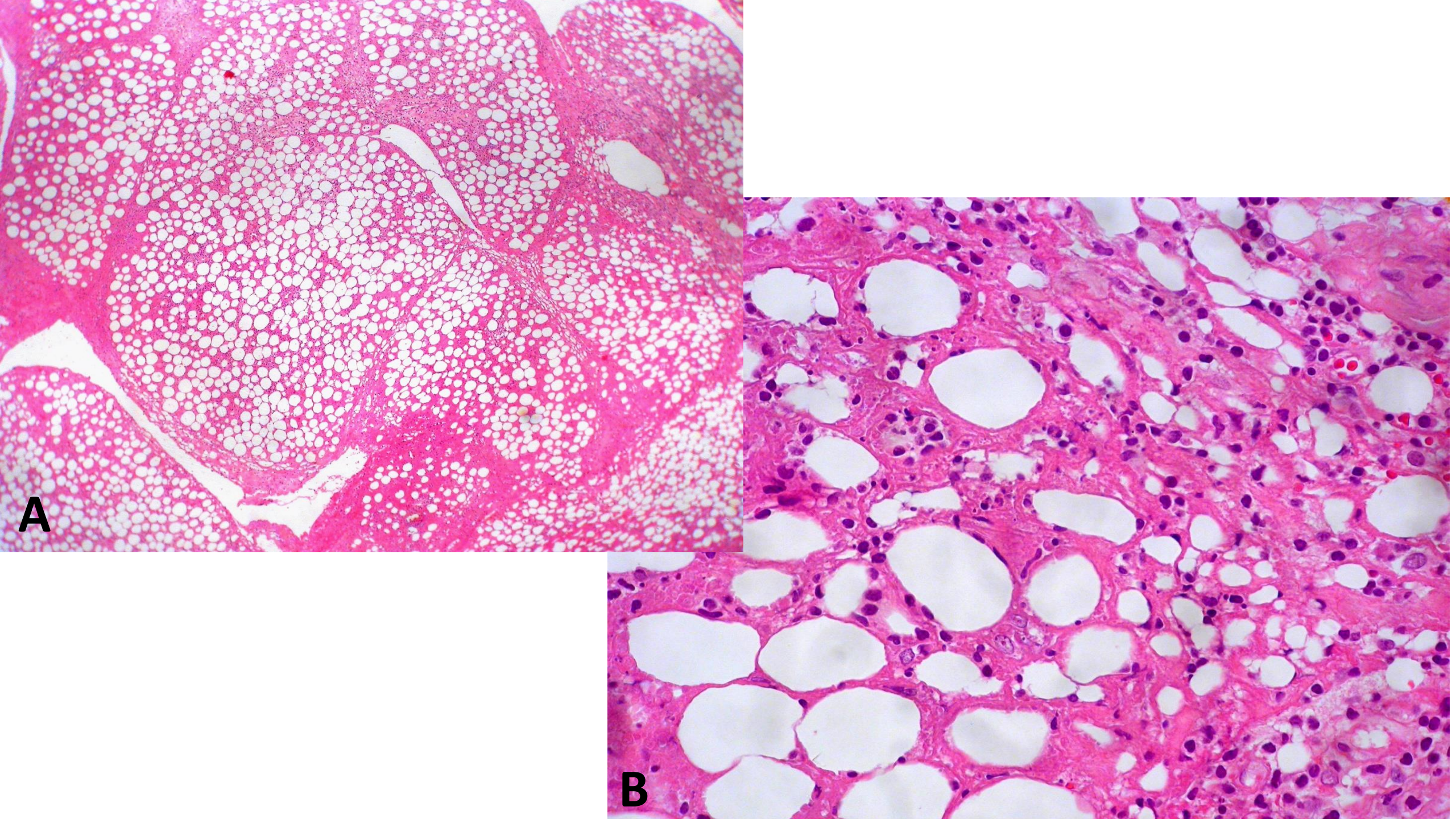
Pathologic features

- Histopathologic features show diffuse infiltration of subcutaneous fat by isolated and aggregates of small to medium lymphocytes with hyperchromatic nuclei, irregular nuclear contours and scanty pale staining cytoplasm. Many apoptotic bodies are seen. There is also typical rimming of the adipocytes by infiltrating atypical lymphoid cells(Fig: 1).
