Pathology 7

Lymphoid neoplasms

- The most specific markers for T cell differentiation
  - CD19
  - CD10
  - CD20
  - CD3
  - CD79

- All the following are good prognostic factors in B-ALL, except:
  - Age 2-10 years
  - Low WBC count
  - T(12;21)
  - Hypodiploidy
  - T(9;22)

- MYC gene translocations are associated with
  - Follicular lymphoma
  - Burkitt lymphoma
  - DLBCL
  - CLL
  - Mantle cell lymphoma

- The most common lymphoma is
  - Follicular lymphoma
  - Burkitt lymphoma
  - DLBCL
  - CLL
  - Mantle cell lymphoma

- What tumor is positive for Cylcin D1
  - Follicular lymphoma
  - Burkitt lymphoma
  - DLBCL
  - CLL
  - Mantle cell lymphoma

Important terms

- Leukemia: neoplastic cells mainly circulating in the blood
- Lymphoma: neoplastic process involving the lymph node primarily
- Acute Leukemia: neoplastic proliferation of early cells
- Chronic leukemia: neoplastic proliferation of cells showing advanced degrees of differentiation

- The three major lines of differentiation are
  - Lymphoid
  - Myeloid
  - Histiocytic

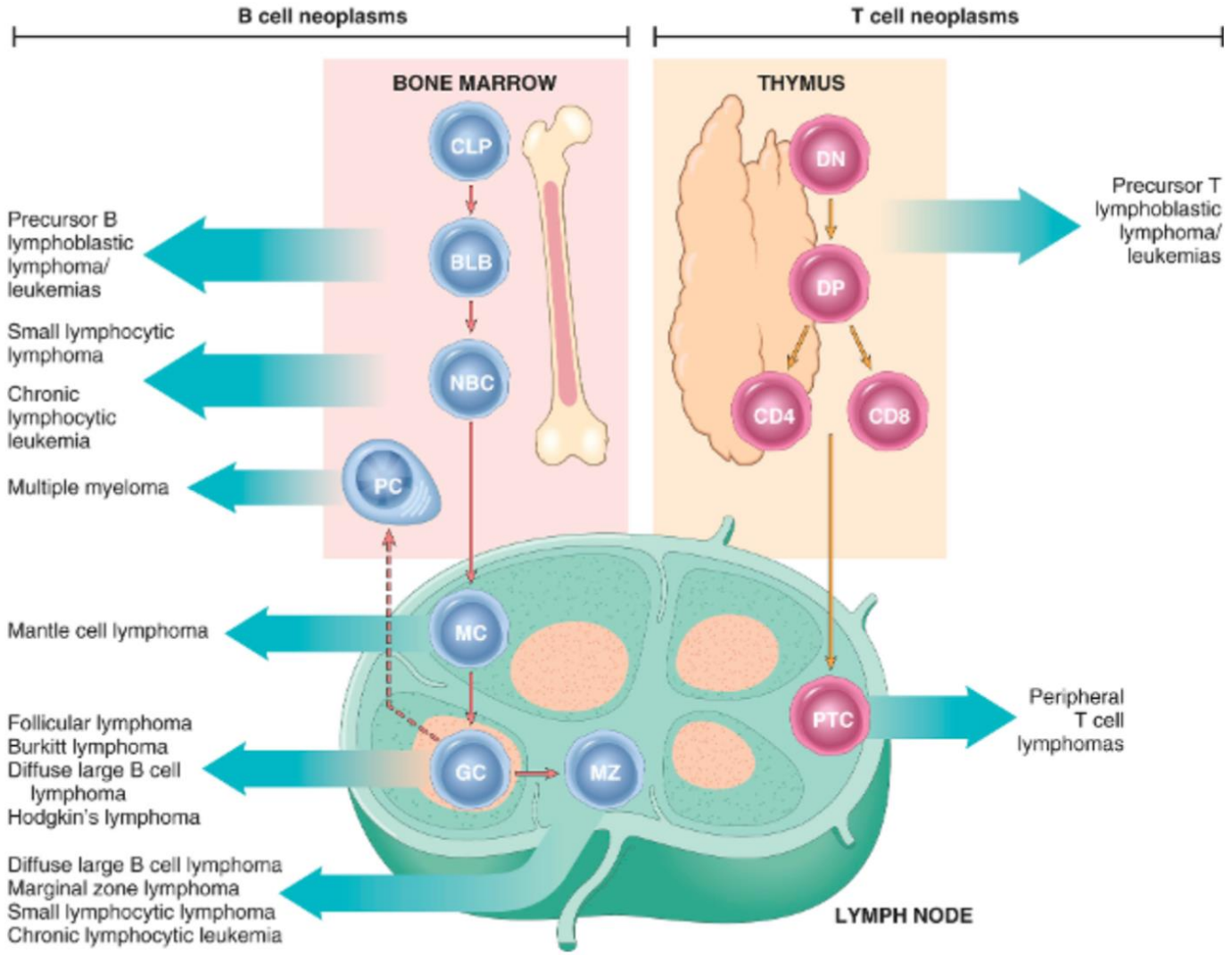
Lymphoid neoplasms
General

- Broadly divided into B or T cell neoplasms
- Could present with leukemia, lymphoma or other (plasma cell neoplasms)
- Overlapping clinical features
- Classification depends on the cell of origin not the clinical presentation

- All lymphoid neoplasms are derived from a single transformed cell and are therefore clonal.
  - Receptor gene rearrangement to determine clonality
  - Expressing only kappa or only lambda indicates clonality
- Relationship between lymphoid neoplasms and immune system
  - Autoimmune disorders and lymphoma
  - Immune deficiency and lymphoma

