lymphocyte predominance = 5- 20%**

- *Nodular*
- *Diffuse*

### **Classical**

- *Lymphocyte rich*            **10%**
- *Nodular sclerosis*        **54%**
- *Mixed cellularity*        **16%**
- *Lymphocyte depletion* **1%**

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# HODGKIN LYMPHOMA

## **H/RS cells of classical HL**

- **Do not show progressive DNA mutations**
- **Result from negative selection**
- **Do not undergo apoptosis = prolonged survival and replication**

## **L/H of NLP-HL**

**Do express progressive DNA mutations**  
**Result from positive selection by antigens**

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# HODGKIN LYMPHOMA

## CLASSICAL HL

Frequency: 15% of all lymphomas

Age: bimodal distribution

a) 15-35 ys.

b) >50 ys.

Sex: slight prevalence in M

Symptoms (inconstant):

Weight loss

Weakness

Fever

Night sweat

Prurigo

Hyper-eosinophilia

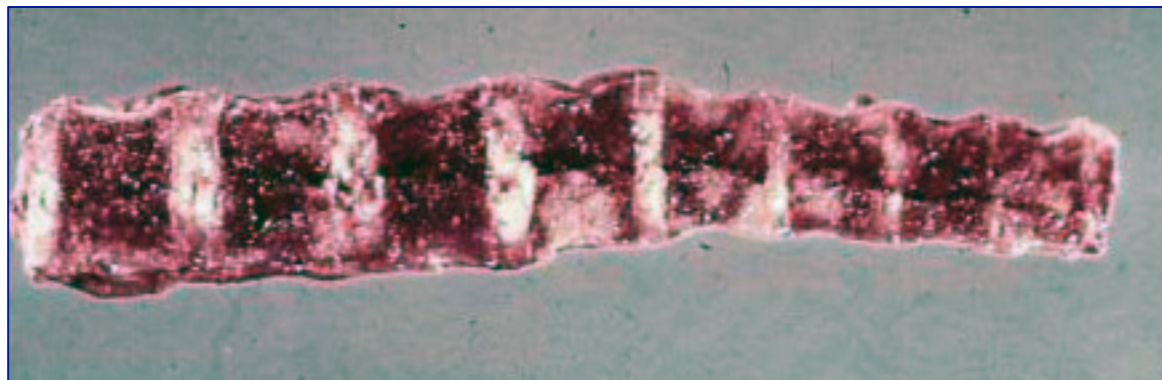
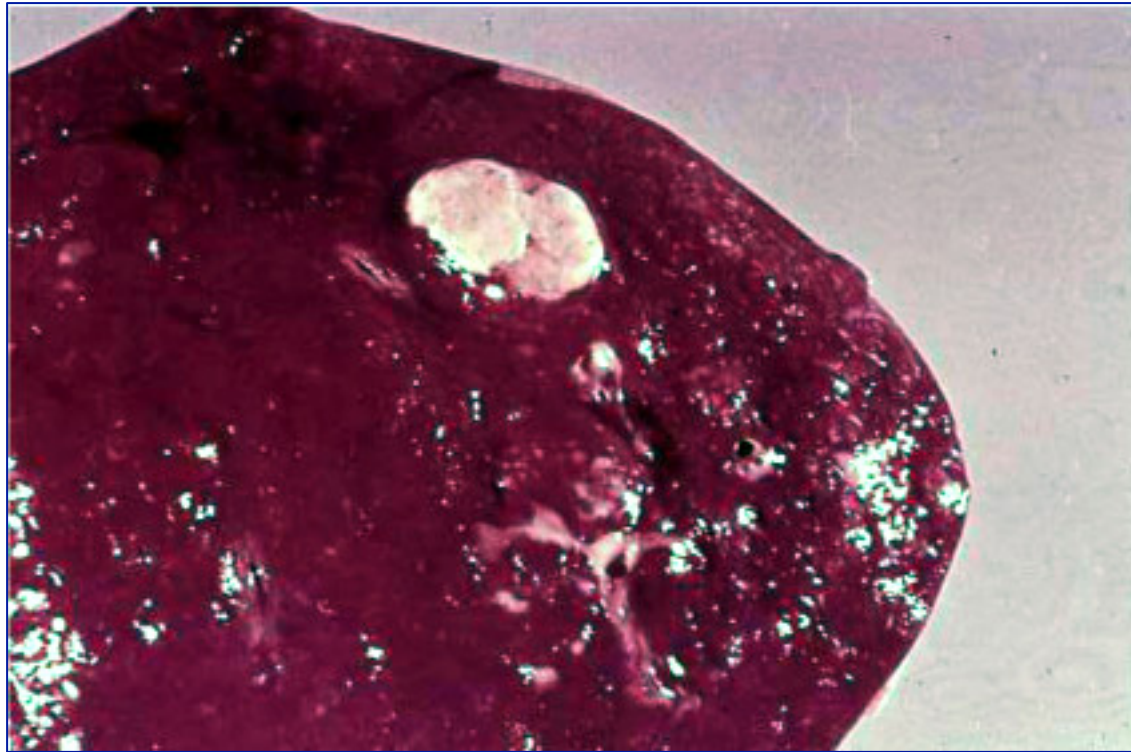
Lymphadenomegaly, hard consistency

} IF- $\gamma$ , IL-6

} IL-5

→ TGF- $\beta$

# HODGKIN LYMPHOMA



# HODGKIN LYMPHOMA

## **CLASSICAL HL**

**Lymphomegaly**

**1-2 lymph node basins**

**Usually superficial (latero-cervical, supraclavicular, mediastinal)**

**Progressive involvement of:**

**Adjacent basins**



**Deeper lymph nodes**



**Spleen, liver, bone marrow**

# CLASSICAL HODGKIN LYMPHOMA

## Morphology

Lymph node architectural effacement

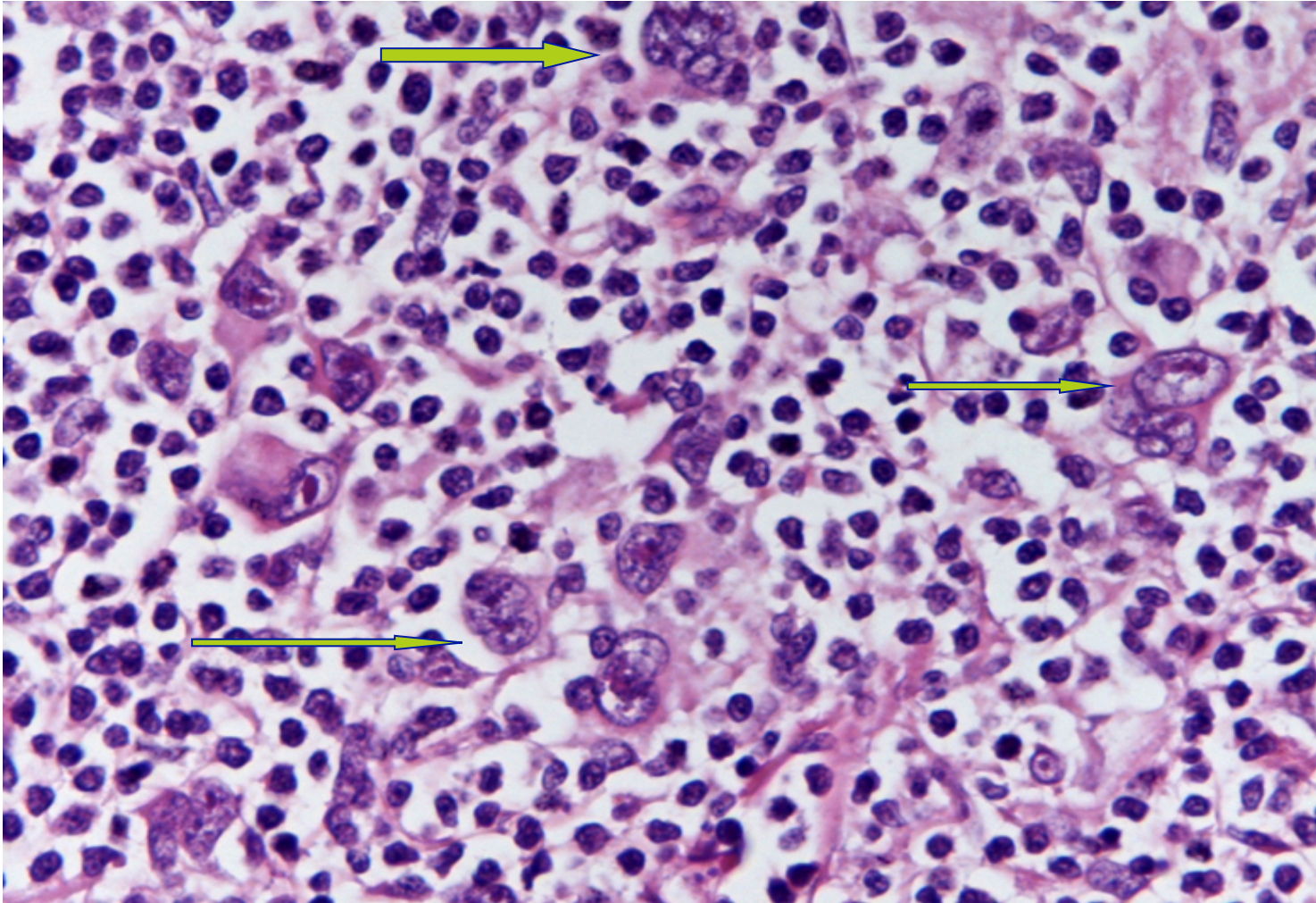
### Neoplastic cells:

- Large RS cells, bi/multinucleated + mononuclear H cells
- Clear nuclei
- Large basophilic nucleoli
- Wide and clear cytoplasm
- CD30 & CD15 +

