Adult T-cell Leukemia/Lymphoma

Definition

- Peripheral T-cell neoplasm
- Most often composed of highly pleomorphic lymphoid cells
- Usually widely disseminated
- Caused by the human T-cell leukemia virus type 1 (HTLV-1)

Epidemiology

- Endemic in
  - Japan
  - Caribbean basin
  - Central Africa
- Disease distribution closely linked to prevalence of HTLV-1 in the population

Epidemiology

- Long latency
- Affected individuals are exposed to the virus very early in life
- Virus transmission
  - Breast milk
  - Blood
  - Blood products

Epidemiology

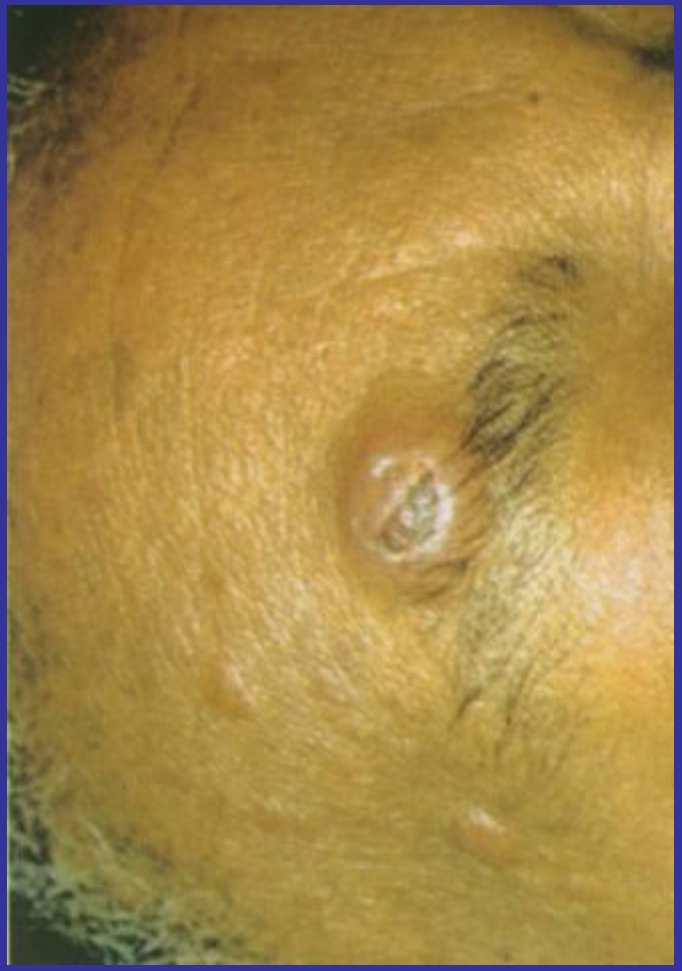
- Incidence of 2.5% among HTLV-1 carriers in Japan
- Sporadic cases found in USA and elsewhere in the world
- Adults (median age 55 years)
- M:F = 1.5:1

Sites of Involvement

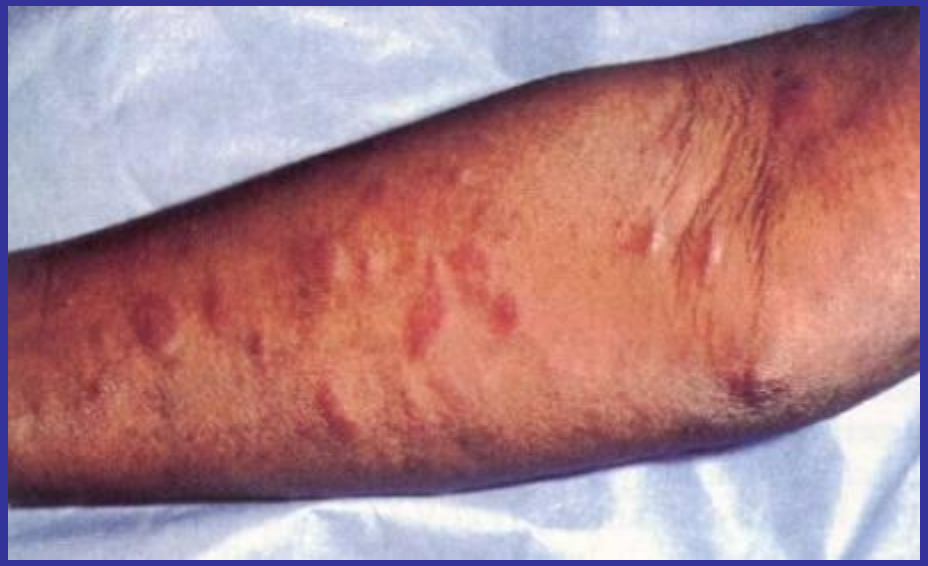
- Widespread LN and PB involvement (most common presentation)
- Number of circulating neoplastic cells does not correlate with degree of BM involvement
  - Circulating cells may be recruited from other organs like skin