- Lymphoma even has the potential to spread anywhere in the body
- WHO classification

Precursor B Cell Neoplasms
Precursor B cell leukemia/lymphoma (B-ALL)
Peripheral B Cell Neoplasms
B cell chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)
B cell prolymphocytic leukemia
Lymphoplasmacytic lymphoma
Mantle cell lymphoma
Follicular lymphoma
Extranodal marginal zone lymphoma
Splenic and nodal marginal zone lymphoma
Hairy cell leukemia
Plasmacytoma/plasma cell myeloma
Diffuse large B cell lymphoma (multiple subtypes)
Burkitt lymphoma
Precursor T Cell Neoplasms
Precursor T cell leukemia/lymphoma (T-ALL)
Peripheral T/NK Cell Neoplasms
T cell prolymphocytic leukemia
T cell granular lymphocytic leukemia
Mycosis fungoides/Sézary syndrome
Peripheral T cell lymphoma, unspecified
Angioimmunoblastic T cell lymphoma
Anaplastic large cell lymphoma
Enteropathy-type T cell lymphoma
Panniculitis-like T cell lymphoma
Hepatosplenic γδ T cell lymphoma
Adult T cell lymphoma/leukemia
Extranodal NK/T cell lymphoma
Aggressive NK cell leukemia
Hodgkin Lymphoma
Nodular sclerosis
Mixed cellularity
Lymphocyte-rich
Lymphocyte-depletion
Lymphocyte predominance, nodular


B cell neoplasms
T cell neoplasms
BONE MARROW
THYMUS
CLP
DN
BLB
DP
NBC
CD4
CD8
PC
MC
PTC
GC
MZ
Precursor B lymphoblastic lymphoma/ leukemias
Small lymphocytic lymphoma
Chronic lymphocytic leukemia
Multiple myeloma
Precursor T lymphoblastic lymphoma/ leukemias
Mantle cell lymphoma
Follicular lymphoma
Burkitt lymphoma
Diffuse large B cell lymphoma
Hodgkin's lymphoma
Peripheral T cell lymphomas
Diffuse large B cell lymphoma
Marginal zone lymphoma
Small lymphocytic lymphoma
Chronic lymphocytic leukemia
LYMPH NODE