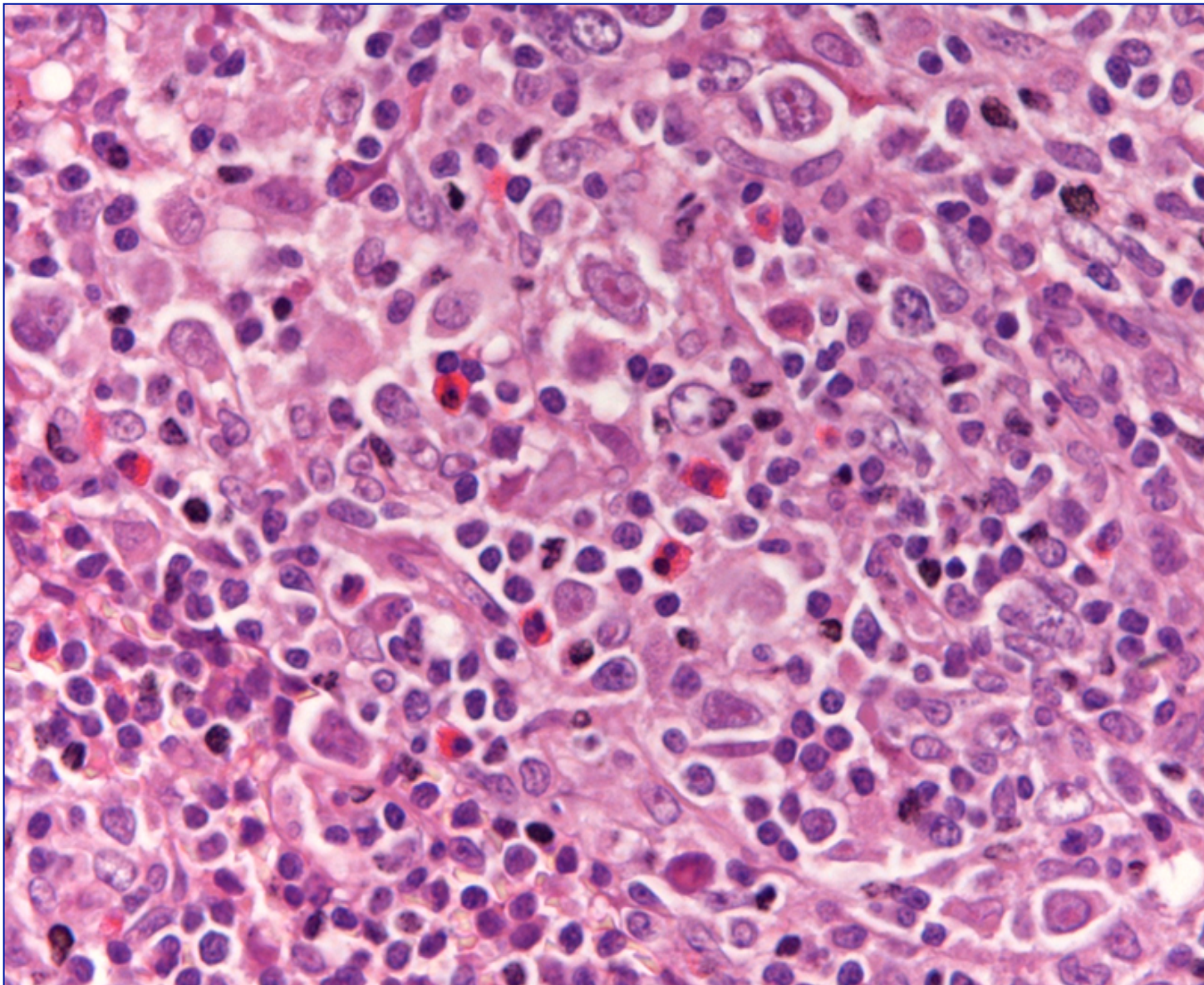
### Reactive cells

- Present in all subtypes, variable number

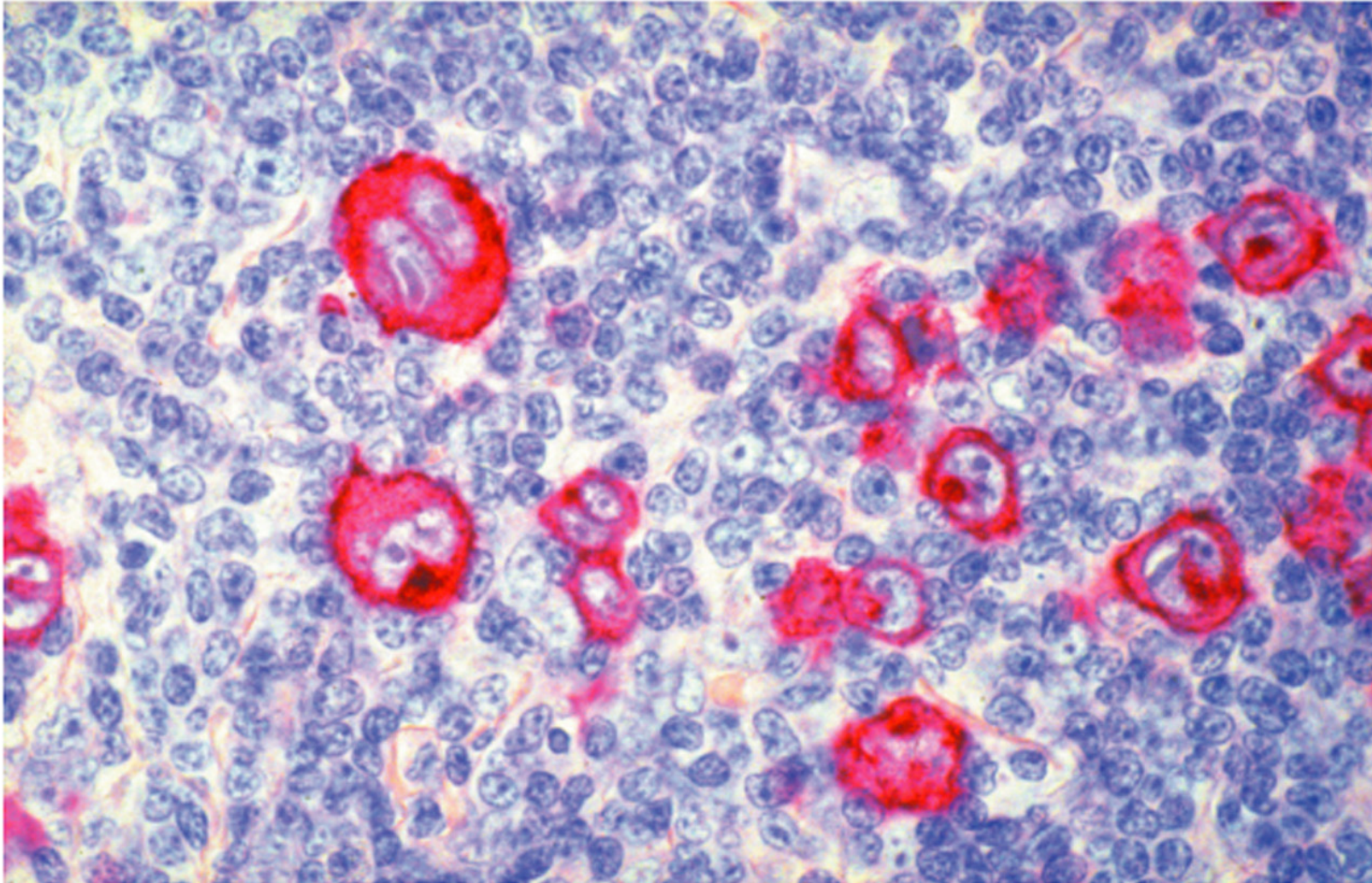
# HODGKIN LYMPHOMA



# HODGKIN LYMPHOMA



# HODGKIN LYMPHOMA – CD30



# CLASSICAL HODGKIN LYMPHOMA

## **Lymphocyte rich**

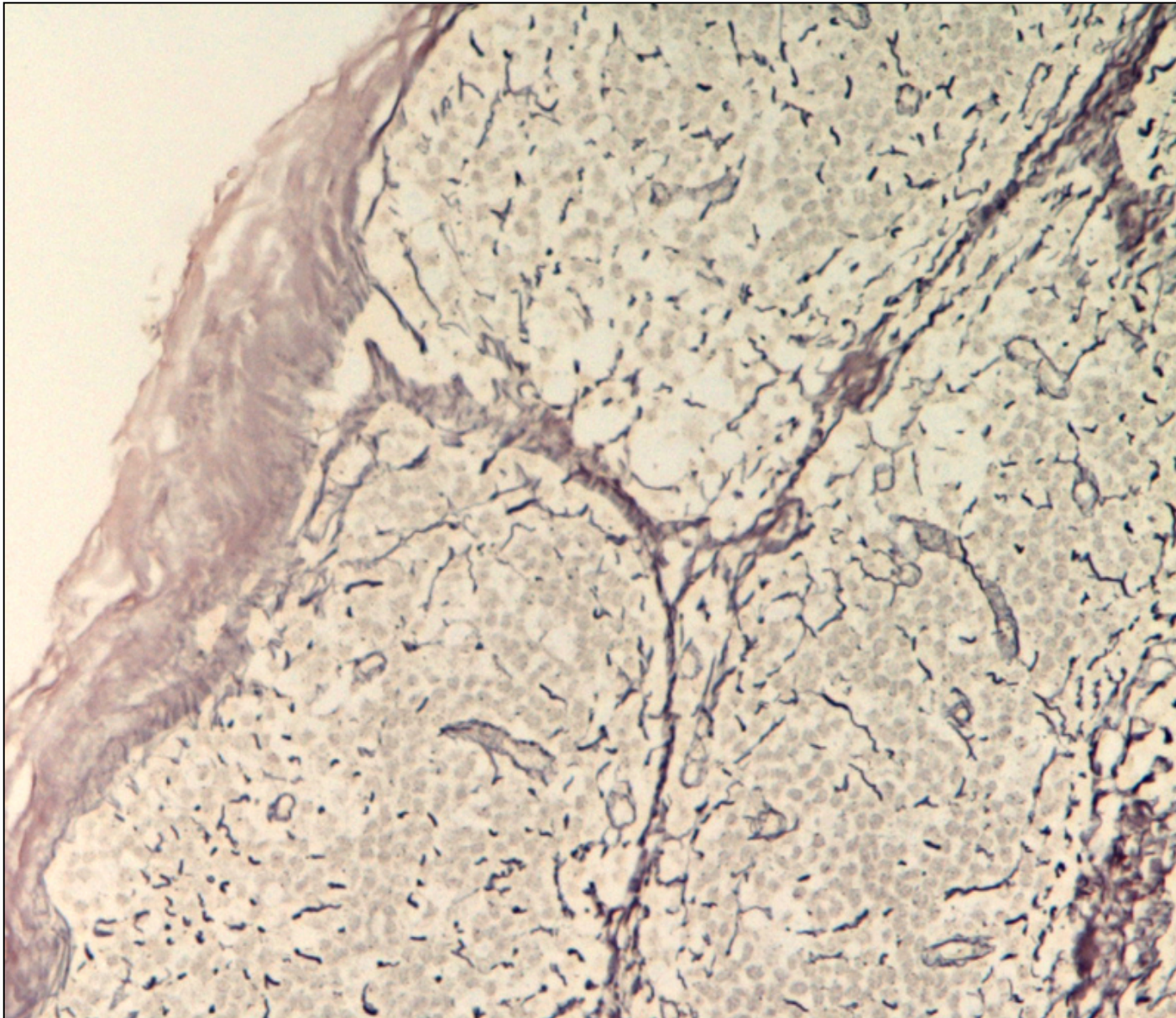
- **Abundant small T-cell population**
- **Scattered H & RS cells**
- **Indolent progression**