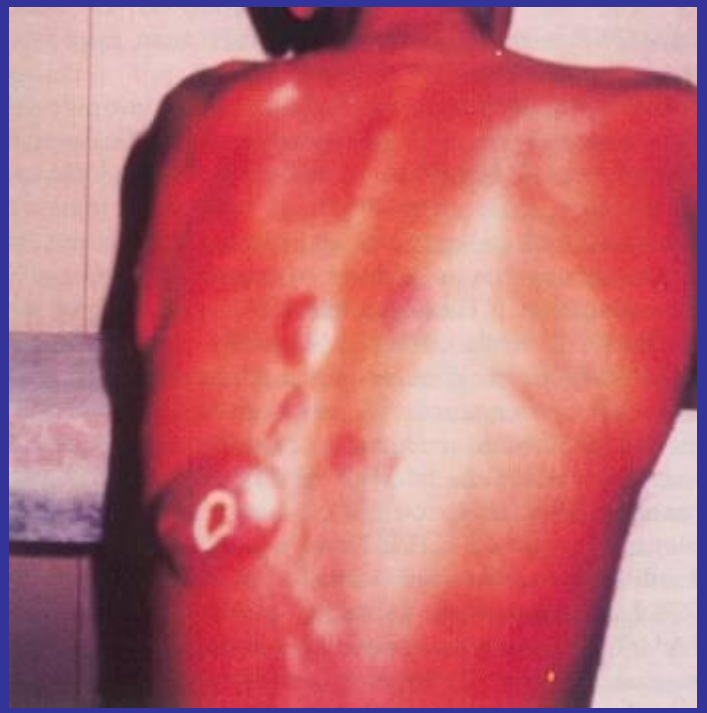
Sites of Involvement

- Systemic disease with involvement of
  - Spleen
  - Skin (most common extralymphatic site of involvement; >50%)
  - Lung
  - GI
  - CNS



Sites of Involvement





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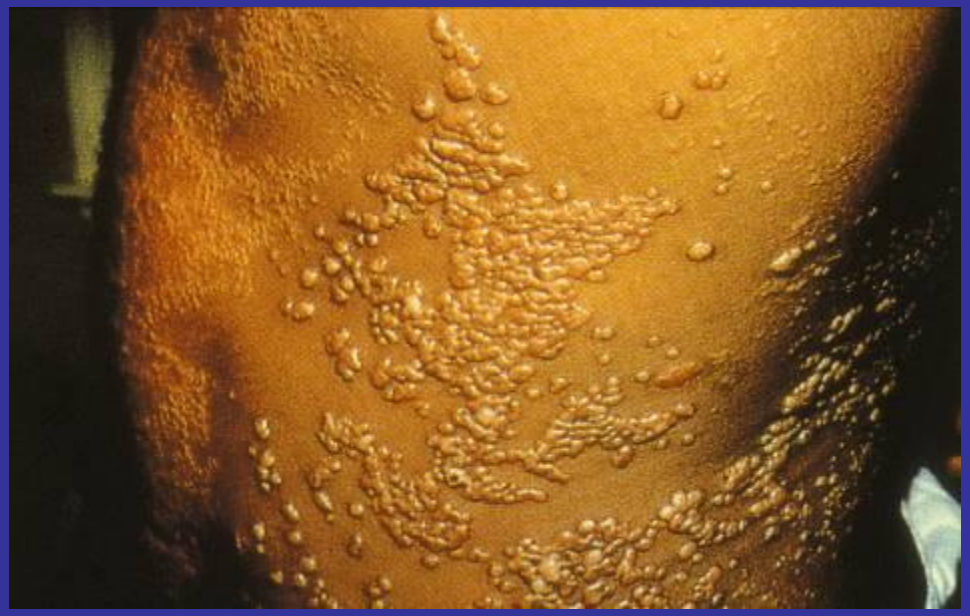
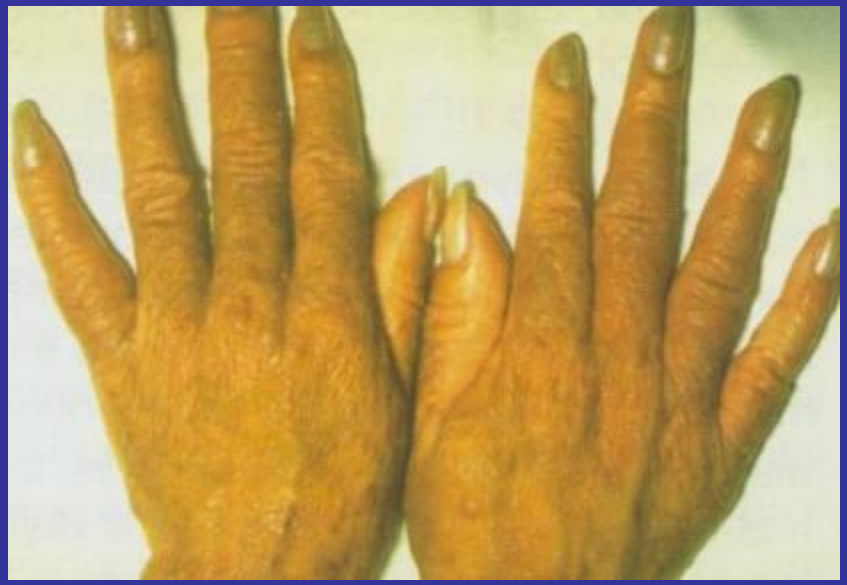