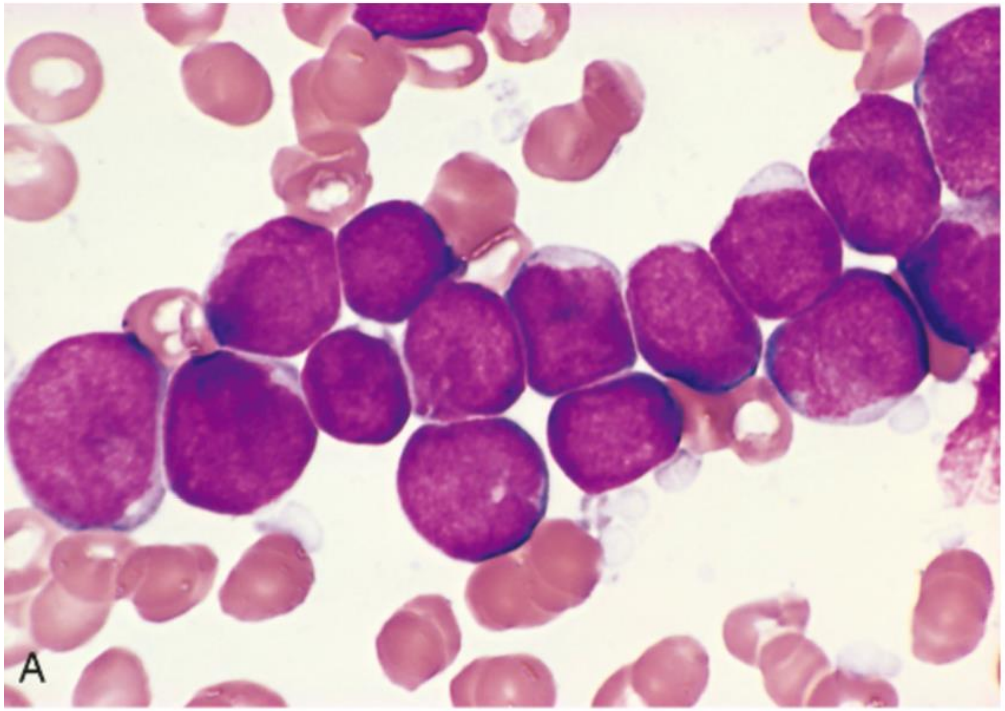
- Precursor B and T cell lymphoblastic lymphoma/ leukemia—commonly called acute lymphoblastic leukemia (ALL)
- Chronic lymphocytic leukemia/small lymphocytic lymphoma
- Follicular lymphoma
- Mantle cell lymphoma
- Diffuse large B cell lymphomas
- Burkitt lymphoma
- Multiple myeloma and related plasma cell tumors
- Hodgkin lymphoma

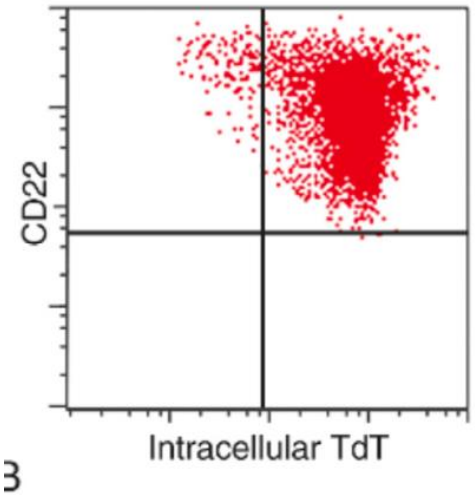
Precursor B and T cell lymphoblastic lymphoma/ leukemia—commonly called acute lymphoblastic leukemia (ALL)