## **Nodular sclerosis**

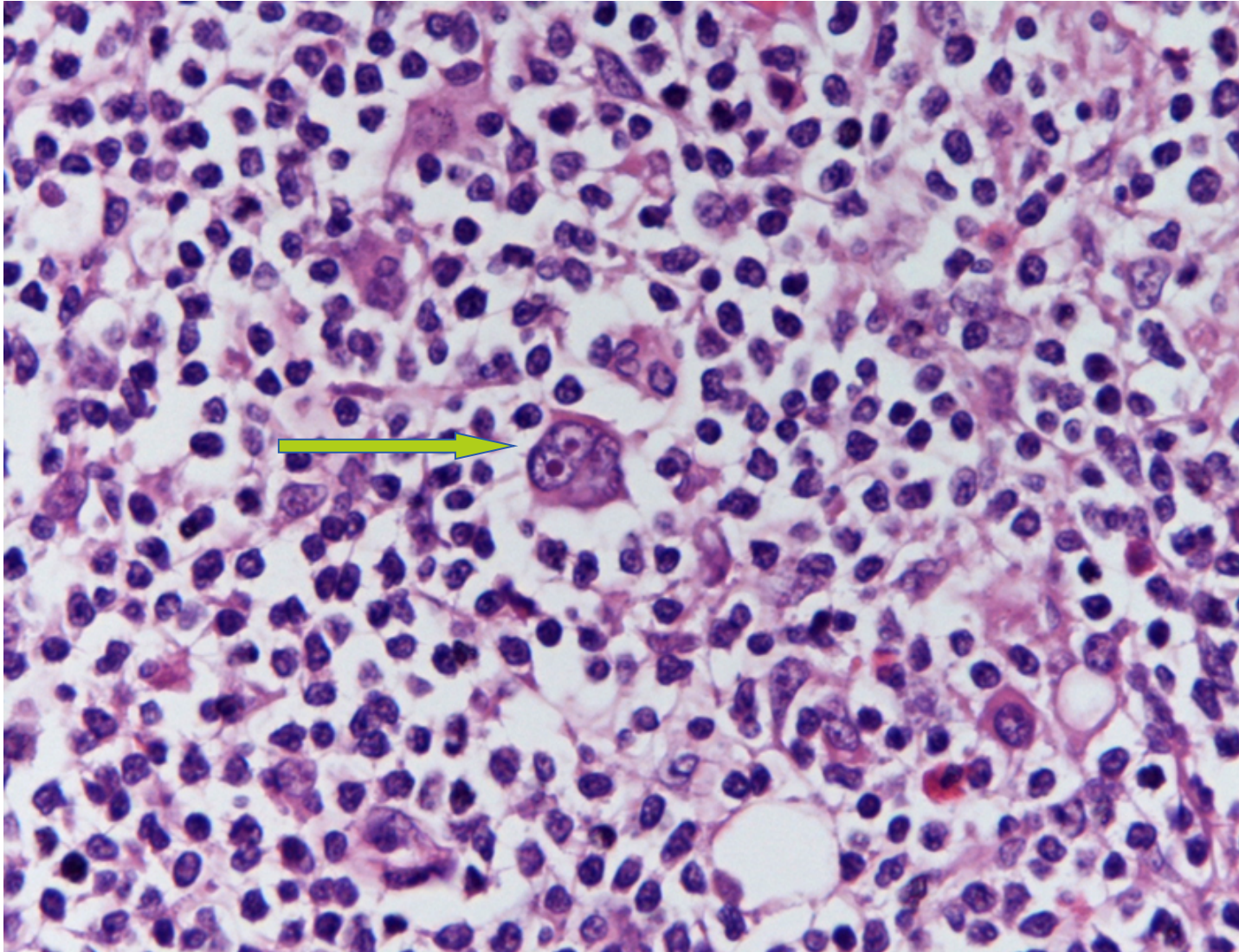
- **More frequent in young women**
- **Mediastinal involvement**
- **Nodular pattern due to active collagen deposition**
- **RS & H cells, wide clear cytoplasm (lacunar)**
- **Reactive cells (T-lymphocytes, eosinophils, plasma cells)**
- **Small necrotic foci**