- On immunohistochemical staining, the tumor cells show positive CD3, CD8, and granzyme B (Fig: 2); and negative CD20, CD4, and CD123.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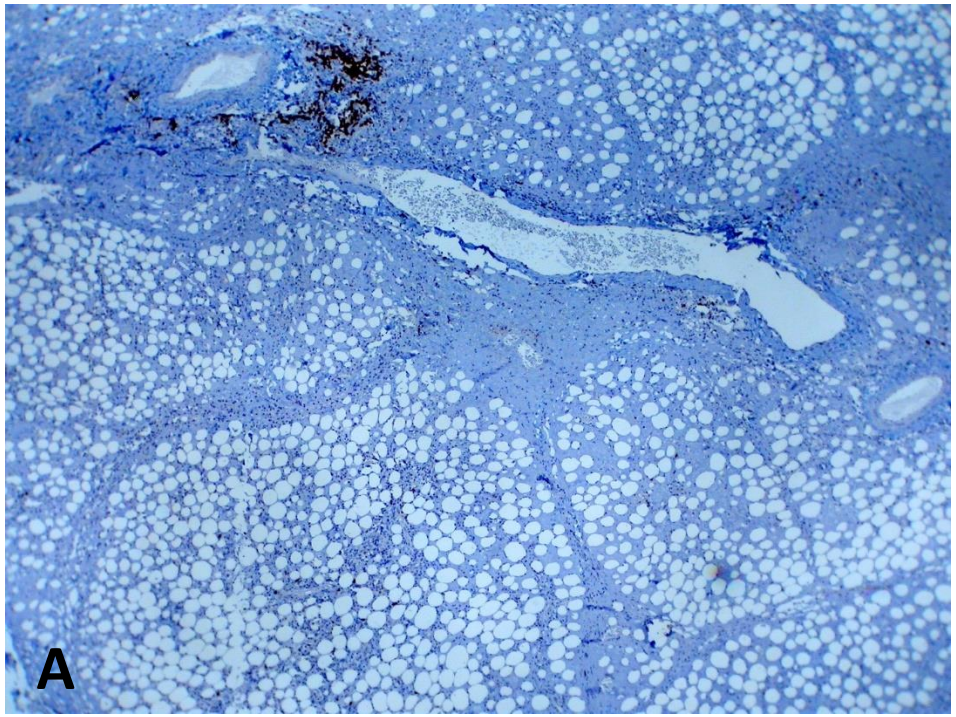
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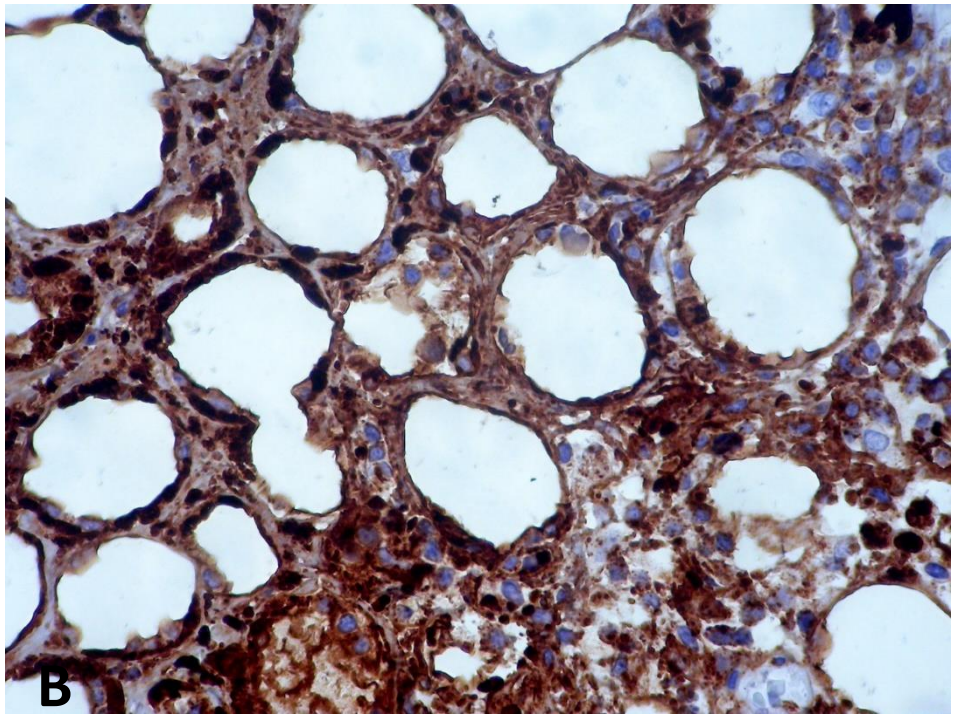