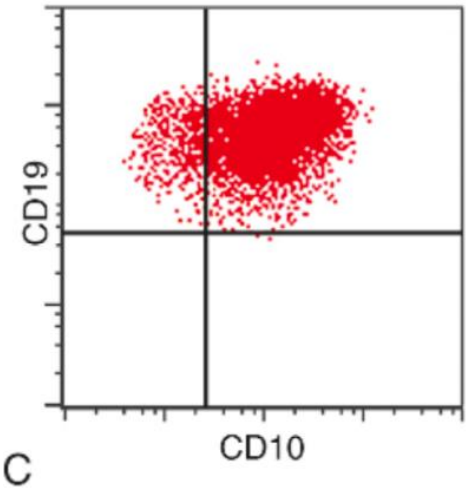
- B 85%, LEUKEMIA
  - The most common malignancy in children
  - Peak age: 3 years
- T 15%, thymic lymphoma
  - Peak age adolescence

Morphology

- Hypercellular marrow in B-ALL
- Cellular thymus or lymph nodes in T-ALL
- Blasts: large cells with scanty cytoplasm, large nucleus, fine chromatin and prominent nucleoli
- On routine staining, no difference between B and T, immunophenotype is needed.


A


CD22
Intracellular TdT
B


CD19
CD10
C

Important markers

- CD19, CD79, pax5, CD22 and CD20 indicate B cell origin
  - CD19 is the most specific
- CD3 indicates T cell origin