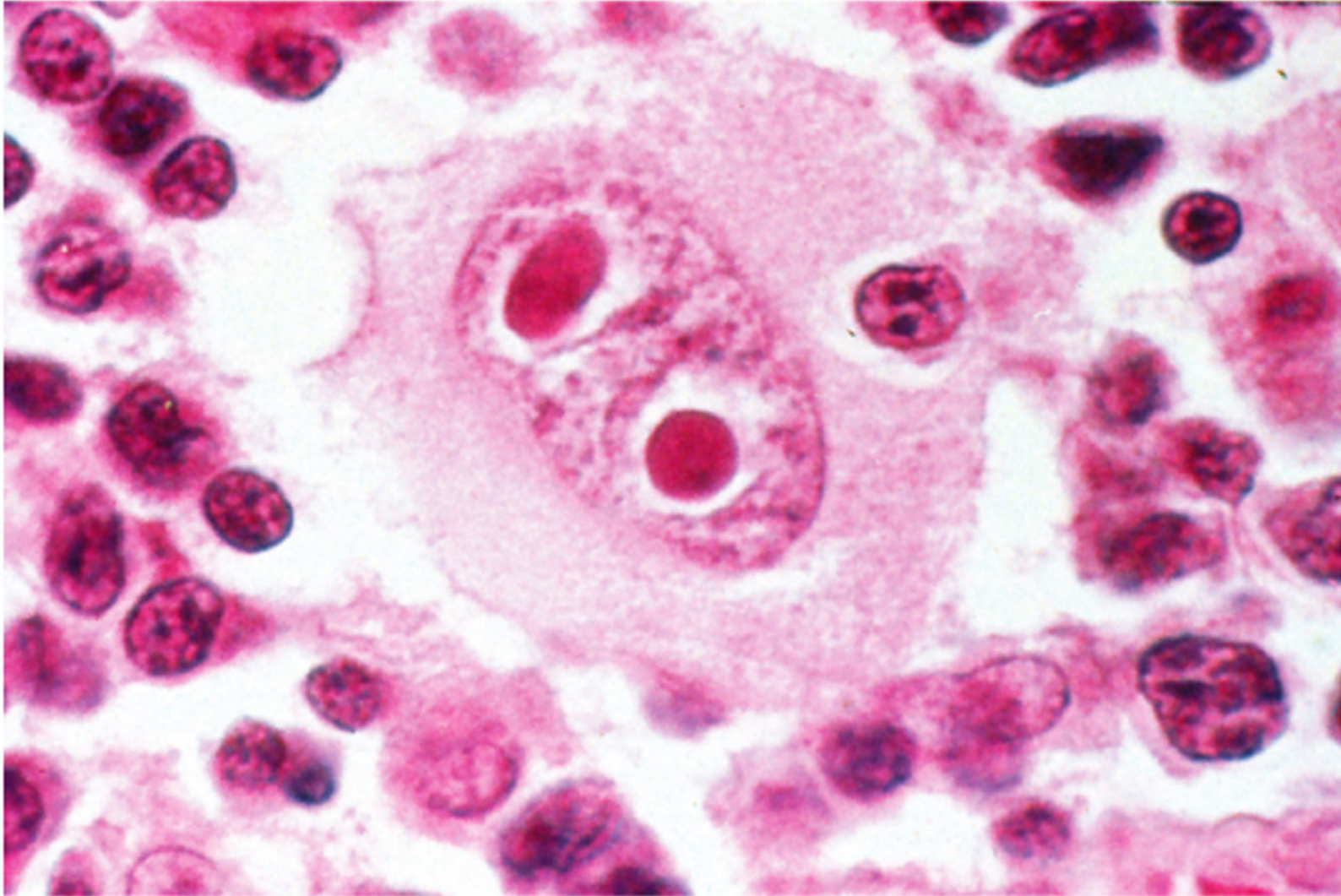


## CLASSICAL HL – Nodular sclerosis



## CLASSICAL HL – Nodular sclerosis





# CLASSICAL HODGKIN LYMPHOMA

## **Mixed cellularity**

M>F

B symptoms frequent

Abundant RS & H cells

Large necrotic foci

Reactive cells in granuloma-like clusters

## **Lymphocyte depletion**

1%, older patients

B symptoms frequent

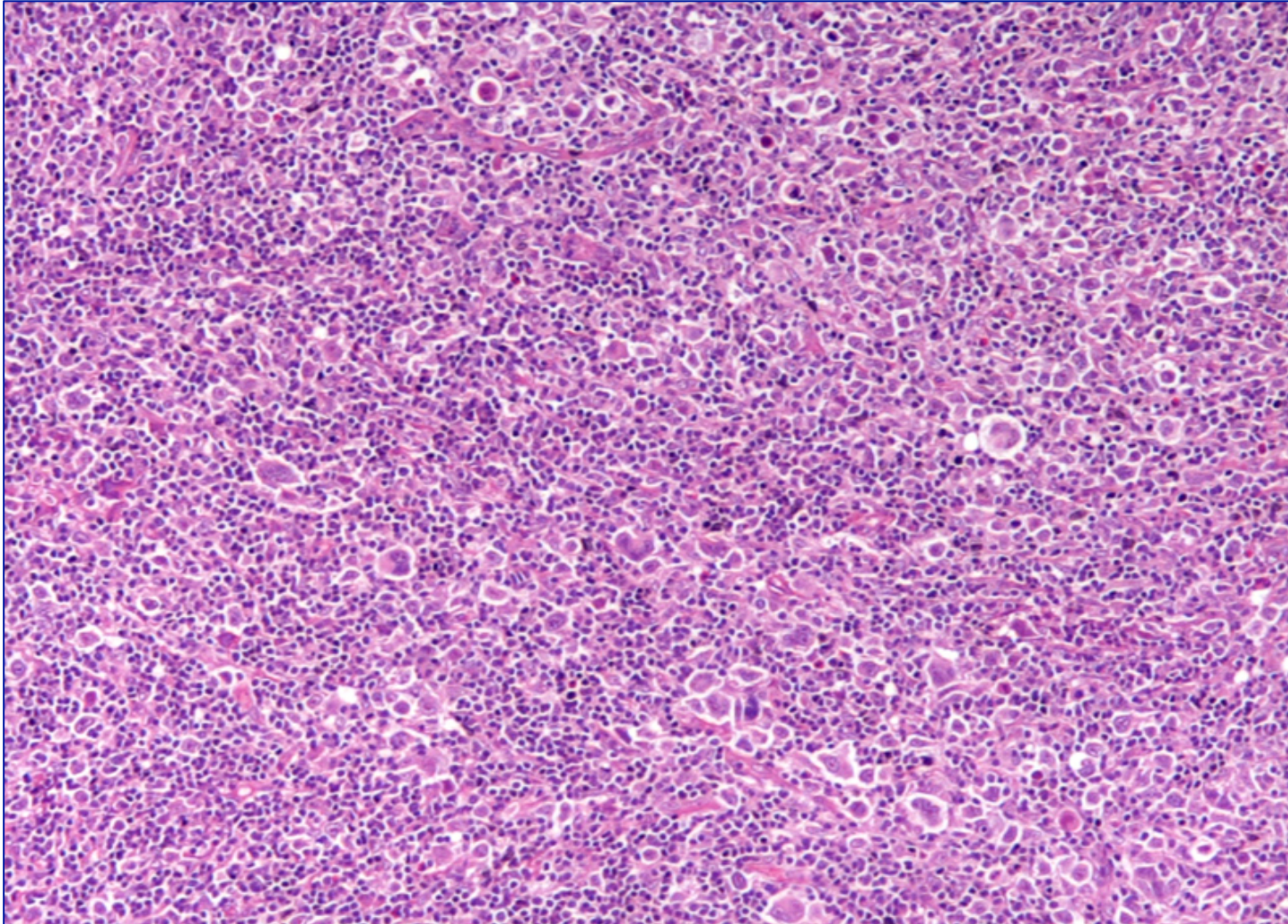
Stage III / IV at presentation

**Prevalent RS & H** cell population

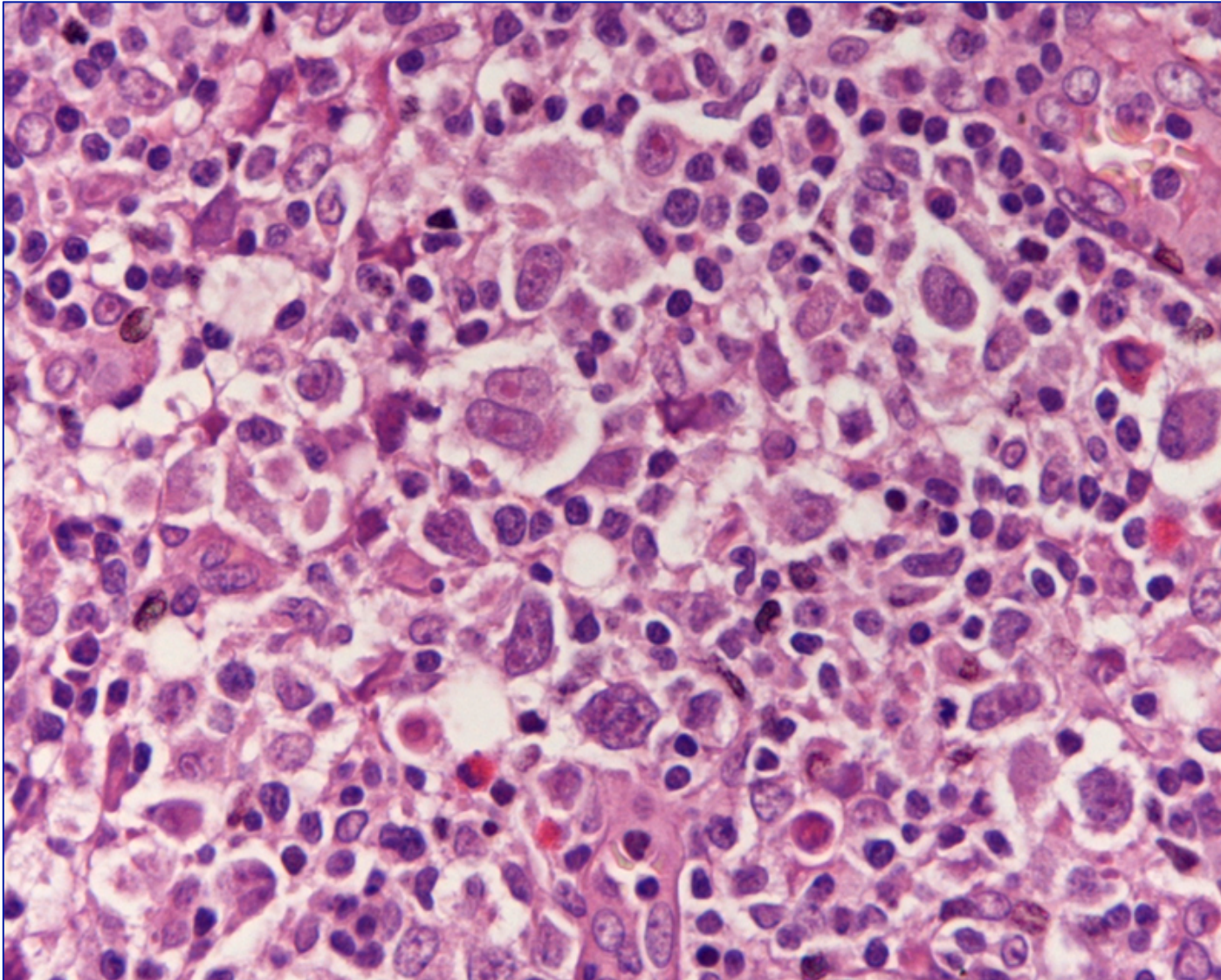
Rare reactive cells (lymphocytes)