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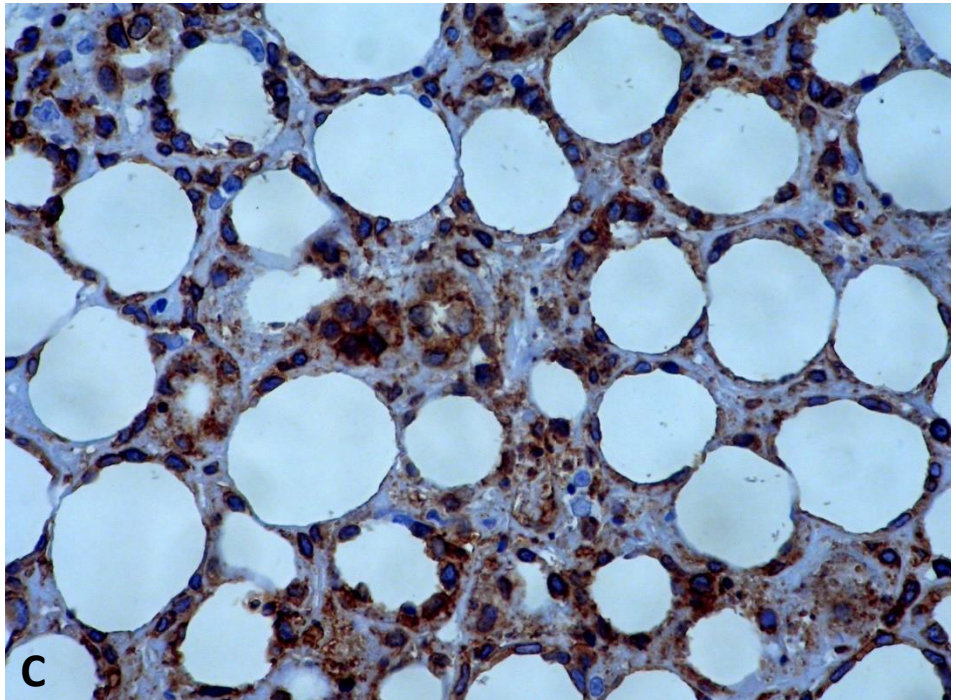
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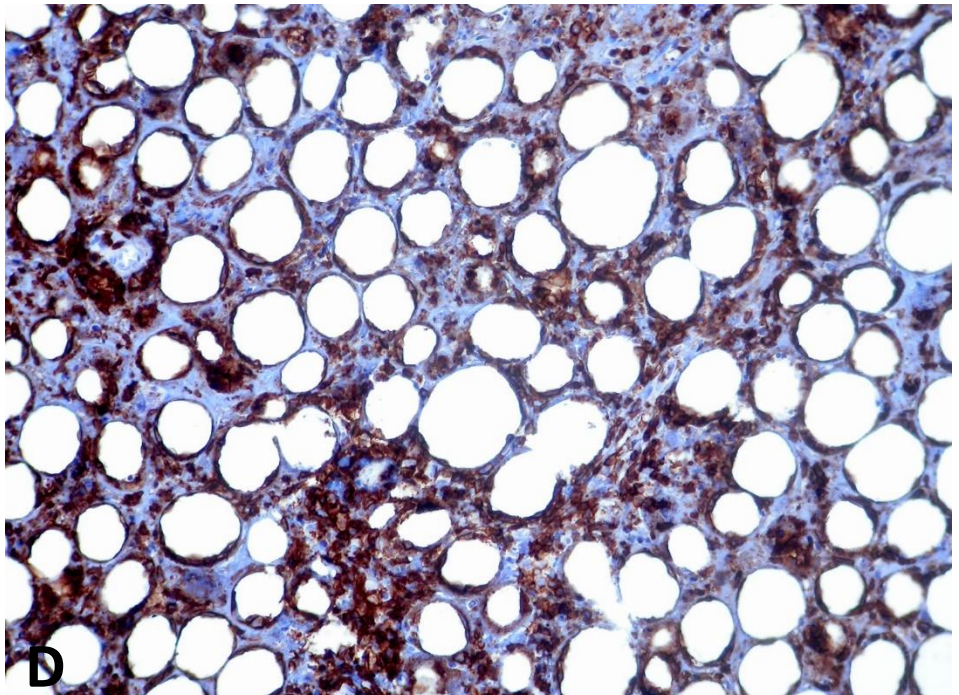
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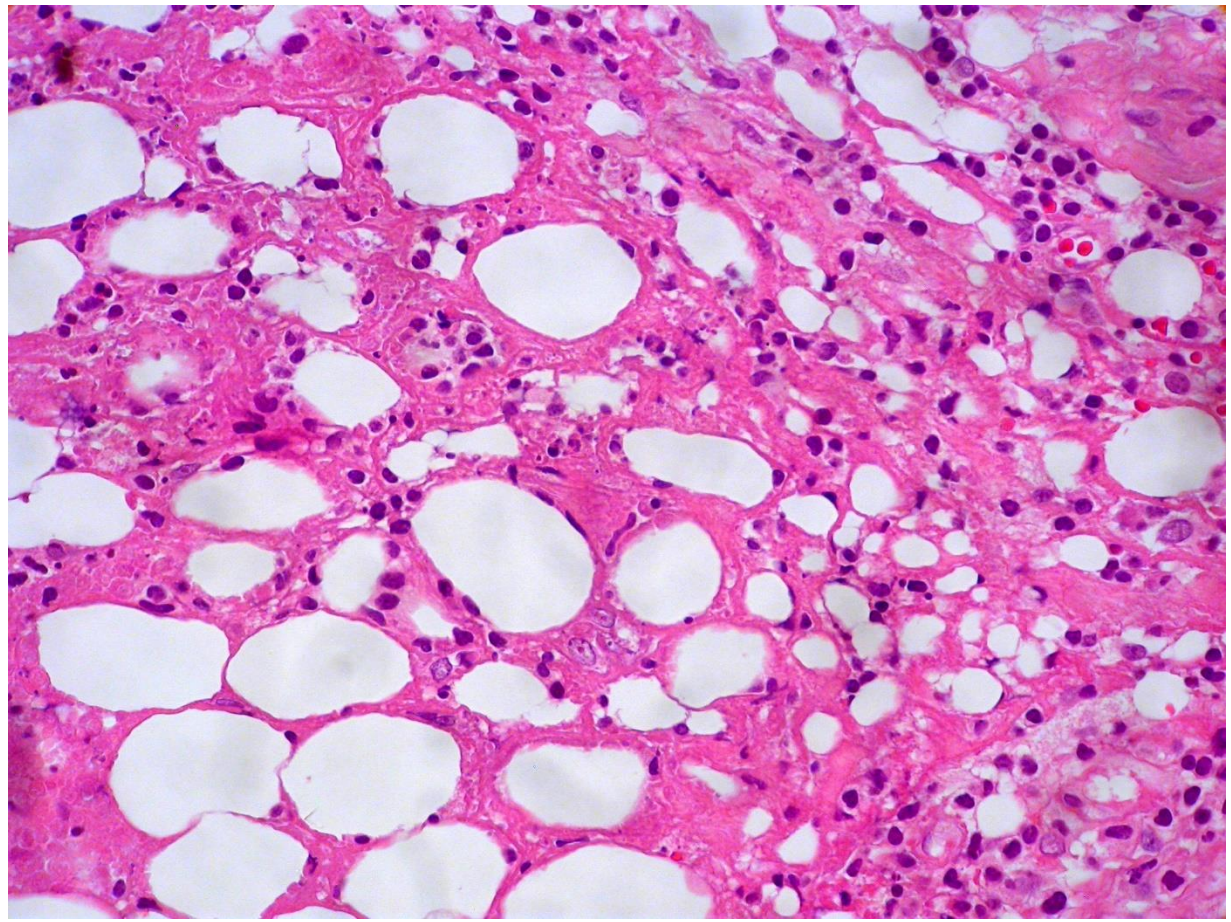
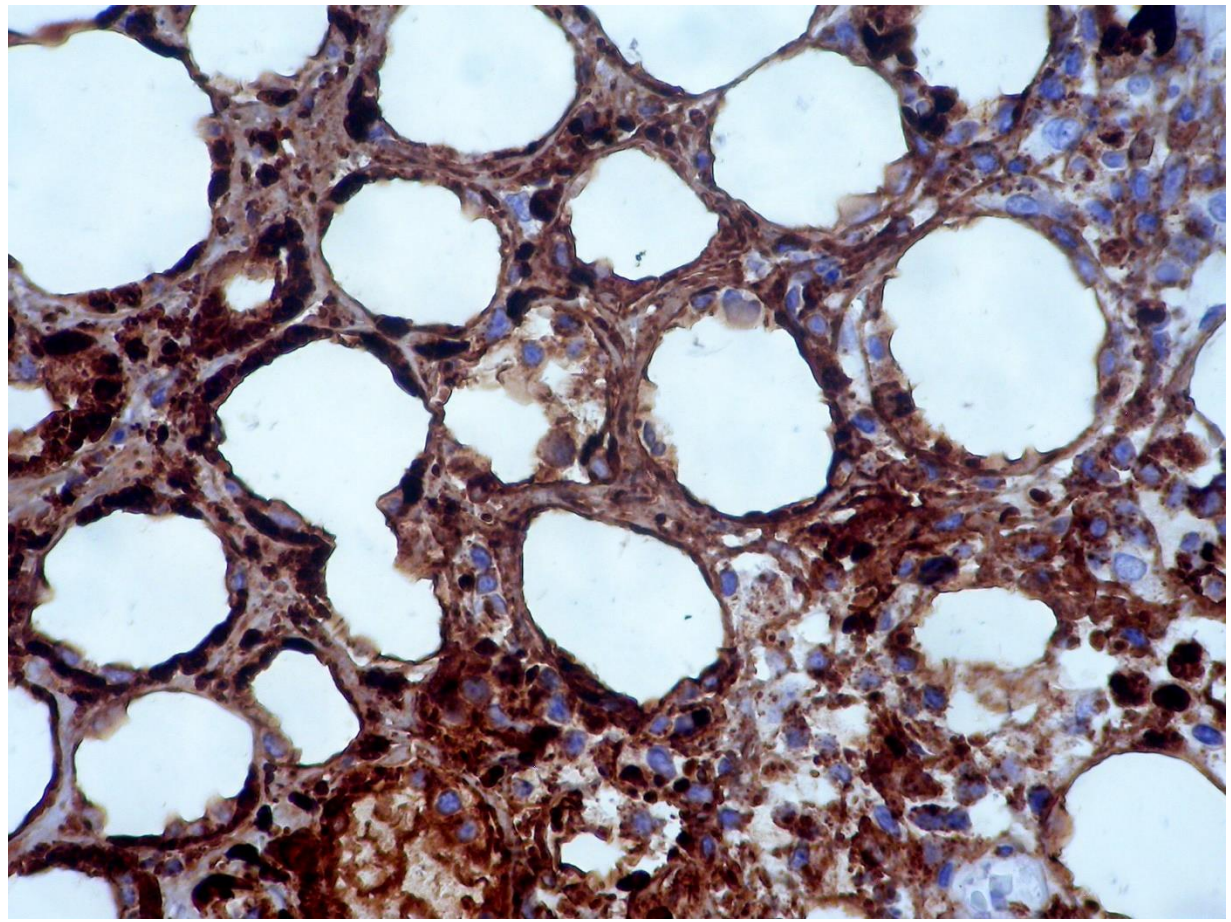
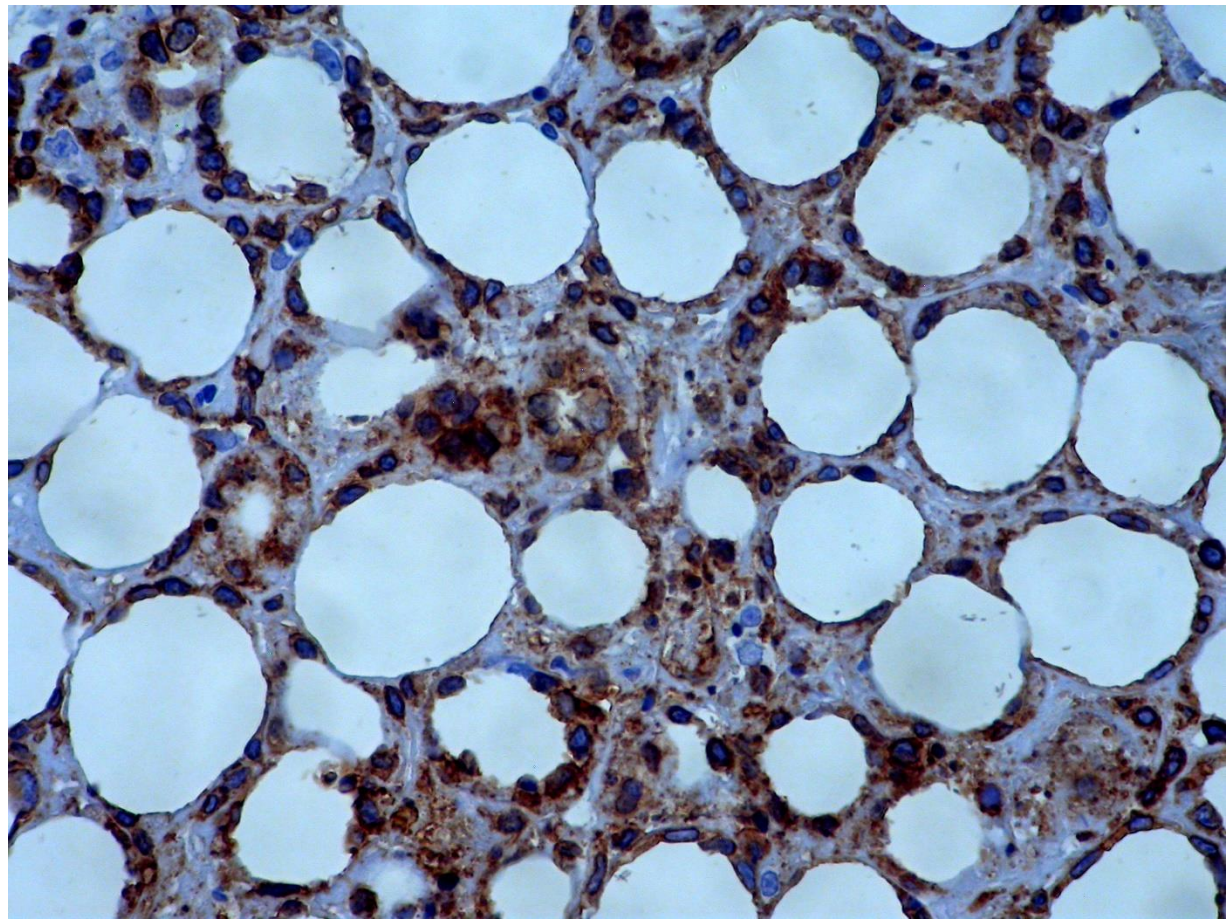
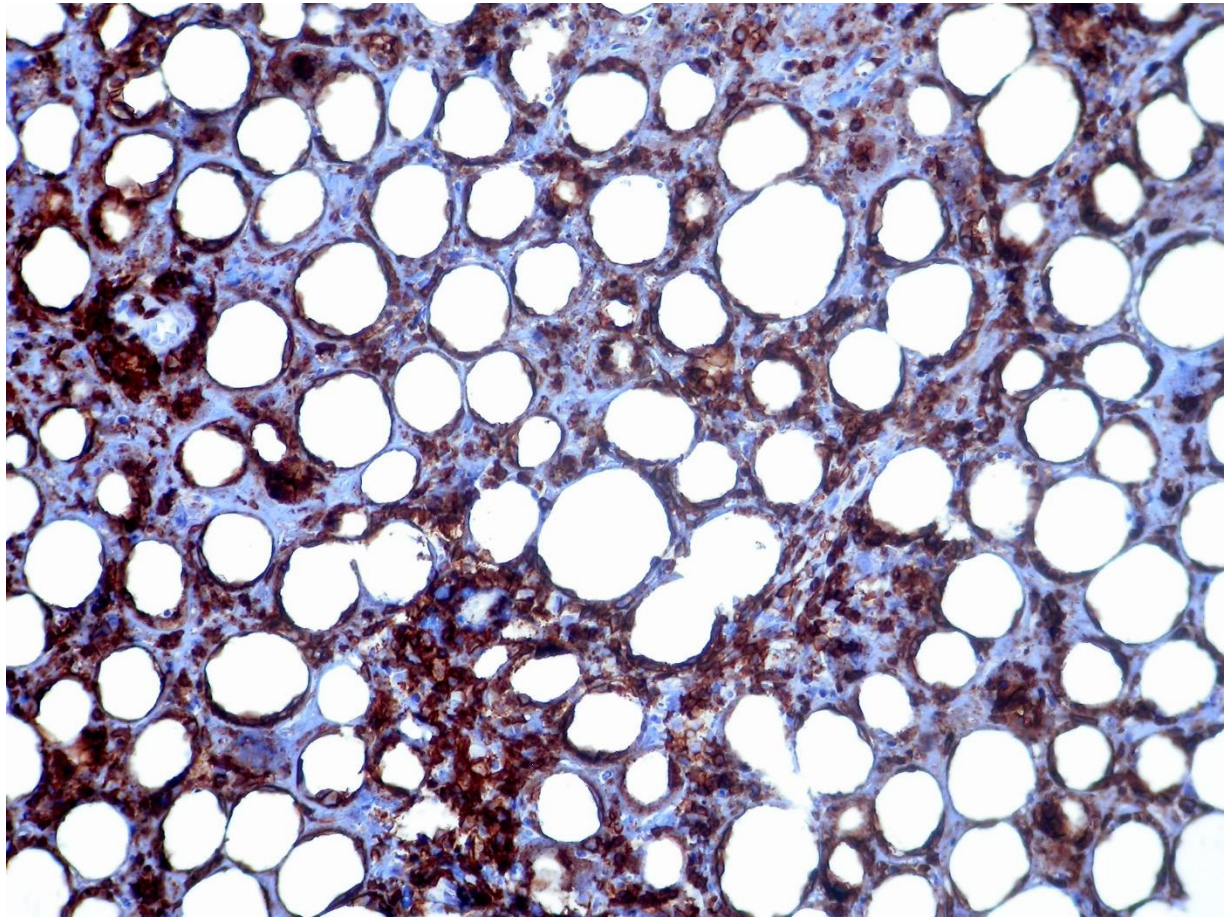