- TdT indicates early lymphoid origin (for both B and T, not myeloid!)
- CD34: blast marker for B, T and Myeloid

genetics

- B-ALL:
  - T(12;21)…good prognosis
  - T(9;22)…bad prognosis
- T-ALL:
  - NOTCh
  - PTEN
  - CDKN2A

Clinical features

- Depression of bane marrow
- Mass effect
- CNS manifestations

- Agressive tumor but curable!!!
  - 80% cure rate in children
  - 40% in adults

Bad prognostic factors

- Age less than 2 or more than 10
- Peripheral blood count more than 100,000
- Normal ploidy or hypodiploidy
- T(9;22)

Good prognostic factors

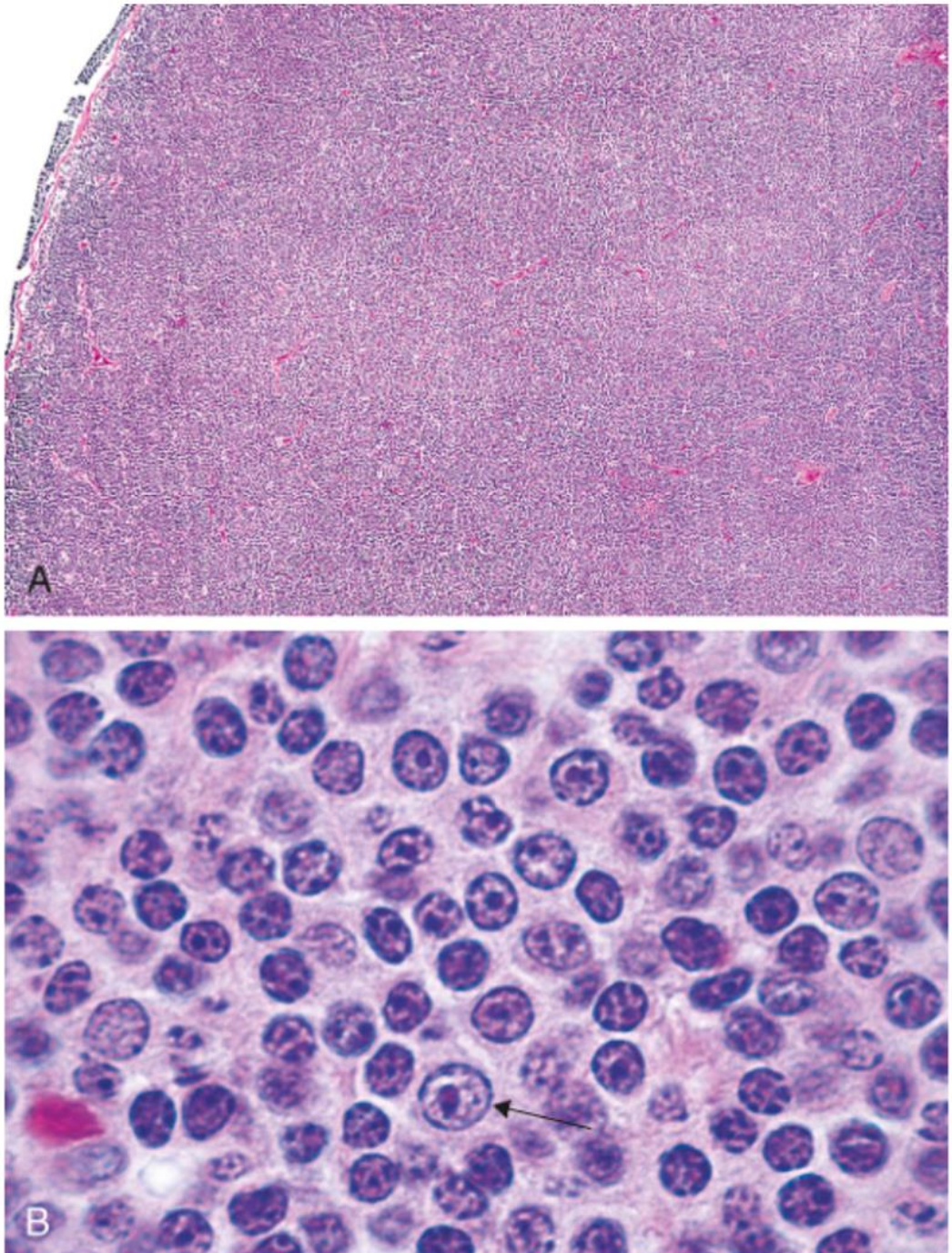
- Age 2-10
- Low WBC count
- Hyperdiploidy
- T(12;21)