Correlated with Diffuse Large B-Cell NHL

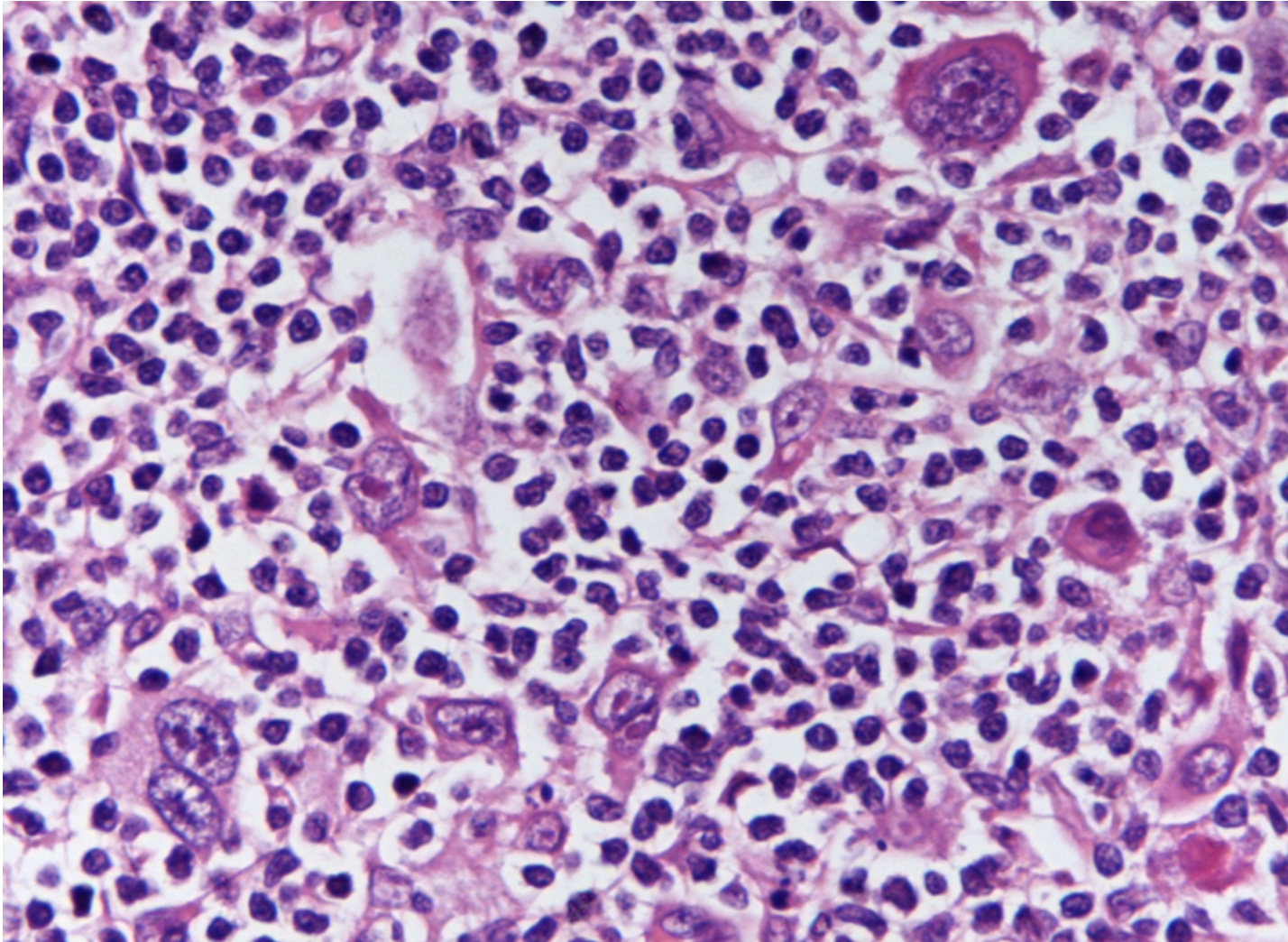
## CLASSICAL HL – Mixed cellularity



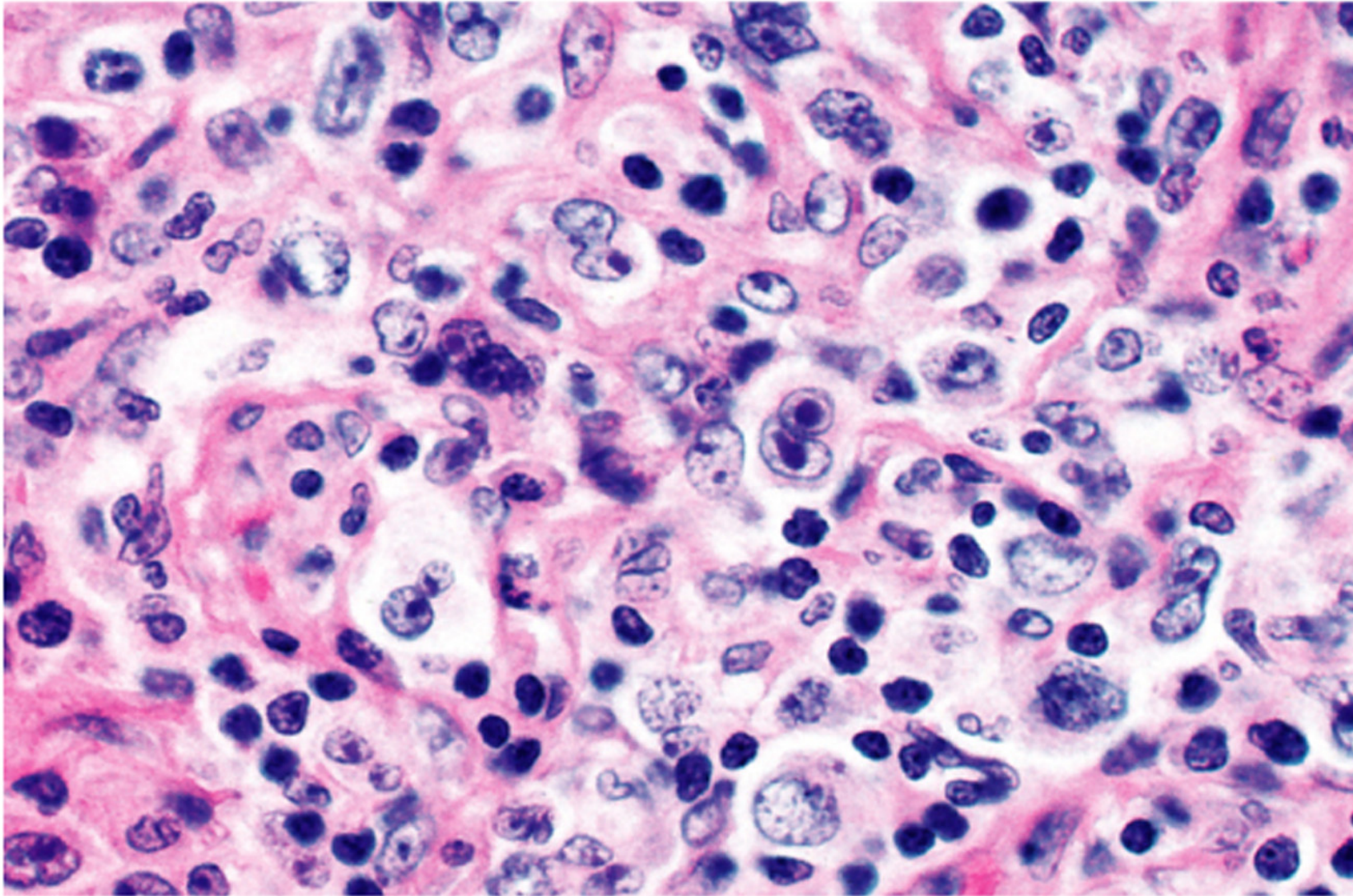
## CLASSICAL HL – Mixed cellularity



## CLASSICAL HL – Mixed cellularity

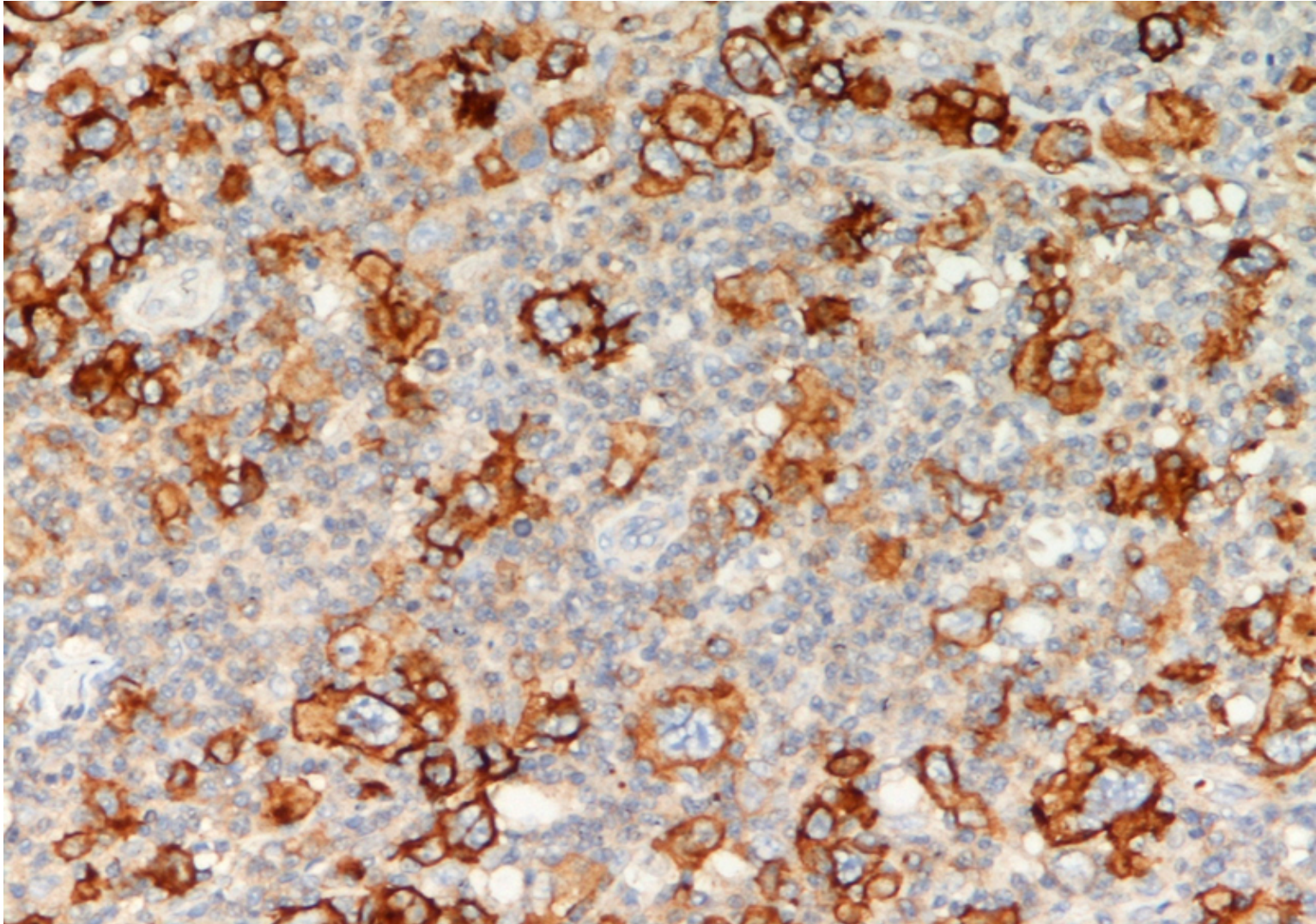


# CLASSICAL HL – Lymphocyte depletion

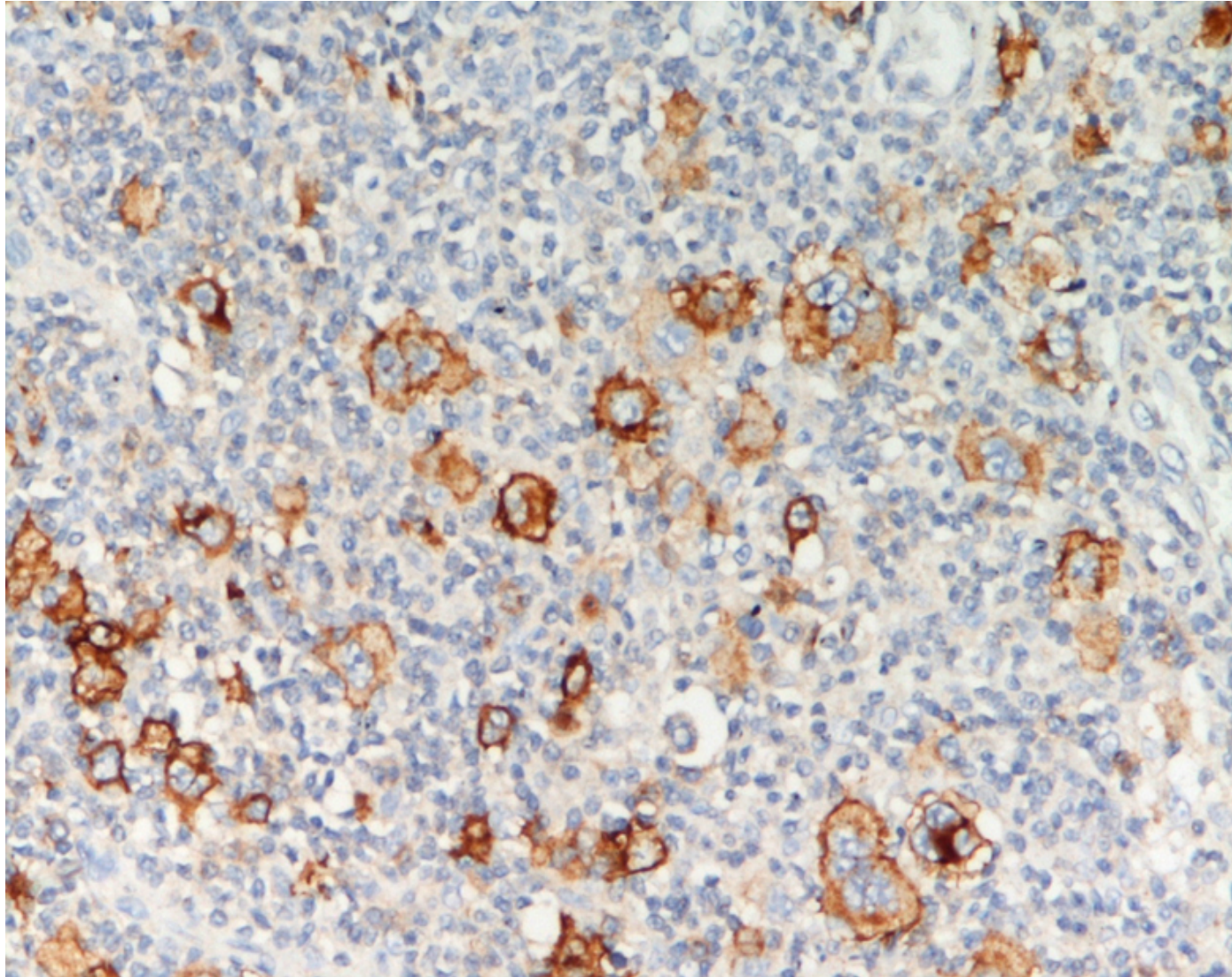