110 of 524

Patient Clinical Data: Name: Baran Surname: Ghadiri Gender: female Age: 11 y/o Birth Date: 24.06.2008 Dear Robert Dear Mighdel This is an 11 y/o female with his

56

Hasserjian, Robert Paul,M.D. <RHASSERJIAN@mgh.harvard.edu> Jul 15, 2019, 12:15 PM

to me, mapirispinilla@gmail.com

Dear Farid:

I reviewed these images. The cells are very atypical, definitely cytotoxic T-cell type. The clinical presentation of orbital disease in a child does seem unusual, but I would also favor a PTCL, subcutaneous panniculitic type. Can you do TCR alpha-beta/gamma delta? EBER would also be of interest. Does the child have an evidence of hemophagocytic syndrome?

12 Best,

Rob

12

From: Farid Kosari <faridkosari@gmail.com>

Sent: Sunday, July 14, 2019 11:22 AM

To: Hasserjian, Robert Paul,M.D.; mapirispinilla@gmail.com

Subject:

External Email - Use Caution

56

mapiris <mapirispinilla@gmail.com>

to me, Robert

Jul 15, 2019, 1:22 PM

Dear Farid, I basically concur with Bob, this looks like a panniculitic T-cell lymphoma
A pair of comments
- Ki67 staining is useful, should depict a rim of Ki67-positive cells surrounding adipocytes
- Sequencing study could show interesting data. There have been a pair of papers describing (Nat Genet. 2018 Dec;50(12):1650-1657) mutations associating STCL with hemophagocytic lymphohistiocytic syndrome.
- Cerroni has described some overlapping cases (Am J Surg Pathol. 2015 Feb;39(2):206-11.) between lupus and STCL, this could be a case

12

In case you are interested we can do the sequencing for you
Warmest wishes
Miguel

12

Dr Miguel A Piris
Associate Medical Chief
Pathology Service
Fundación Jiménez Díaz
Av Reyes Católicos, 2
28040 Madrid
Tel 34 91 550 4804
e-mail: miguel.piris@quironsalud.es
http://www.fjd.es/iis_fjd

Subcutaneous Panniculitis type T cell lymphoma

Definition

- A cytotoxic T cell lymphoma that preferentially infiltrates subcutaneous tissue with atypical cells of varying size, showing prominent fat necrosis and karyorrhexis
- Cases expressing the γδ T-cell receptor are excluded and now reclassified as primary cutaneous γδ T-cell lymphoma