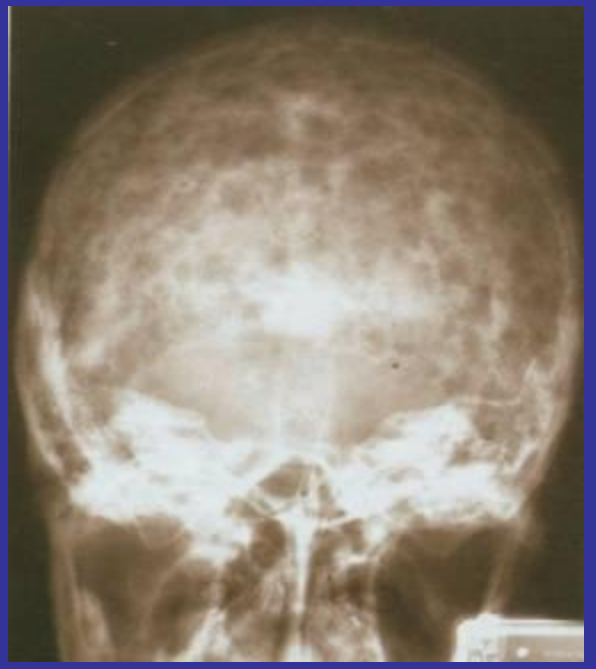


Clinical Variants

- Acute
- Lymphomatous
- Chronic
- Smoldering

Clinical Features

- Acute variant
  - Most common
  - Leukemic phase
  - Markedly elevated WBC
  - Skin rash
  - Generalized lymphadenopathy
  - Hypercalcemia, with or without lytic bone lesions



Clinical Features

- Acute variant
  - Systemic disease
    - Hepatosplenomegaly
    - Constitutional symptoms
    - Elevated LDH
  - Eosinophilia
  - T-cell immunodeficiency (PCP; Strongyloidiasis)

Clinical Features

- Lymphomatous variant
  - Prominent lymphadenopathy without PB involvement
  - Advanced stage disease
  - Hypercalcemia is less often seen

Clinical Features

- Chronic variant
  - Skin lesions (exfoliative rash)
  - May have absolute lymphocytosis (but atypical lymphocytes are not numerous in PB)
  - No hypercalcemia
  - Progression to acute variant in 25% of cases, but after a long duration

Clinical Features

- Smoldering variant
  - Normal WBC with <3-5% neoplastic cells
  - Skin or pulmonary lesions are frequent
  - No hypercalcemia
  - Progression to acute variant in 25% of cases, but after a long duration

Clinical Features

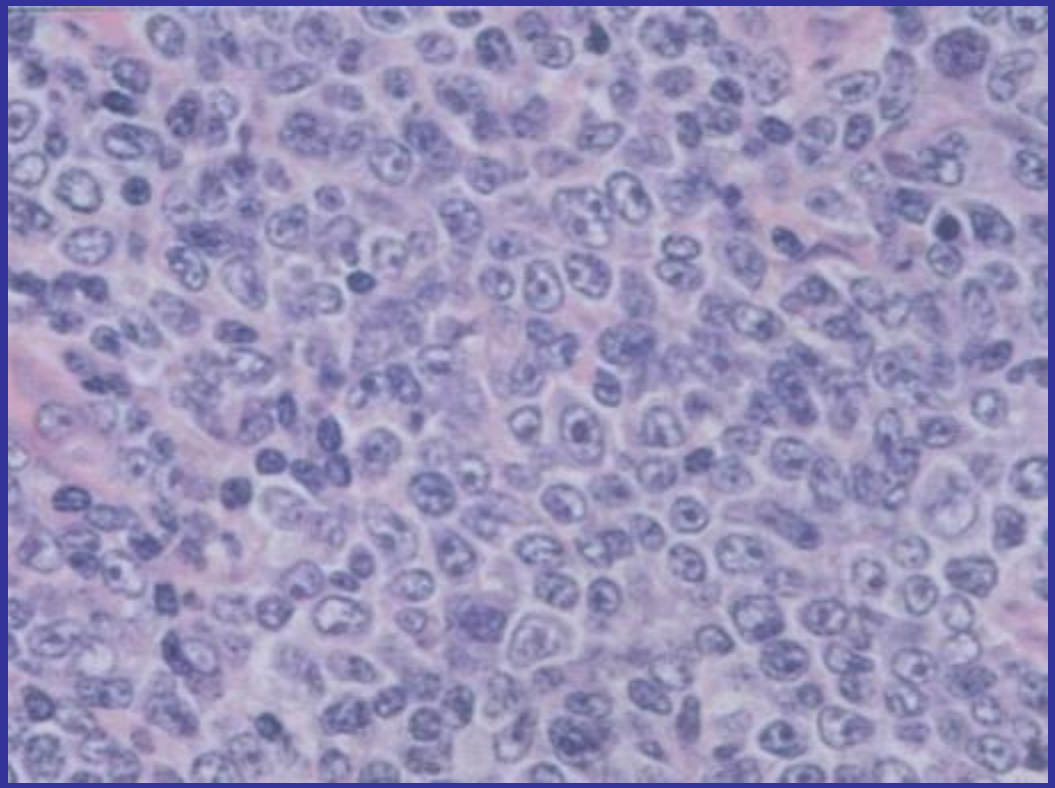
	ACUTE	LYMPHOMATOUS	CHRONIC	SMOLDERING
Leukemic phase	+	-	ATLL cells >10%	ATLL cells <3-5%
WBC	↑↑↑		↑	Normal
LN	+	+	Mild	-
Hypercalcemia	Common	Uncommon	-	-
Hepatosplenomeg	+	+	Slight	-
LDH	↑	↑	Slight ↑	Normal
Skin rash	+		+	+
Infections	+	+		
Survival	2 wks to >1 yr	2 wks to >1 yr	< 2 yrs	> 2 yrs