Chronic lymphocytic leukemia/small lymphocytic lymphoma

- If PB count of neopalstic cells is more than 5000/microliter……CLL
- If less WITH LYMPH NODE INVOLVEMENT…..SLL
- If no lymph node and less than 5000……monoclonal B cell lymphocytosis-CLL type.

morphology

- Small mature lymphocytes with dense chromatin and small or indistinct nucleoli
  - Small percentage of lymphocytes show prominent nucleoli, called prolymphocytes.
- Lymph node effaced with sheets of lymphocytes


A
B

Immunophenotype

- B cell markers positive
- CD5 positive..VERY IMPORTANT
  - The other CD5 positive B cell lymphoma is mantle cell lymphoma

Clinical manifestations

- Old age
- Asymptomatic
- Nonspecific symptoms, fatigue, anorexia, weight loss or lymphadenopathy, hepatosplenomegaly
- Lymphocytosis
- Hypogammaglobulinemia
  - 15% have autoimune hemolytic anemia

- Prolonged survival
- Not curable without stem cell transplantation
  - Only in young patients
- Small fraction might progress into diffuse large B cell lymphoma
  - Survival is less than 1 year

Follicular lymphoma

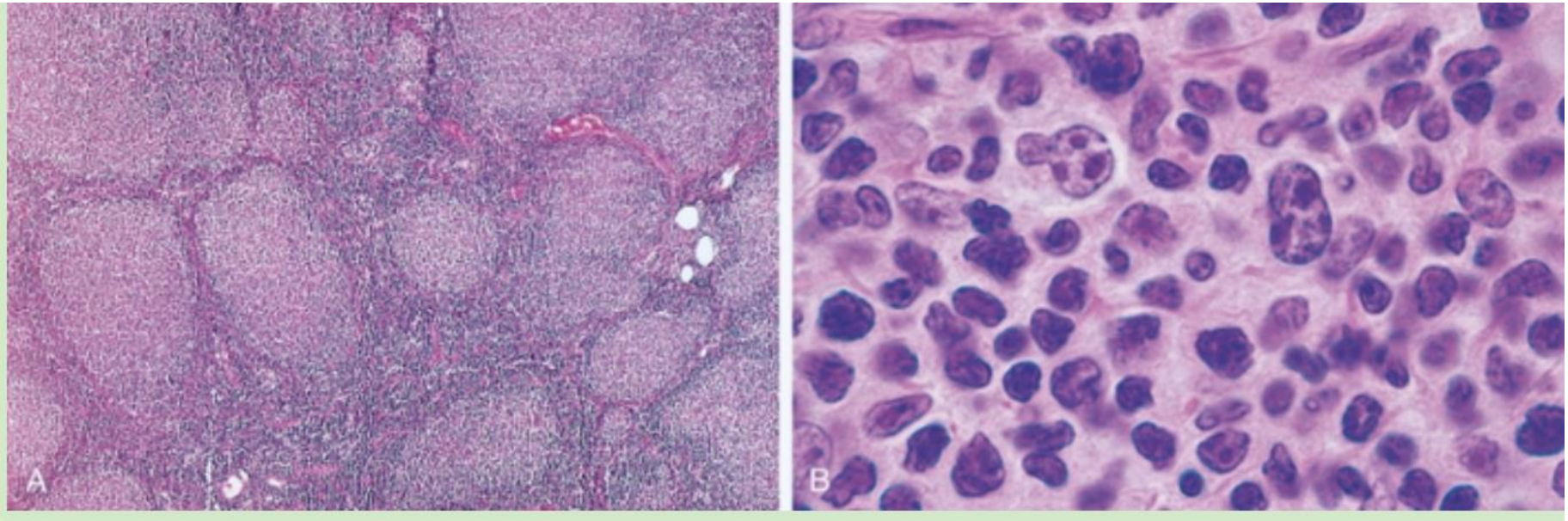
- Common low grade lymphoma
  - 40% of nonhodgkin lymphoma
- T(14;18) placing BCL2 under control of IgH gene

Morphology

nodular or follicular arrangement

two types of cells

centrocytes and centroblasts



Immunophenotype

- B cell markers
- CD10…very important
  - Other tumors are Burkitt and some cases of DLBCL in addition to B-ALL

Clinical manifestations

- Older than 50
- Generalized lymphadenopathy
- Bone marrow is involved in 80% of cases
- Prolonged survival, not curable
- 40% transform into DLBCL, dismal prognosis

Mantle cell lymphoma

- t(11;14) (IgH and cyclin D1)

Morphology

- Lymph nodes are effaced by sheets of medium sized cells with similar morphology to mature lymphocytes (slightly larger)
  - A small percentage of cases have blastic morphology
- Bone marrow is involved in most cases
- GI can be involved by polyposis

Immunophenotype

- B cell markers
- CD5 similar to CLL
- Cyclin D1 positive
  - CLL is negative for cyclin D1