Clinical features

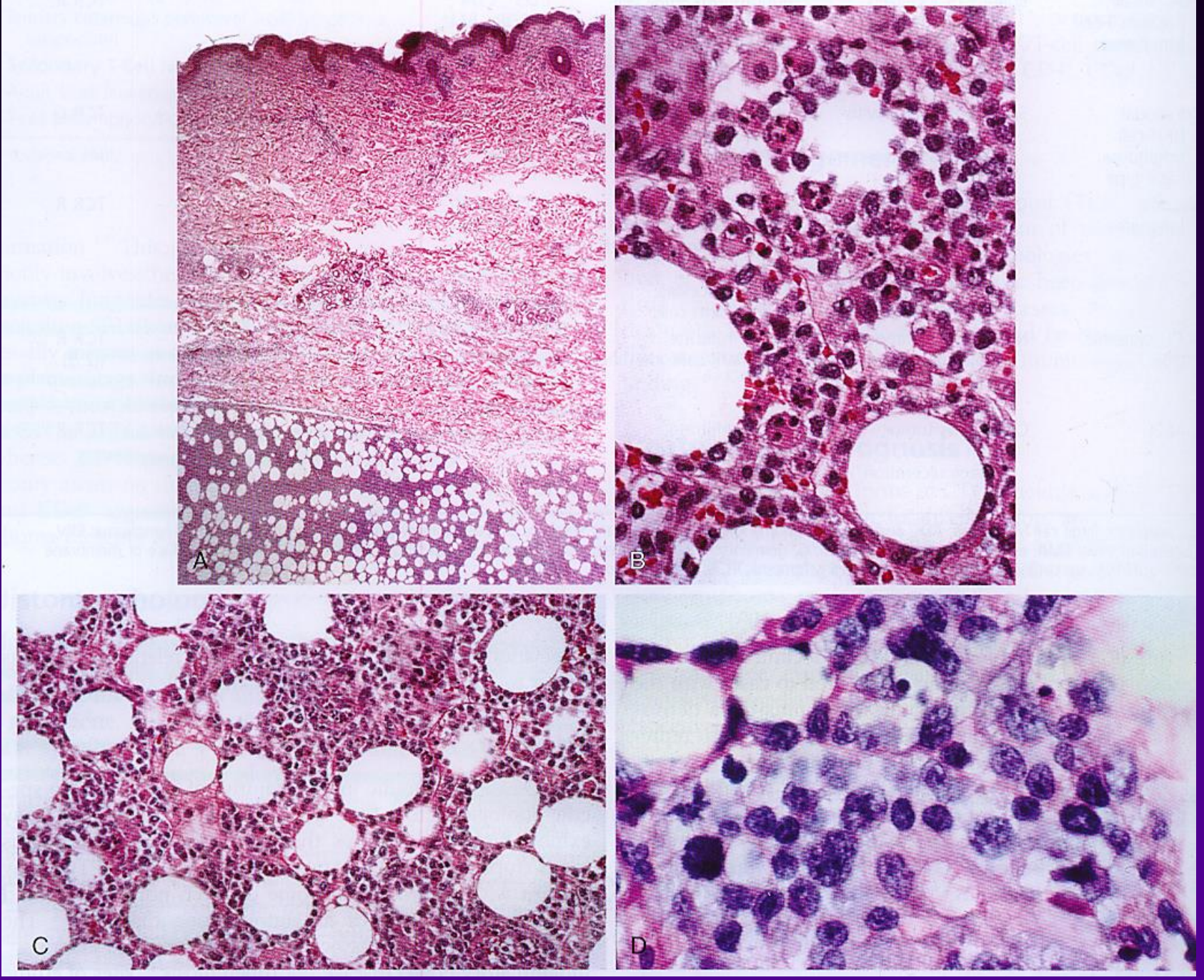
- Slightly more common in females
- Broad age range most (20%) in young adults
- The relationship with SLE is unclear (Jaffe) ➔Up to 20% associated with autoimmune disease most commonly SLE
- The lesions may show overlapping features with lupus profundus panniculitis: fever, polyarthritis, pericarditis
- May be associated with: RA, TB, IBD, or transplantation
- No association with EBV or Borrelia infection

Clinical Manifestation

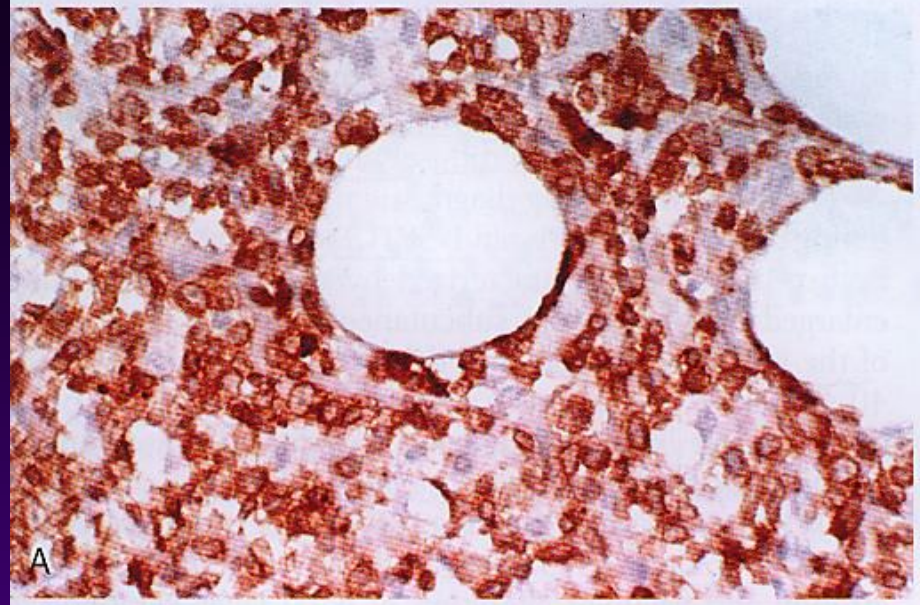
- One or more subcutaneous nodules often misdiagnosed as panniculitis, ulceration is rare
- The most common sites: Lower extremity; Upper extremity and trunk may also involved
- Tumors: may be small or large, but rarely ulcerate, ddx: abscess, may be associated with systemic symptoms: fever, fatigue, and weight loss
- Hemophagocytic syndrome: (pancytopenia, fever, and hepatosplenomegaly) IS RARE (JAFFE) ➔ with signs of marrow failure and associated with aggressive clinical course
- LAP is usually absent

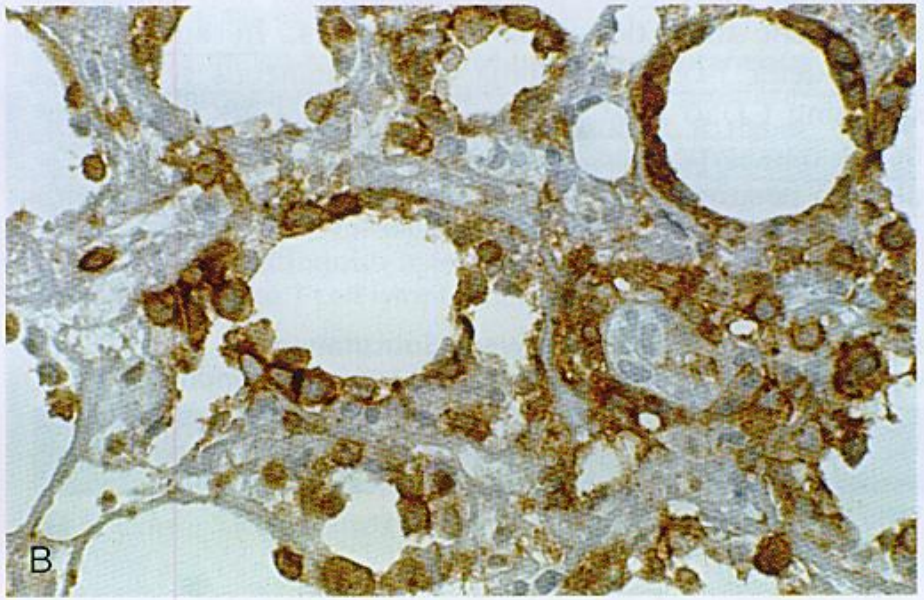
Morphology

- **The overlying dermis and epidermis are minimally involved (Jaffe)**
- Variable mixture of small medium and large atypical cells often containing irregular hyperchromatic nuclei and pale cytoplasm
- Reactive histiocytes with phagocytozed nuclear debris or lipid are numerous
- Granuloma may be present but not a dominant feature
- **Individual adipocytes are rimmed by neoplastic cells: a helpful diagnostic feature**
- **Necrosis and karyorrhexis are common: helpful in the differential diagnosis from other lymphomas**
- **Erythrophagocytosis can be seen but the degree is variable**
- **Other inflammatory cells are typically absent, notably plasma cells: common in lupus panniculitis**
- **Vascular invasion is seen and may be associated with regions of necrosis**