Etiology

- HTLV-1 is causally linked to ATLL
- p40 tax viral protein leads to transcriptional activation of many genes in the infected lymphocytes
- HTLV-1 infection alone is not sufficient for neoplastic transformation. Additional genetic alterations may result in development of a malignancy

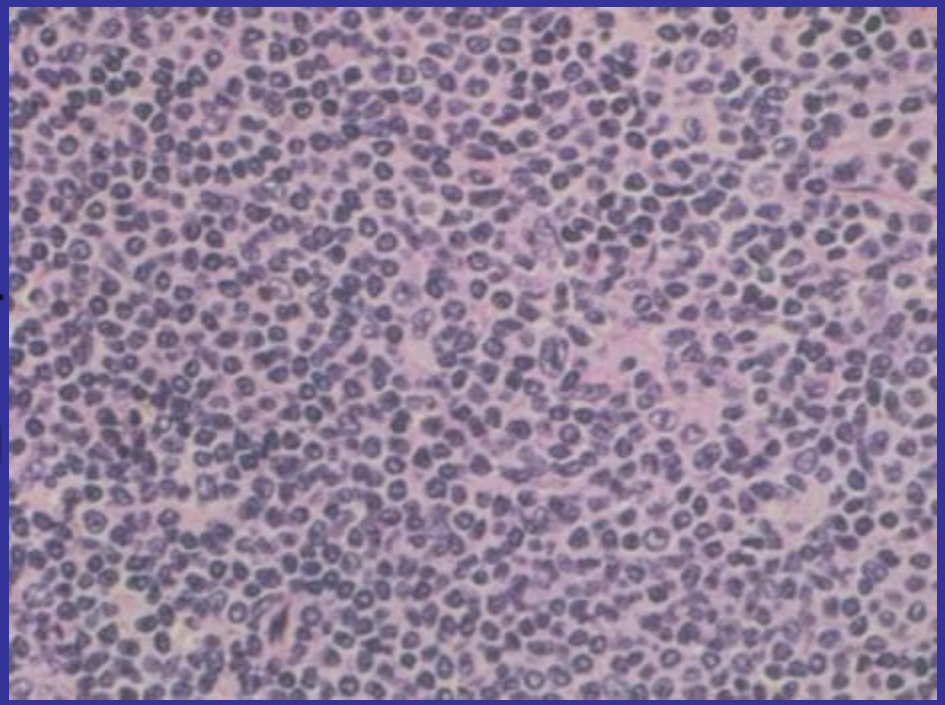
Morphology

- Acute and lymphomatous variants
  - Large to medium-sized cells
  - Pronounced nuclear pleomorphism
  - Coarsely clumped chromatin
  - Prominent nucleoli



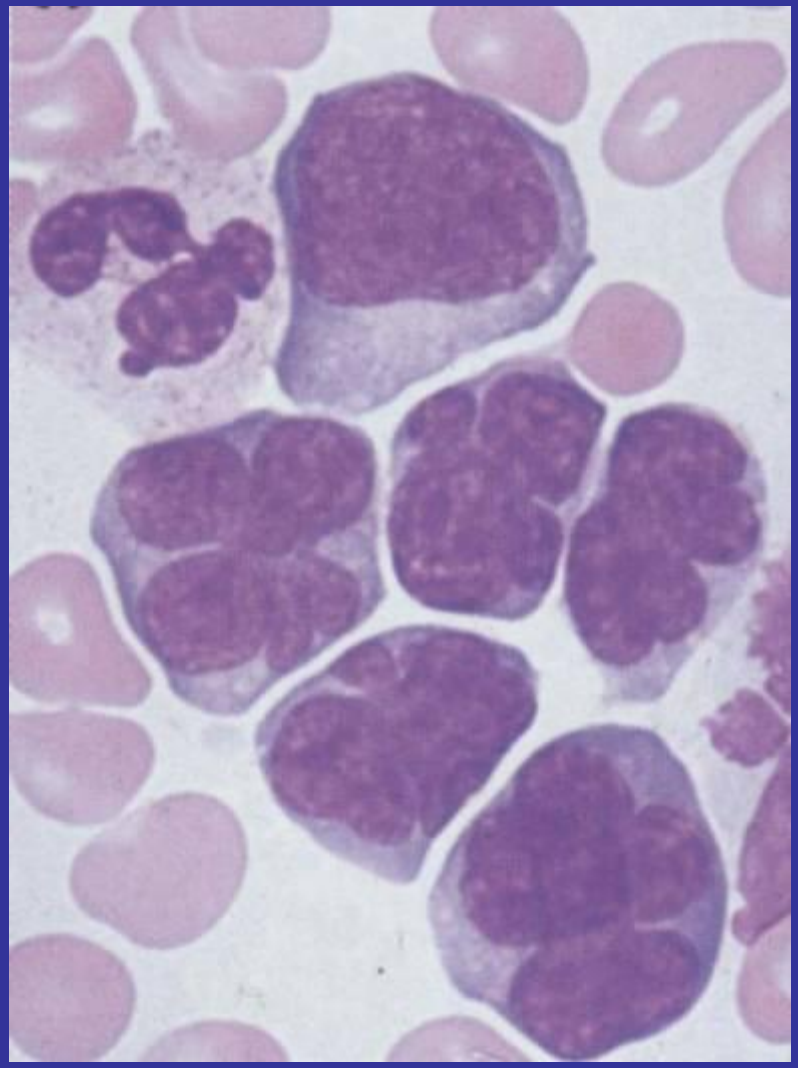
Morphology

- Acute and lymphomatous variants
  - Rare cases may have small atypical lymphocytes with nuclear pleomorphism
  - Clinical course is unrelated to cell size