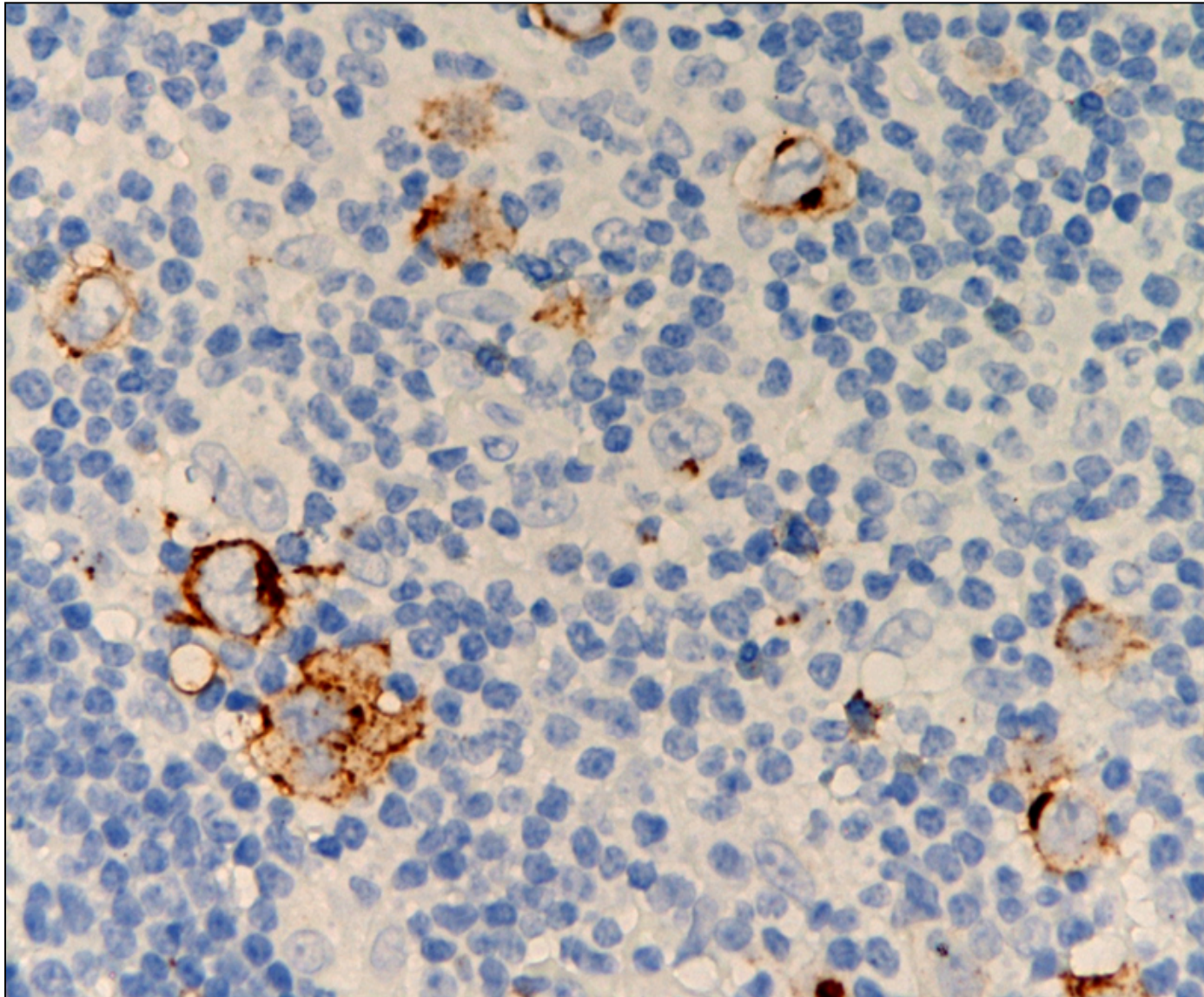
## CLASSICAL HL – CD30



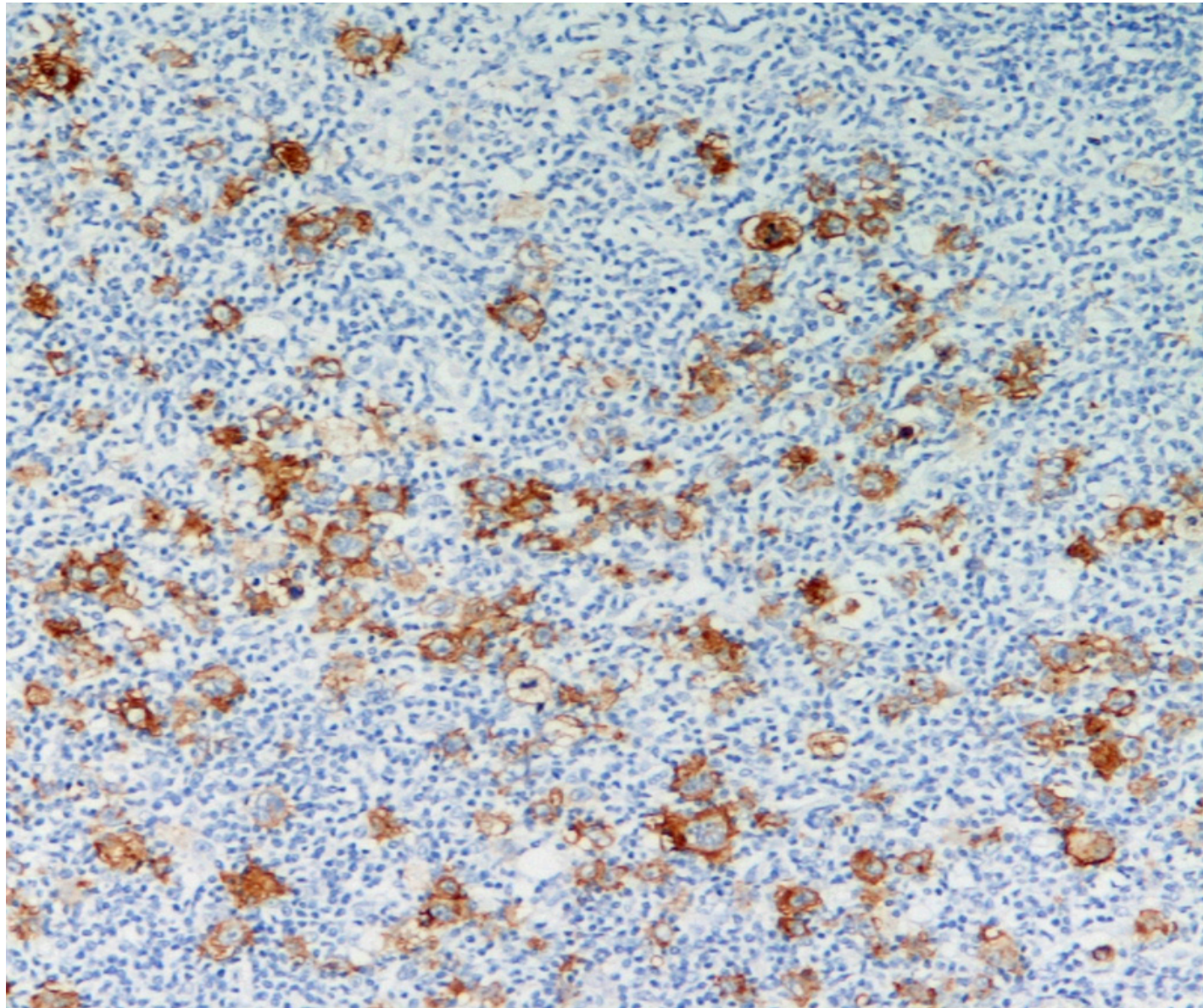
# CLASSICAL HL – CD30



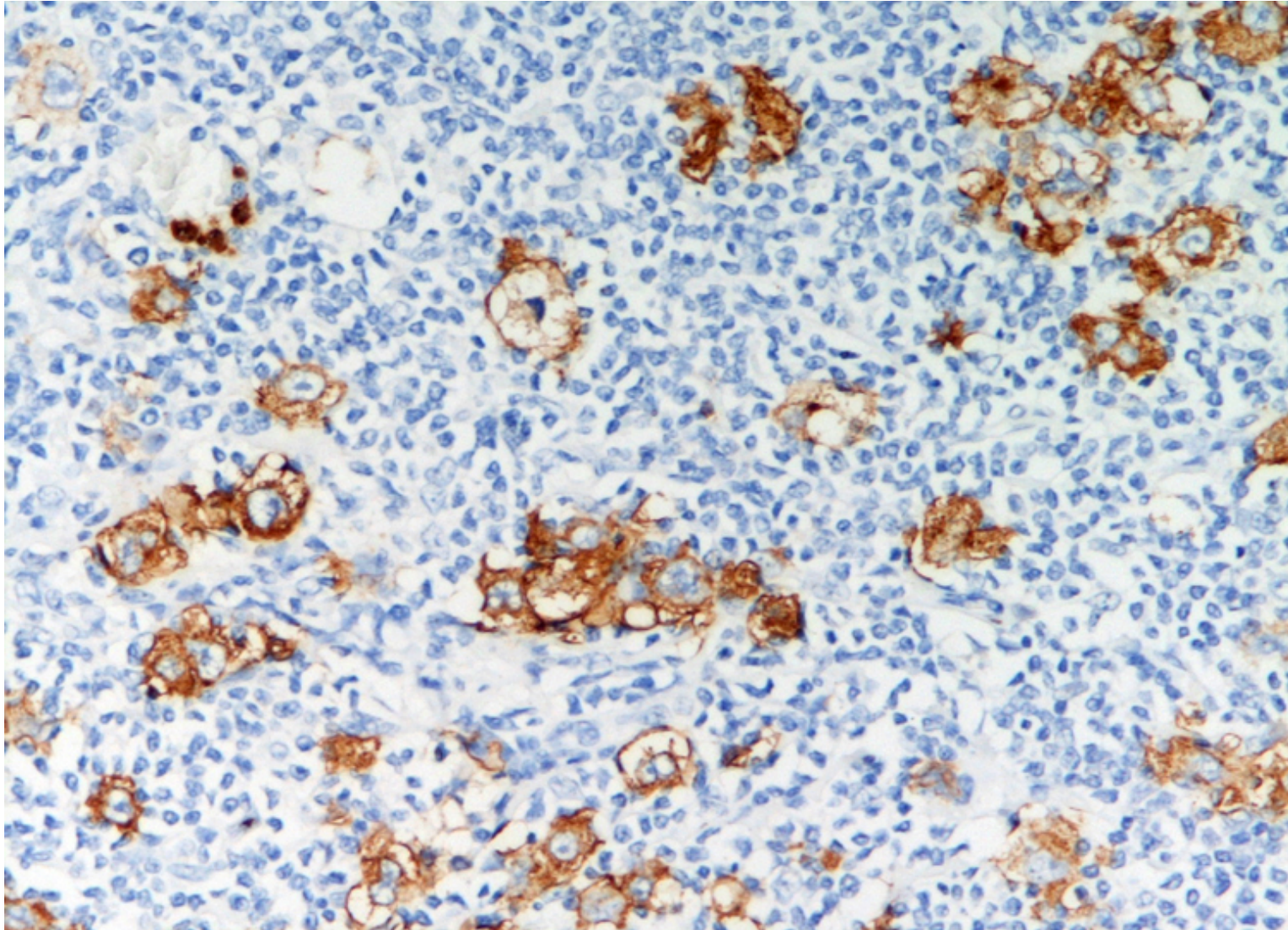
# CLASSICAL HL – CD30



# CLASSICAL HL – CD15



# CLASSICAL HL – CD15



# HL – Lymphocyte predominance

**Age: IV Decade**

**Sex: M**

**Frequency: 5-20%**

**Localized lymphadenopathy**

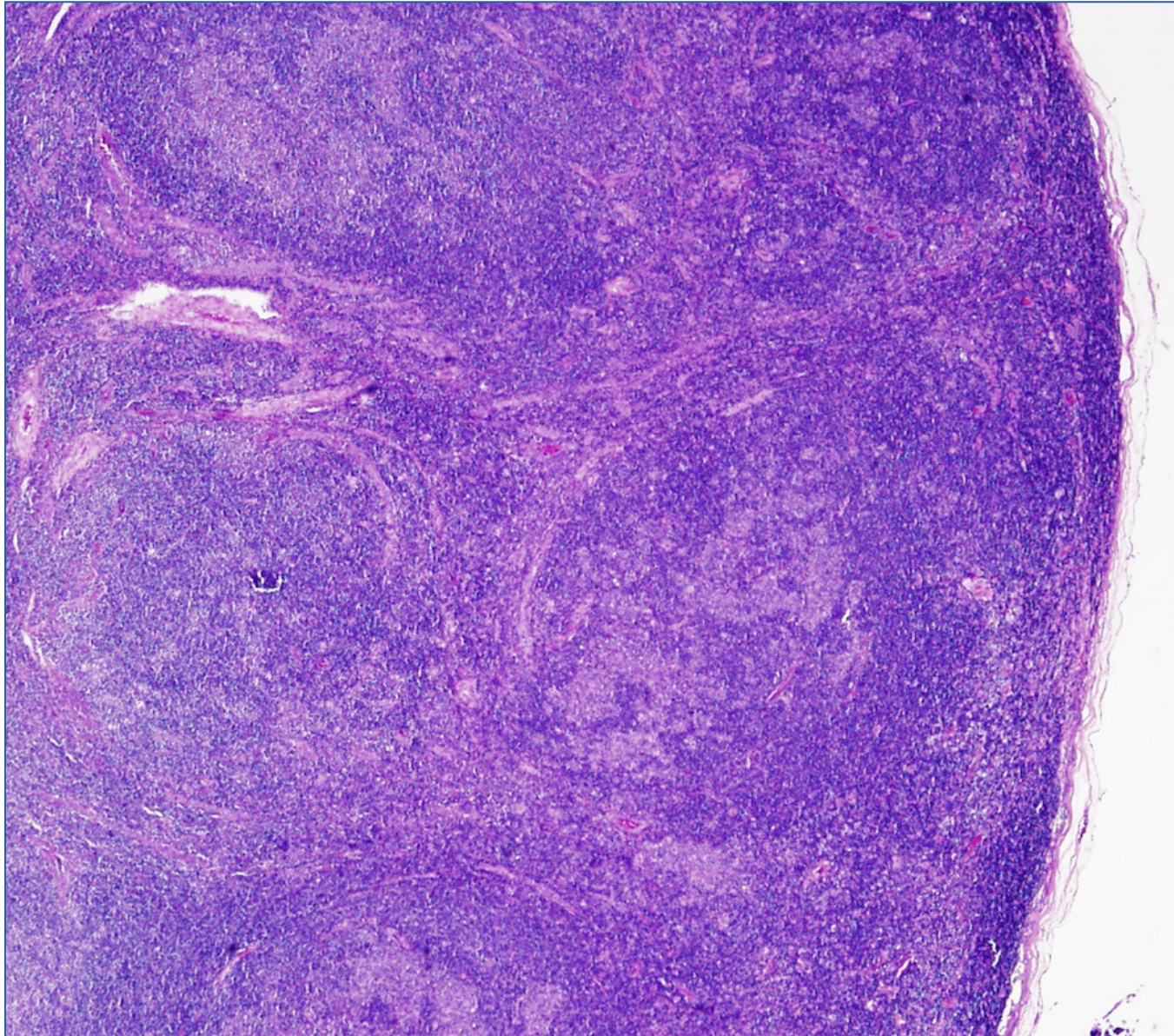