A
B
C
D

- Immunophenotype:
  - Pan T cell Ag +, CD8+, CD4-
  - TIA-1, granzyme B, and perforin +
  - βF1 positive
  - Rarely: CD56, CD30 positive
  - Granzyme M is negative: helpful in distinguishing αβ from γδ tumors
- Genetics:
  - T cell receptor γ gene is rearranged
  - Negative for EBV
- Postulated cell of origin:
  - Mature cytotoxic αβ T cell





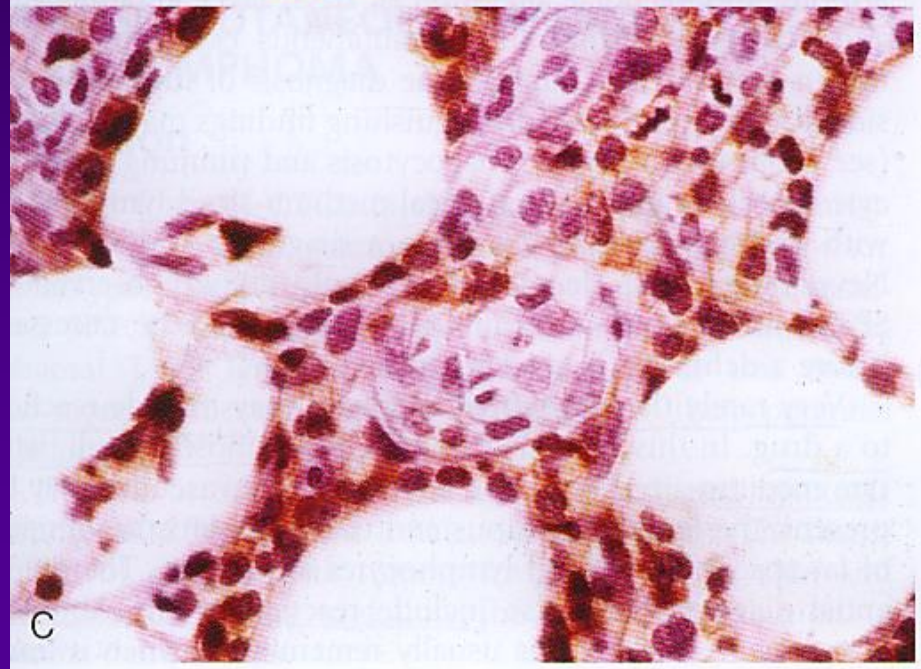
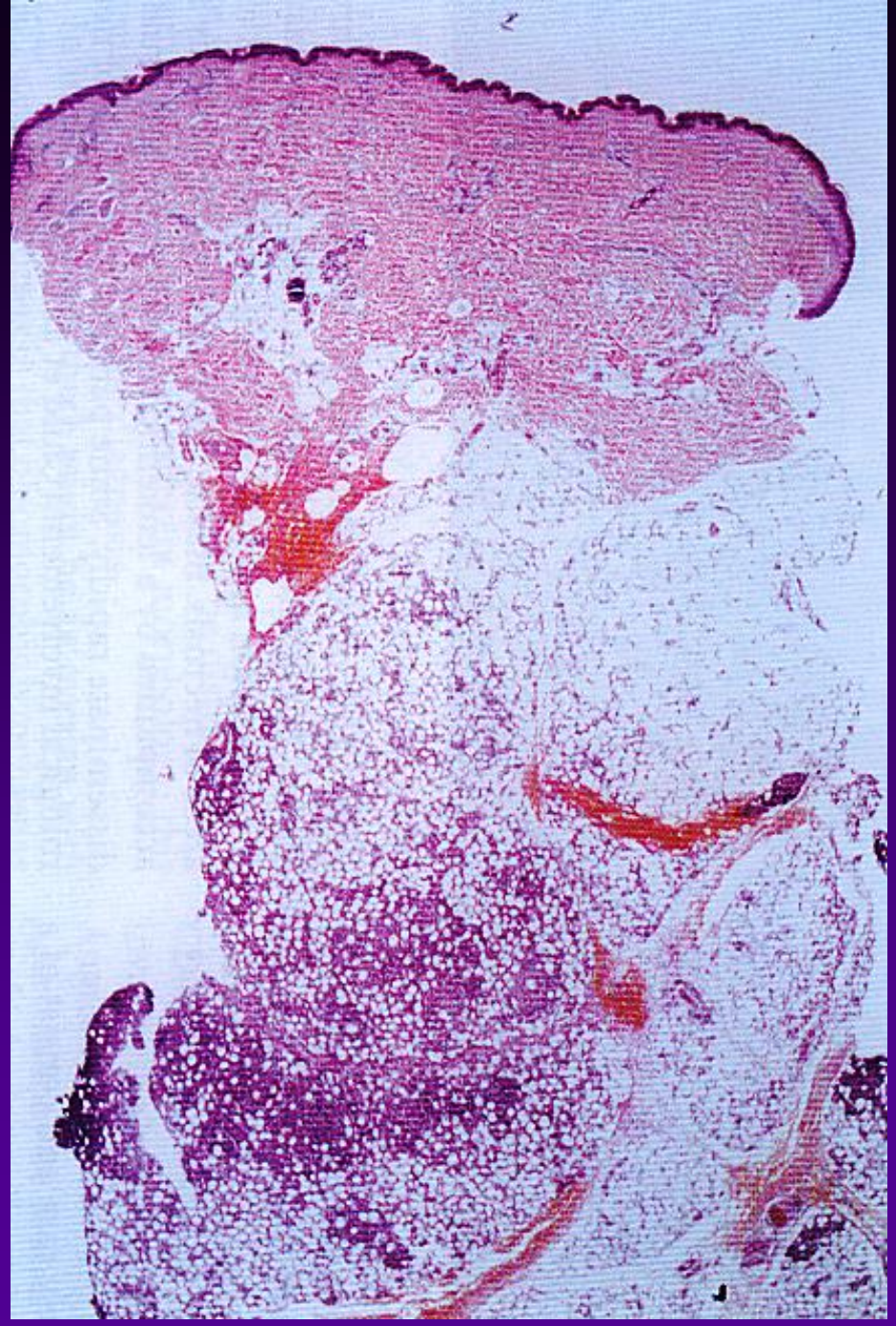