Morphology

- PB
  - Polylobated cells (“flower cells”)
  - Deeply basophilic cytoplasm
  - Small proportion of blast-like cells
- BM
  - Patchy infiltrates
  - Osteoclastic activity may be prominent (even in absence of infiltrate of neoplastic cells)



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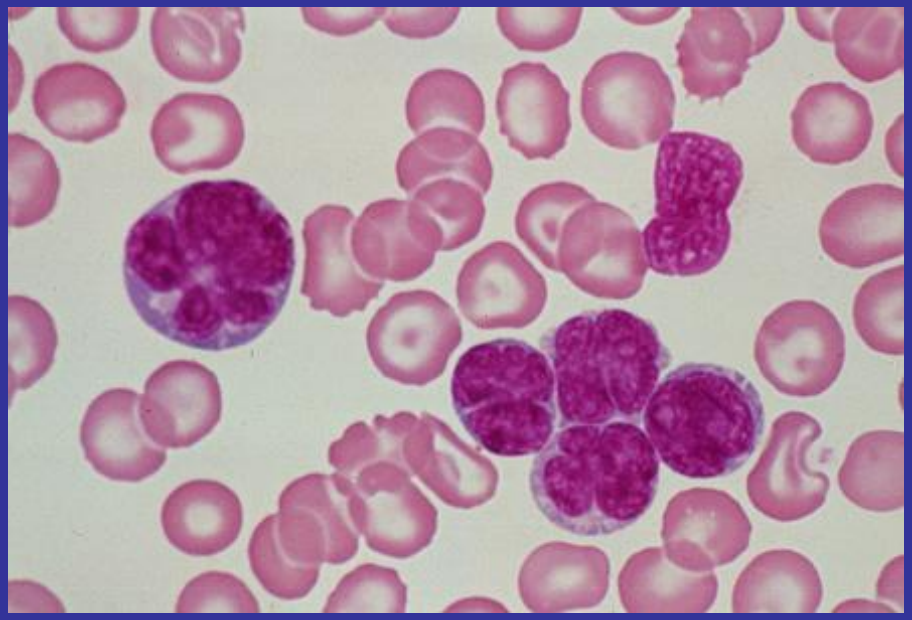