Clinical manifestations

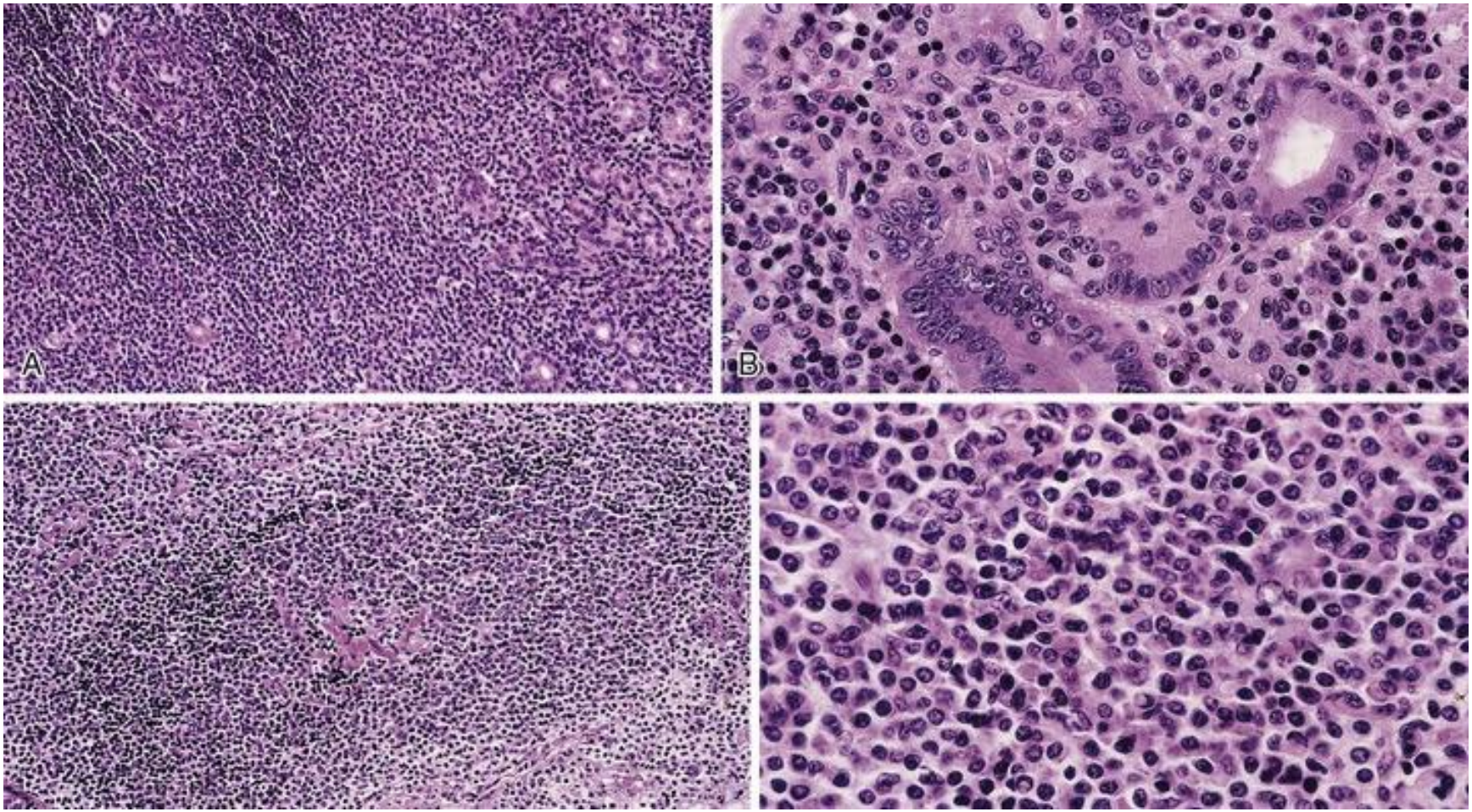
- General nonspecific symptoms
- Lymphadenopathy
- Incurable
  - Survival rate is 4-6 years!!!

Extranodal marginal zone lymphoma

- Low grade B cell neoplasm arising in tissue such as GI, thyroid, skin, salivary gland and orbit
- Associated with chronic inflammation whether infectious or autoimmune

Morphology

- Lymphoepithelial lesions.
- Small to medium size lymphocytes with variable cytoplasm.