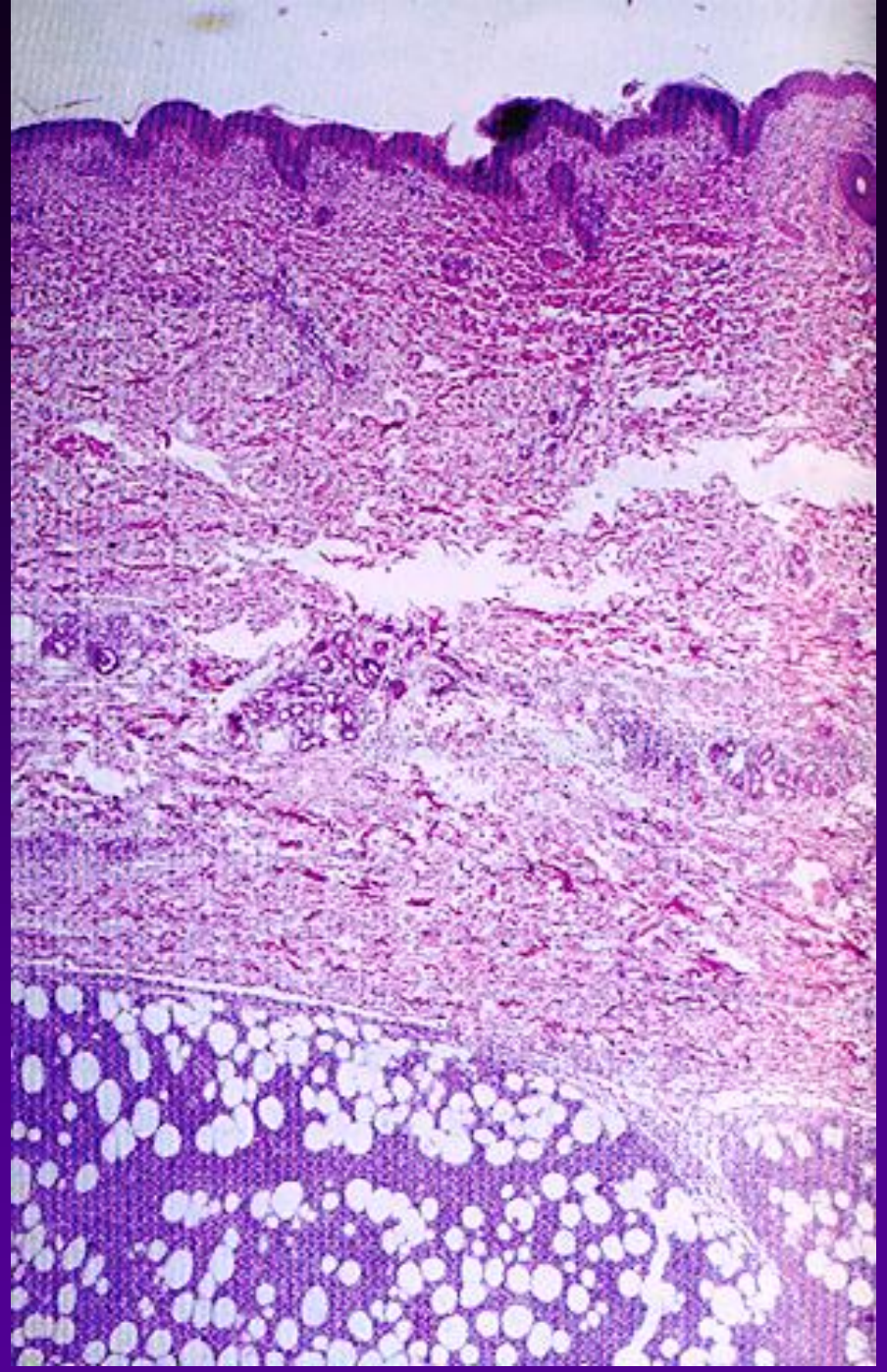
Figure 40-2. Immunophenotype of subcutaneous panniculitis-like T-cell lymphoma. A, The neoplastic cells are $CD3^+$. **B**, The rimming of fat spaces by tumor cells is highlighted by staining for CD8. **C**, The neoplastic cells express βF1. Note negative staining in the endothelial cells and a mitotic figure. (Courtesy Dr. E. Jaffe, Bethesda, MD)

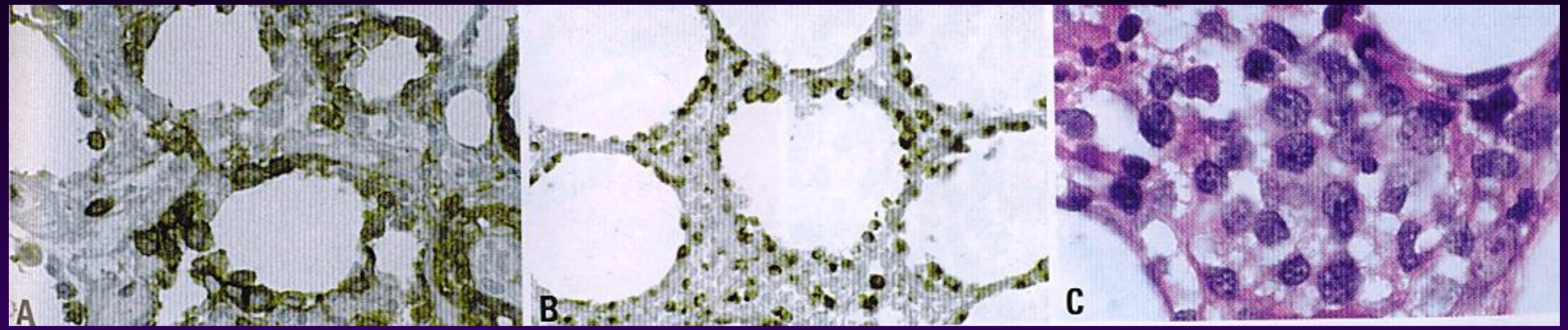
Clinical Course

- 5YS is 80%
- Local recurrences may occur over a period of several years, but the disease remains confined to the subcutis in most pts
- Dissemination to lymph nodes and other organs is rare
- If a hemophagocytic syndrome is present the prognosis is poor
- Distinction from cutaneous γδ T cell lymphoma is important, since SPTCL has a much better prognosis

- Although hemophagocytosis is rarely observed in subcutaneous tumors, histiocytes containing phagocytosed erythrocytes may be evident in BM and in the sinuses of lymph nodes



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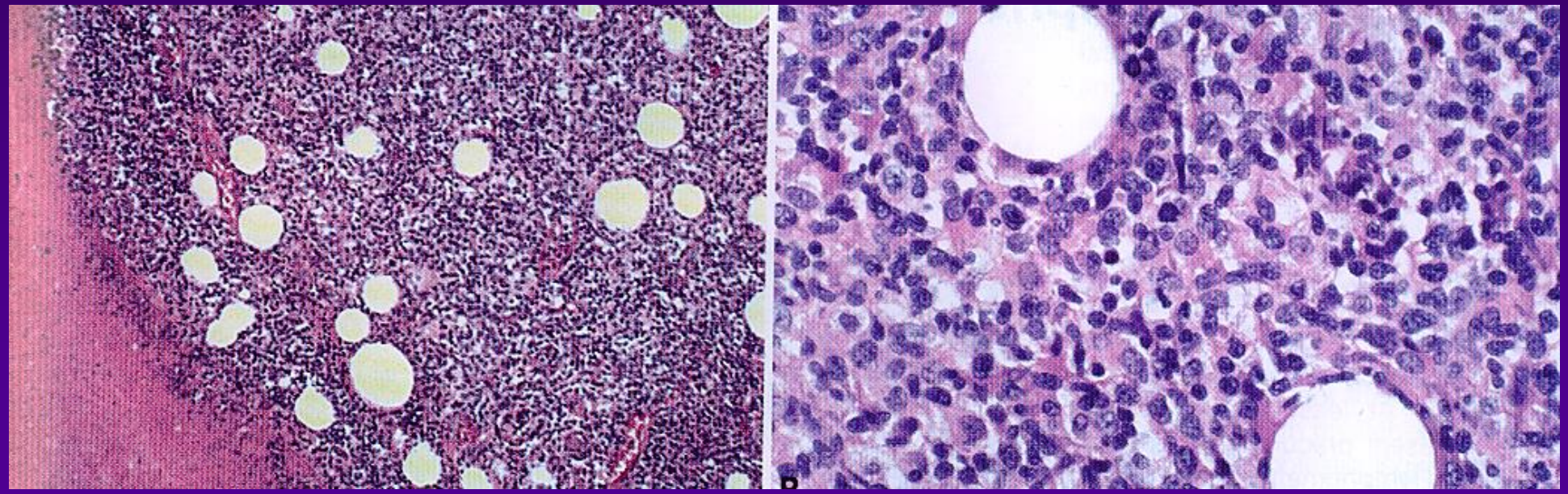