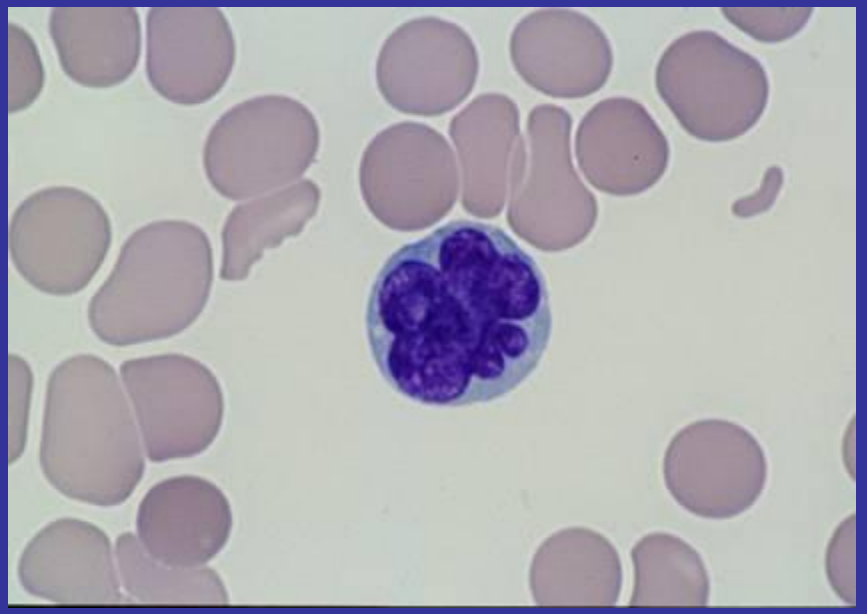

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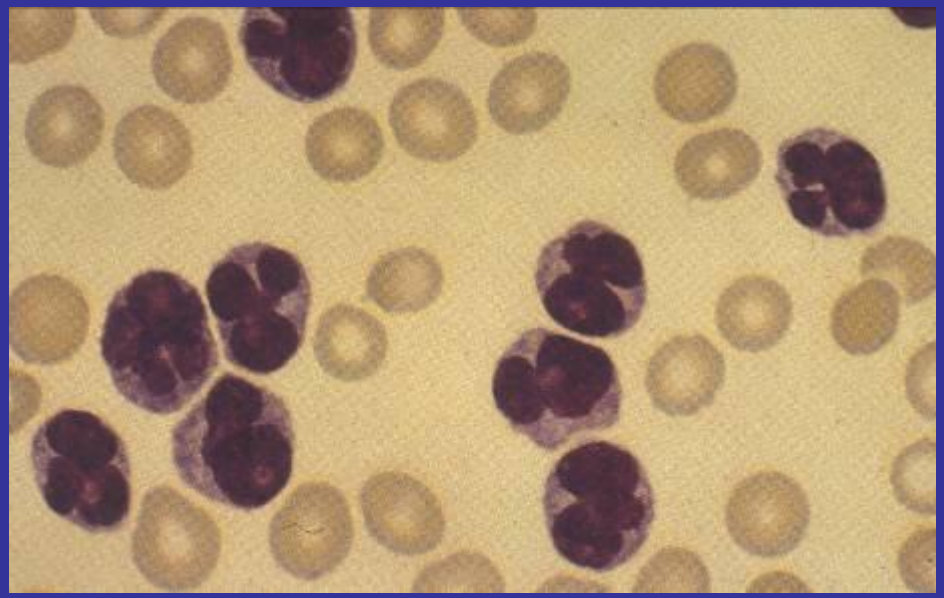
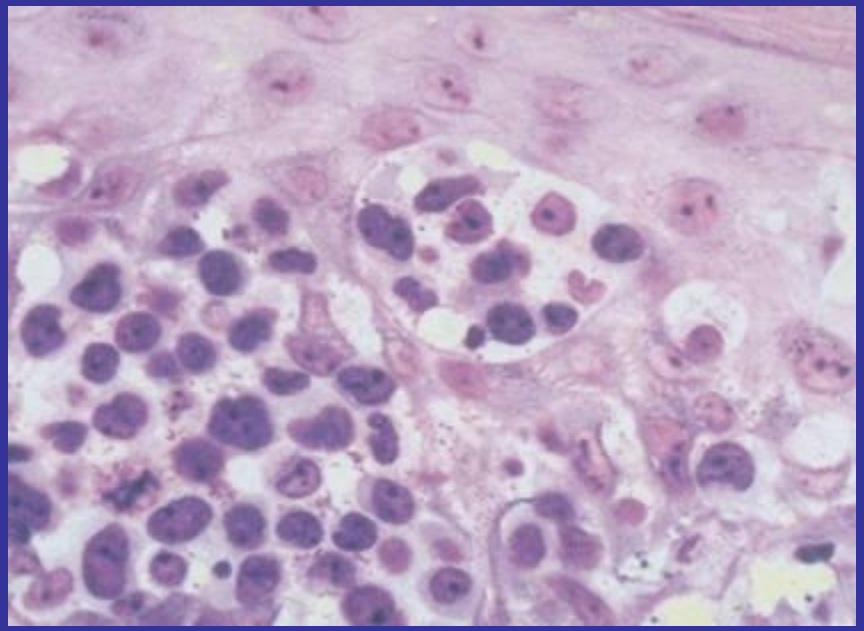


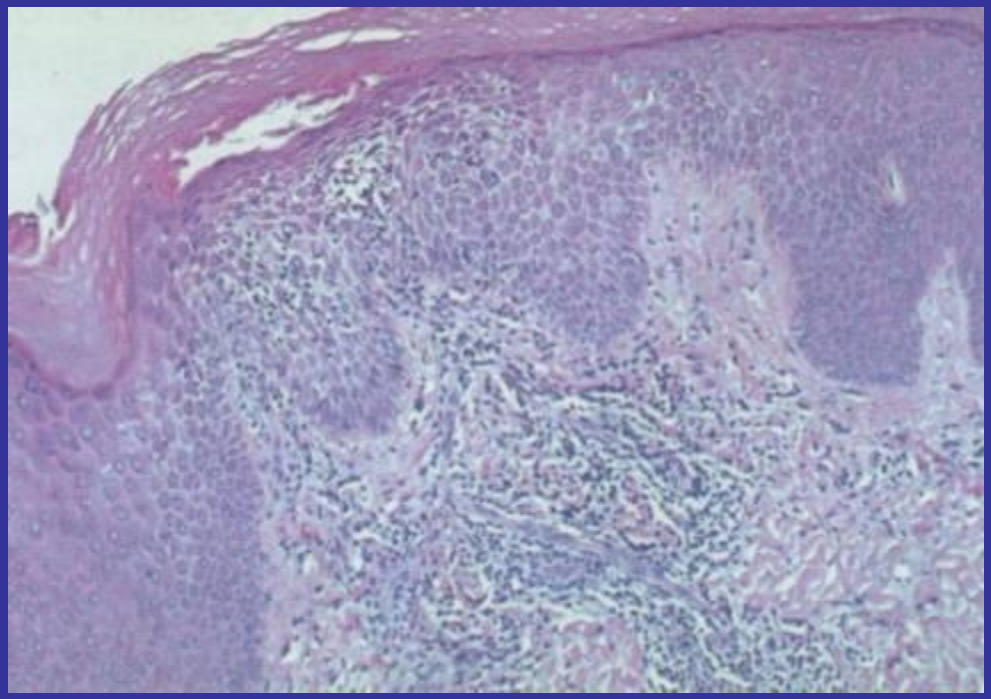
Morphology

- Acute and lymphomatous variants
  - Skin
    - Epidermal infiltration with Pautrier-like microabscesses