**Rare mediastinal involvement**

**Excellent prognosis**

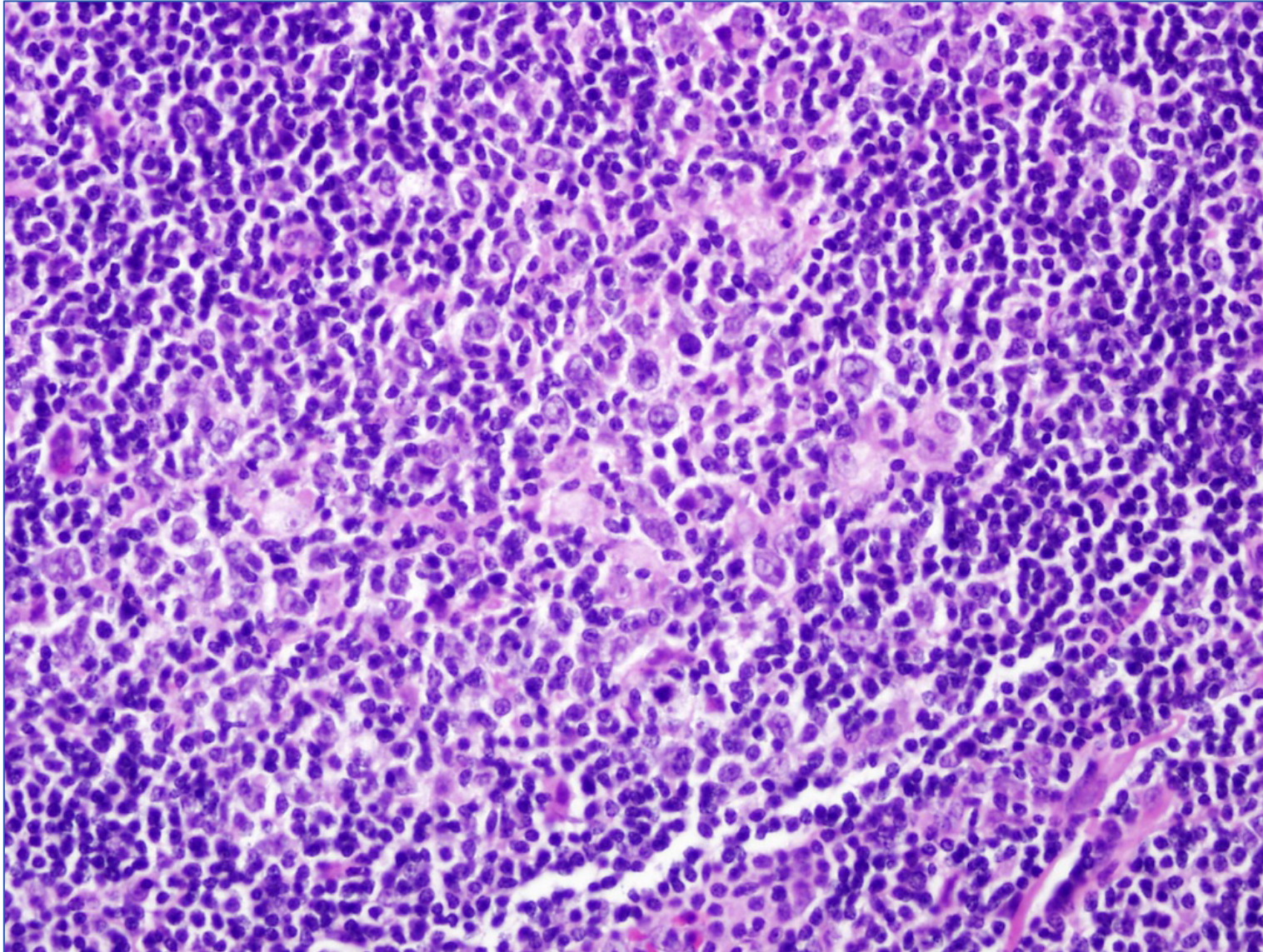
## **Morphology**

- **Multiple nodules, demarcated borders**
- **Small reactive B-lymphocytes**
- **Clustered (granuloma-like) histiocytes**
- **L/H cells with multilobated nuclei**
- **Small nucleoli**
- **Wide, clear cytoplasm**
- **CD20 & CD 79a +**
- **CD30 & CD15-**