A
B

Immunophenotype

- B cell markers

Clinical manifestations

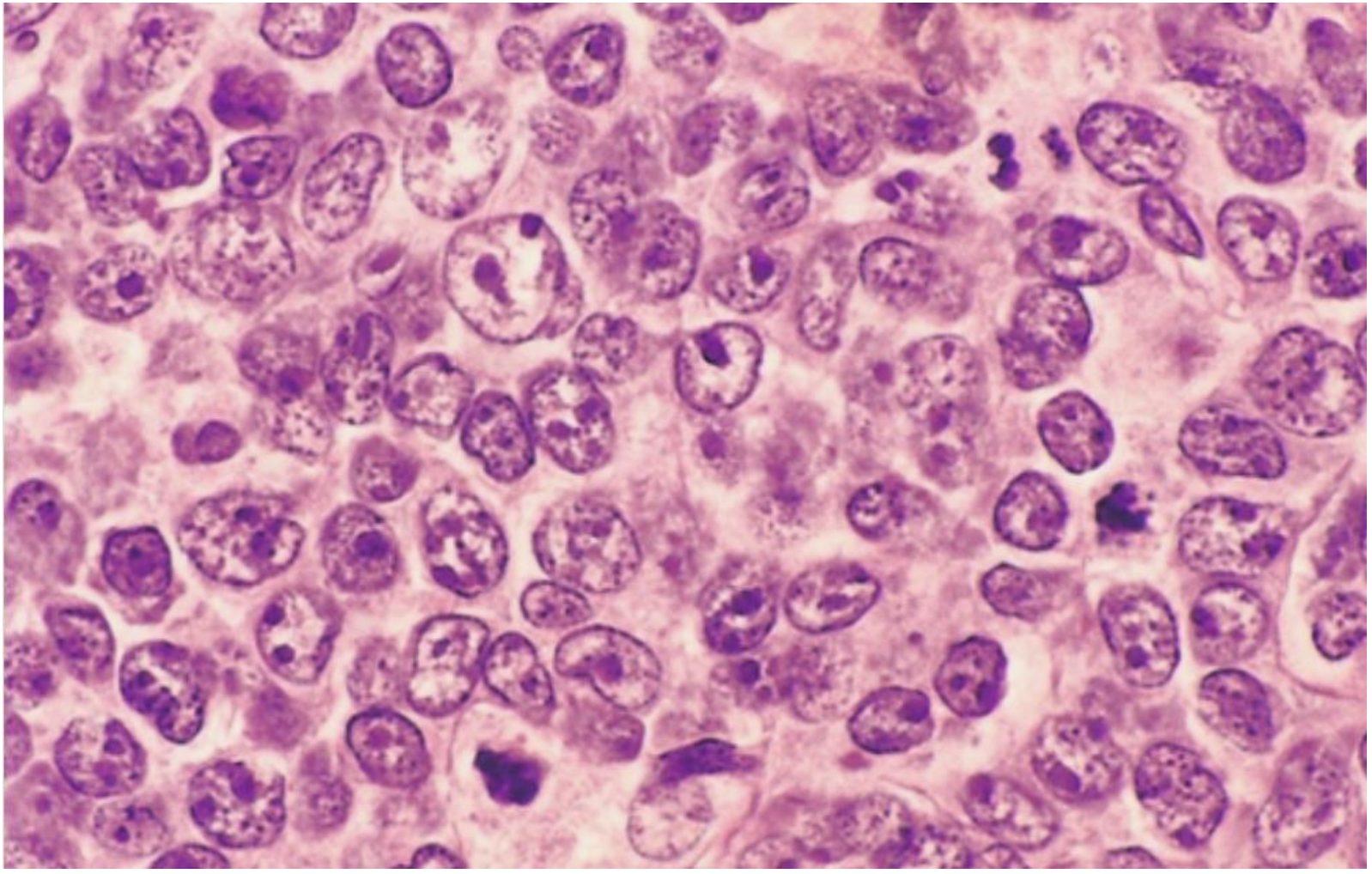
- Mass at the site of involvement
- Low grade, prolonged survival with no cure
  - Exception is H.pylori induced gastric MZL

Diffuse large cell lymphoma

- Most common adult lymphoma
- Either de novo or transformation from other low grade tumors

Morphology

- Large cells!!!
  - At least double that of a normal lymphocyte
  - Diffuse arrangement



Immunophenotype

- B cell markers
- CD10 in a subset of cases

Clinical manifestations

- Older than 60 years of age
  - Can occur at any age
- Generalized lymphadenopathy
- Can occur in extranodal sites
  - Skin, GI…etc.

- Aggressive and rapidly fatal if not treated
- With treatment cure rate is 50%