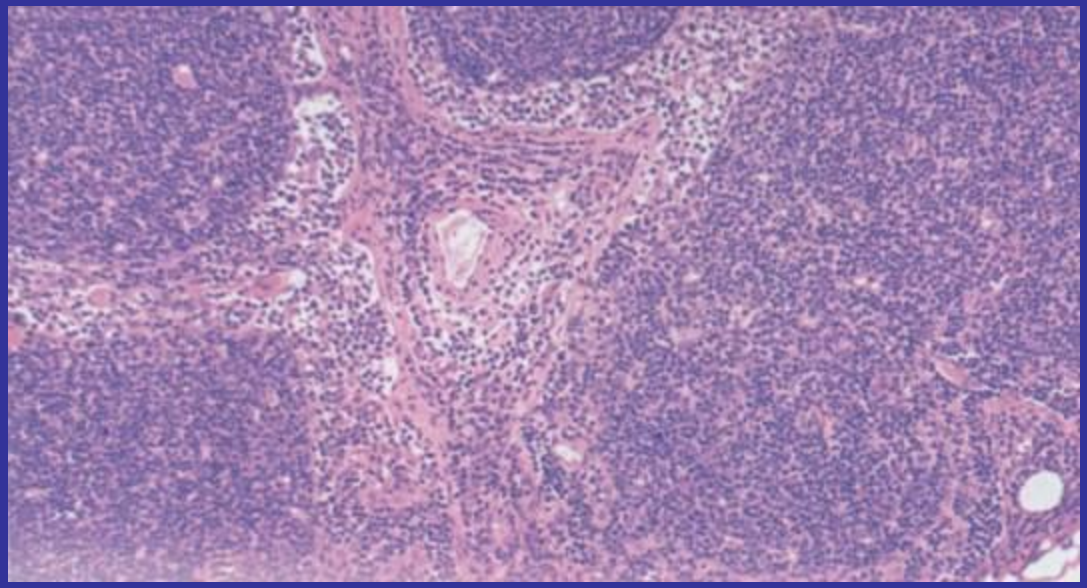
Morphology

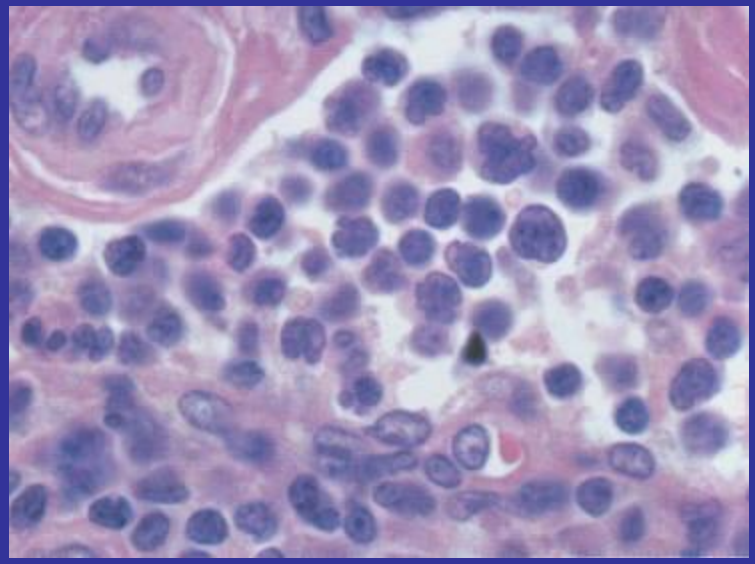
- Chronic and smoldering variants
  - Small cells
  - Minimal cytological atypia
  - Skin
    - Sparse dermal infiltrate
    - hyperkeratosis



Morphology

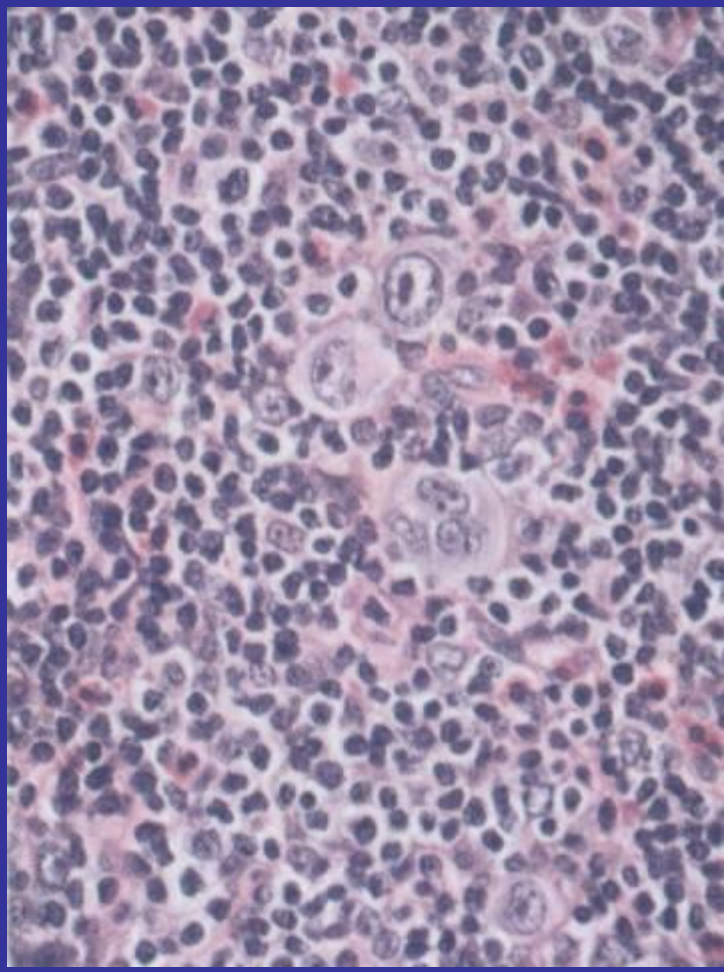
- Lymp node
  - Some cases may show a leukemic pattern of involvement (malignant cells in preserved or dilated sinuses)