# HL – Lymphocyte predominance

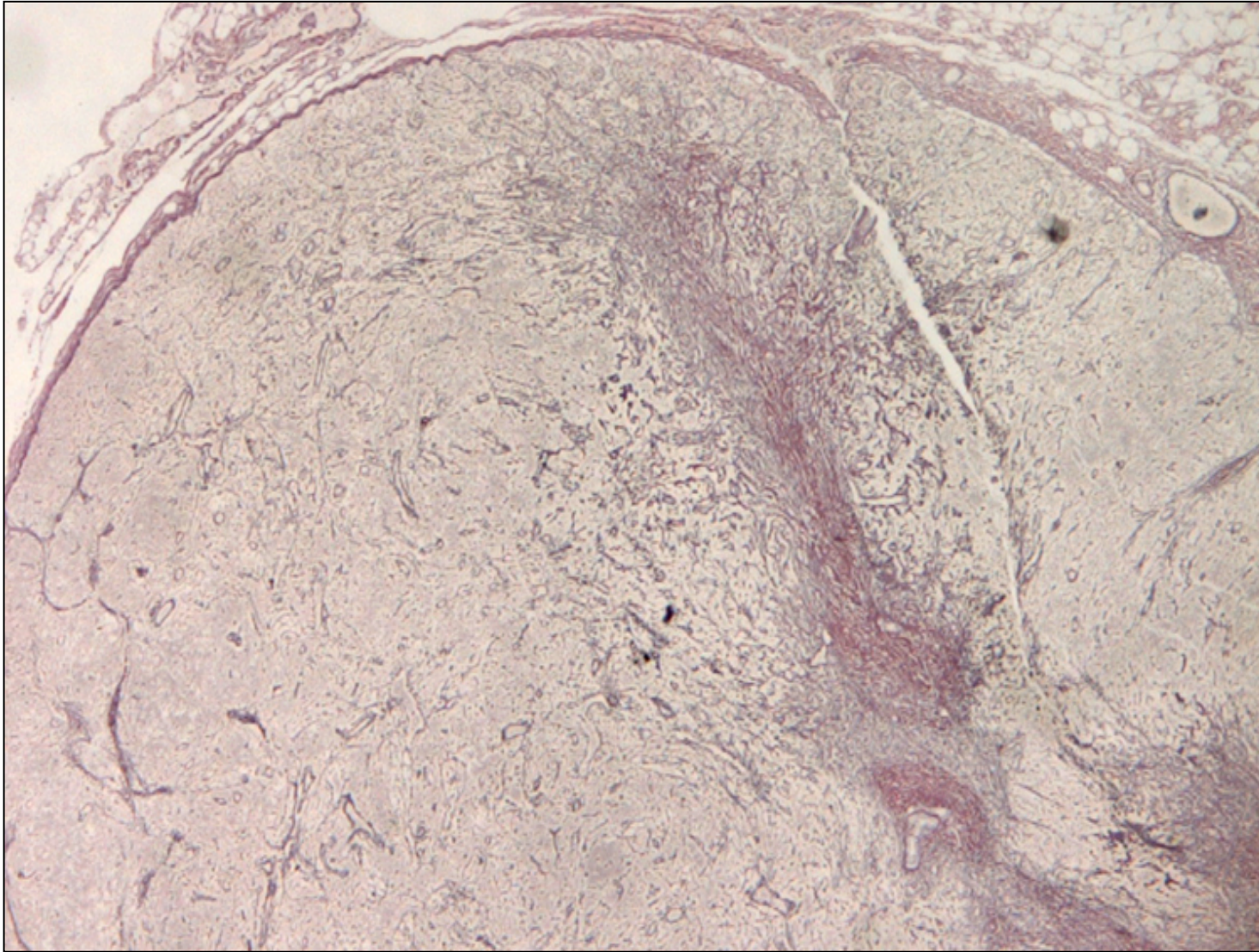


## HL – Lymphocyte predominance

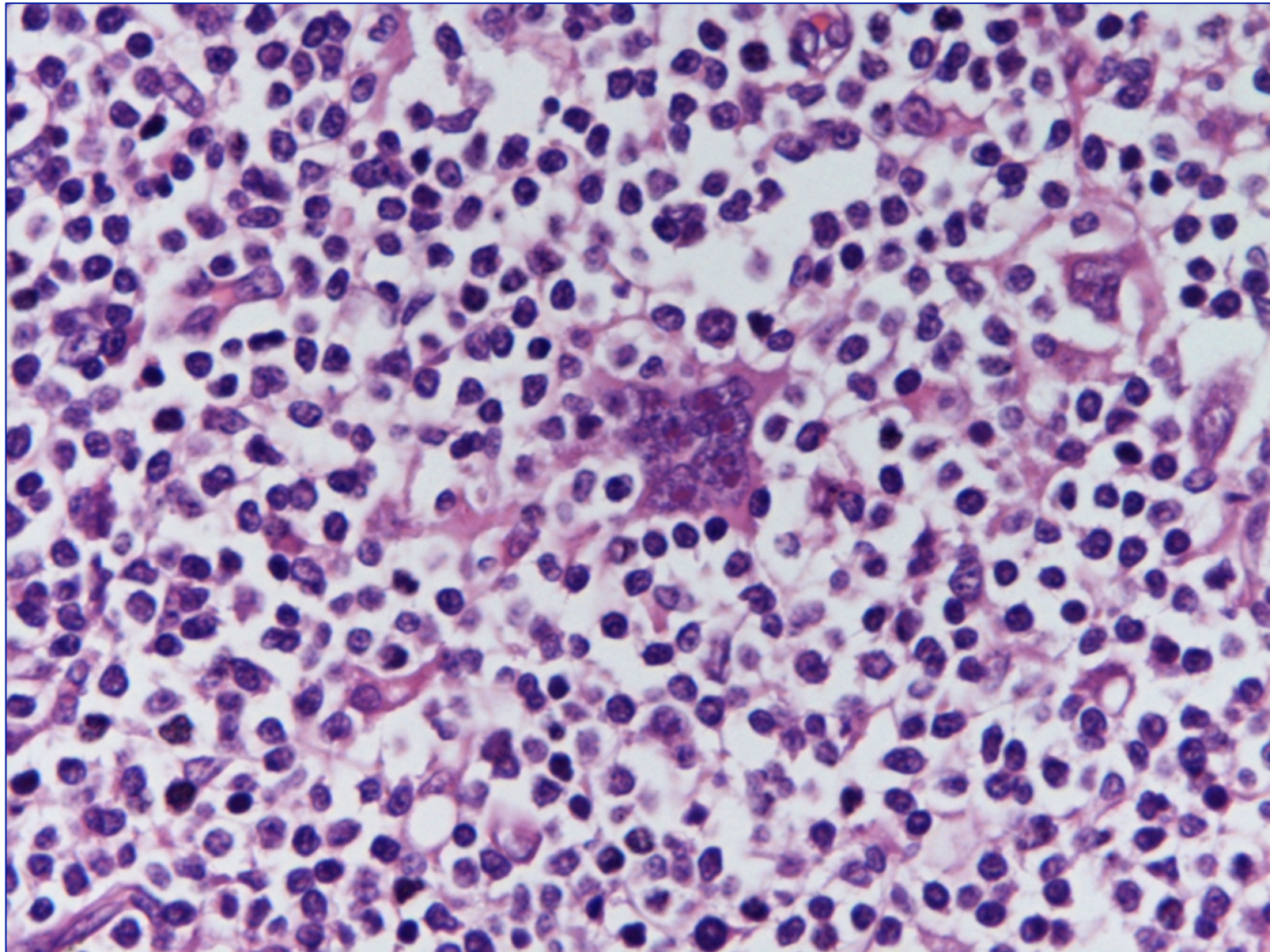


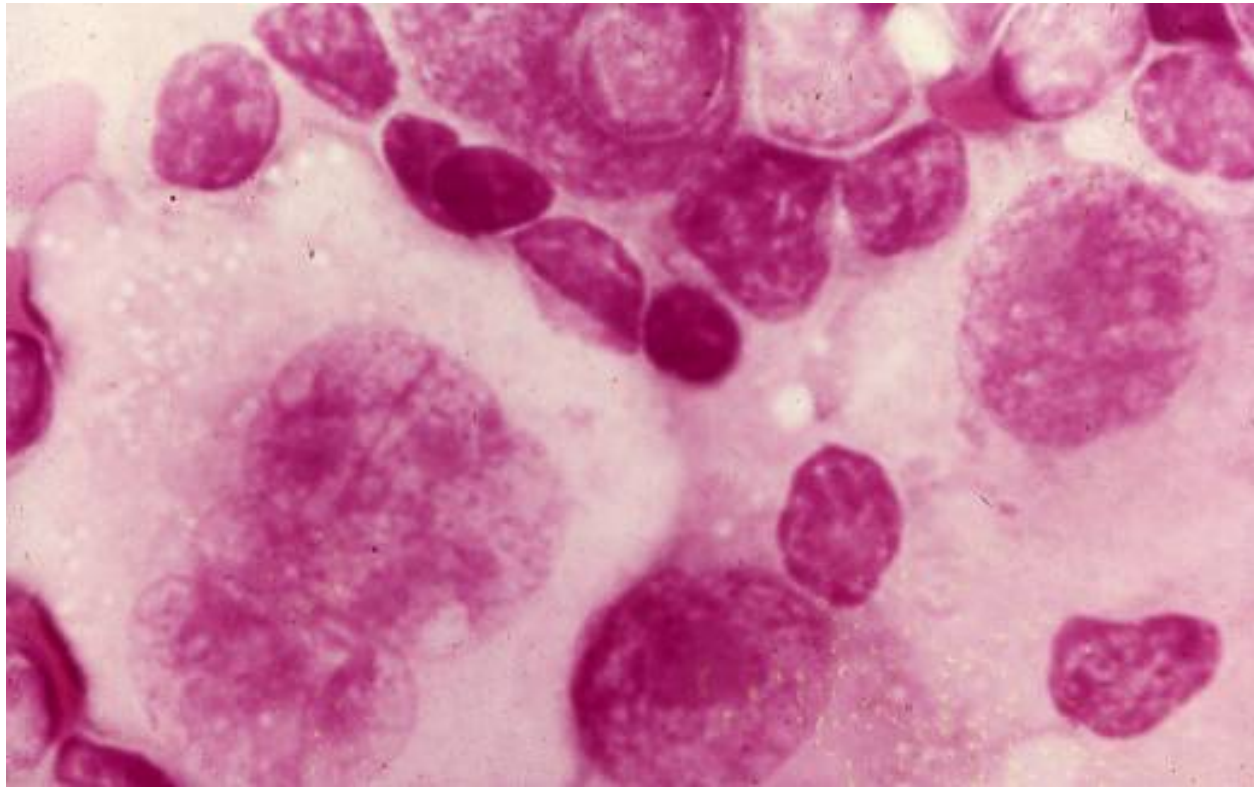


# HL – Lymphocyte predominance



## HL – Lymphocyte predominance





## HL – bone marrow involvement



# HODGKIN LYMPHOMA

## **STAGING (Ann Arbor)**

- I. Single lymph node basin**
- II. Two or more basins, same side of the diaphragm**
- III. Two or more basins, both sides of the diaphragm (+/- spleen (III s))**
- IV. Extra-lymphatic spread**

**For any stage**

**A – lack of symptoms**

**B –**  
    **night sweats**  
    **fever**  
    **weight loss**  
    **weakness**