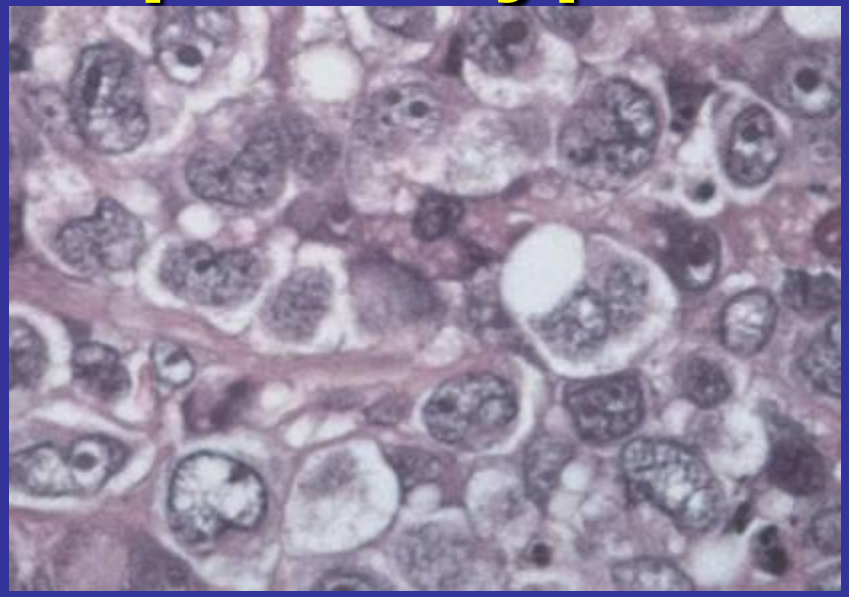
Morphology

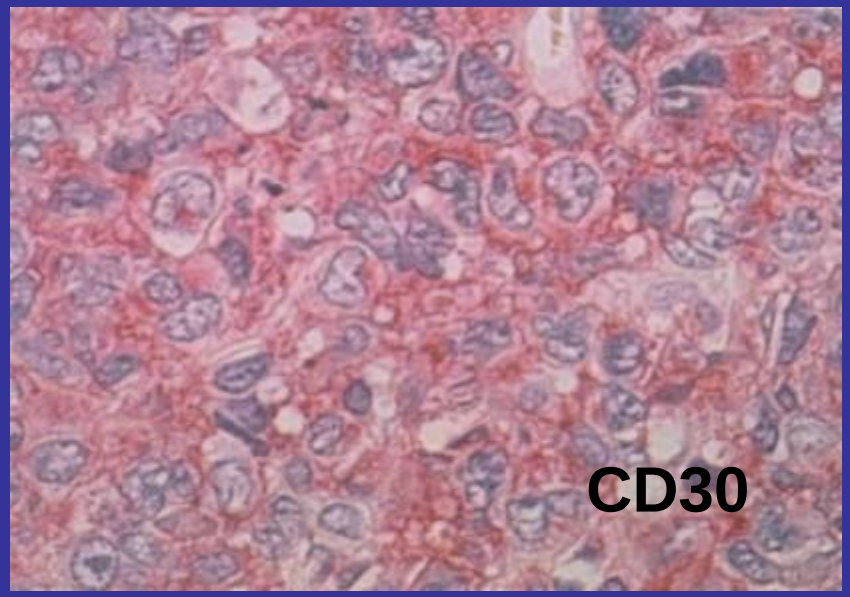
- Early and smoldering variants may show Hodgkin lymphoma-like LN histology
  - **Paracortical areas expanded with a diffuse infiltrate**
  - **Small to medium-sized lymphocytes with mild nuclear irregularities, indistinct nucleoli, scant cytoplasm**
  - **Interspersed RS-like cells and giant cells with lobulated nuclei (EBV and CD15/30 positive)**
  - **Progresses to overt ATLL within months**



ATCLL: Immunophenotype

- Positive for
  - CD2/3/5/25
- Usually negative for
  - CD7
- Most cases are CD4+/CD8-
- Large transformed cells
  - May be CD30+
  - But negative for ALK / TIA-1 / granzyme B





Genetics

- Consistent TCR beta rearrangement
- Clonally integrated HTLV-1 found in all cases
- Possible loss of putative tumor suppressor gene on 6q (6q15-21)
- Alteration of p16 and p53

Postulated Cell of Origin

- Peripheral CD4+ T cells in various stages of activation

Prognosis

- Prognostic factors
  - Clinical subtype
  - Age
  - Performance status
  - Serum Ca
  - Serum LDH

Prognosis

- Survival
  - Acute and lymphomatous variants
    - 2 wks to > 1 year
    - Causes of death
      - Infectious complications
        - » PCP
        - » Cryptococcus meningitis
        - » Disseminated herpes zoster
      - Hypercalcemia
  - Chronic and smoldering variants
    - longer survival
    - Can transform into an acute phase (aggressive)