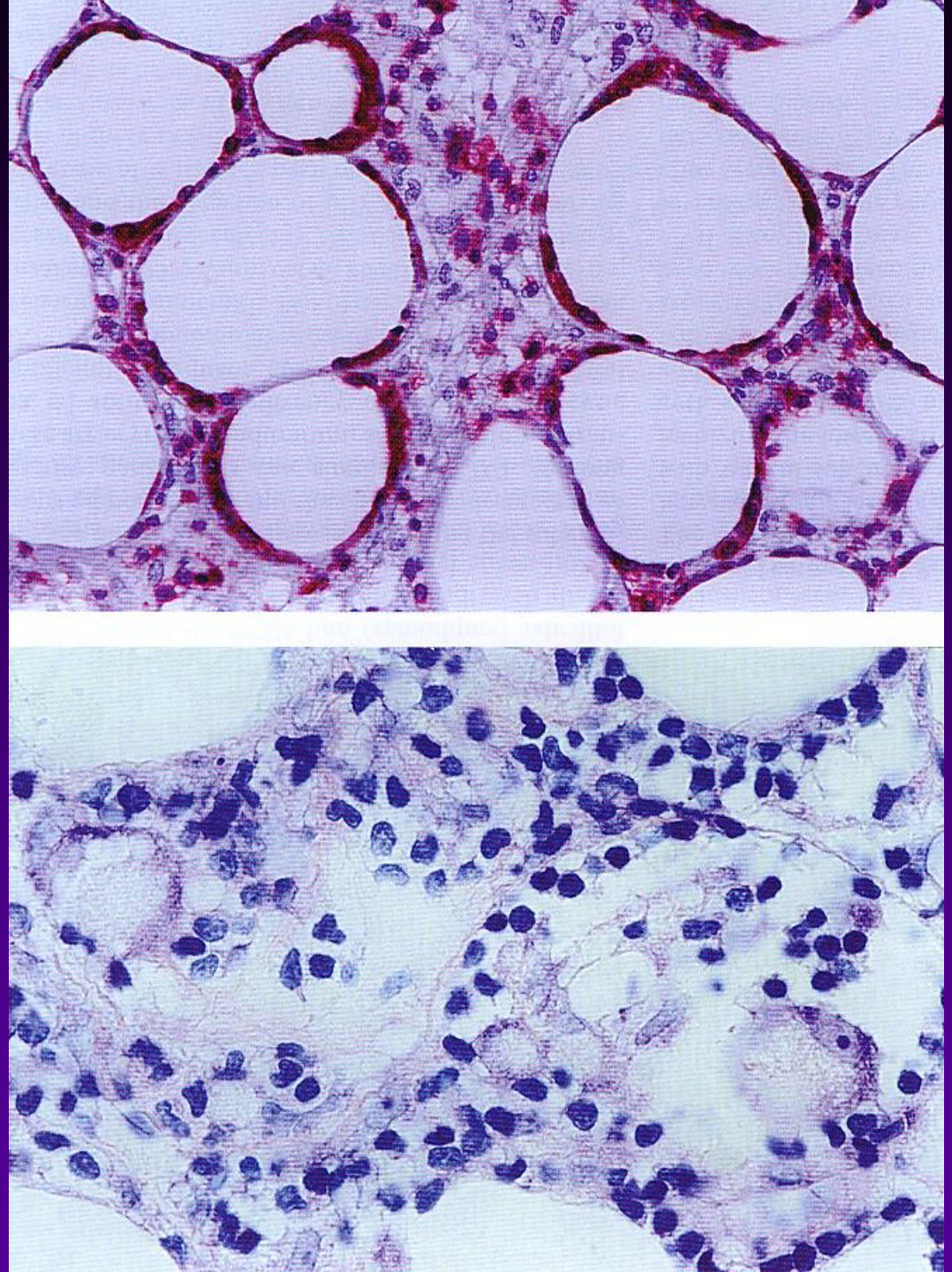

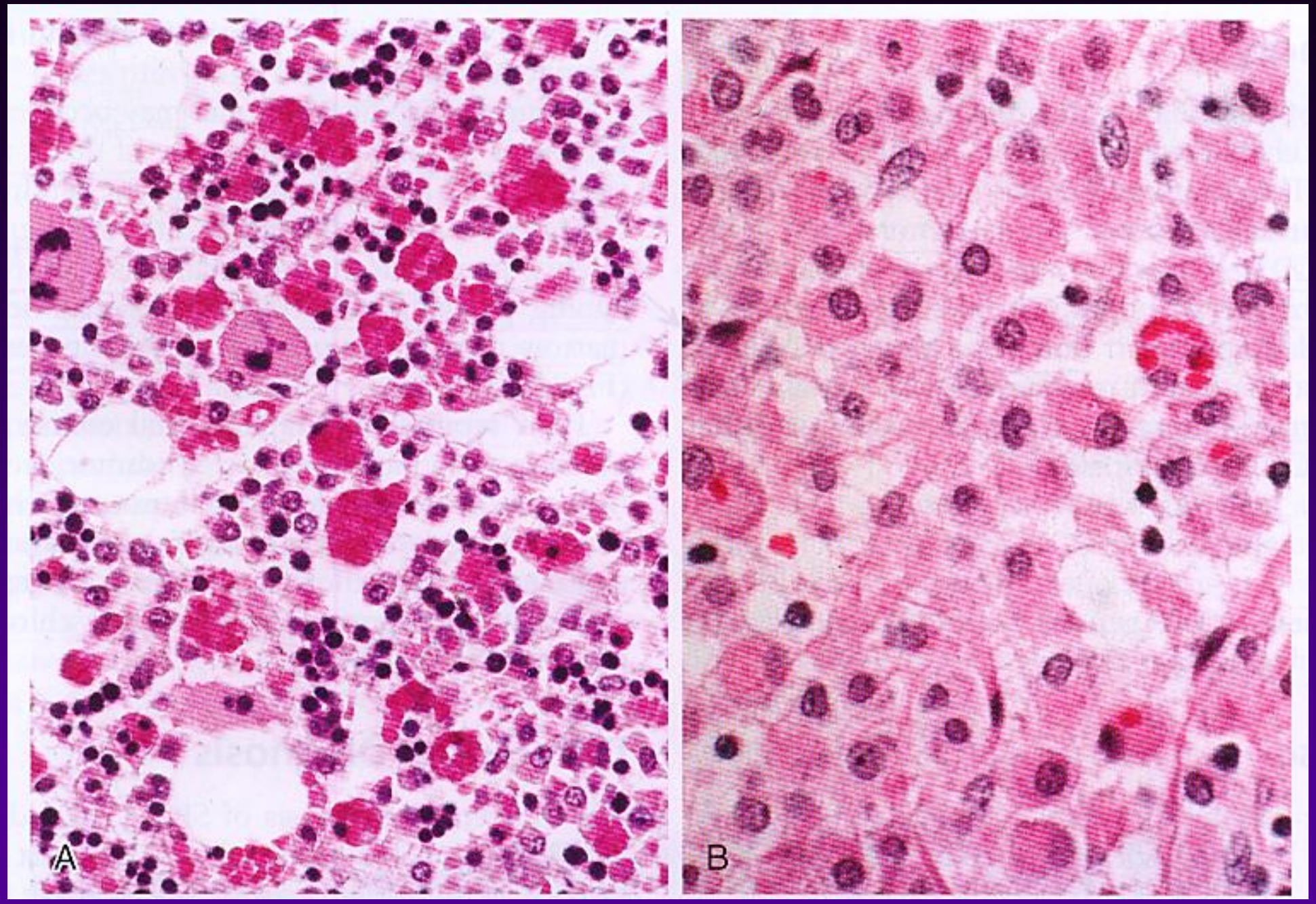
A
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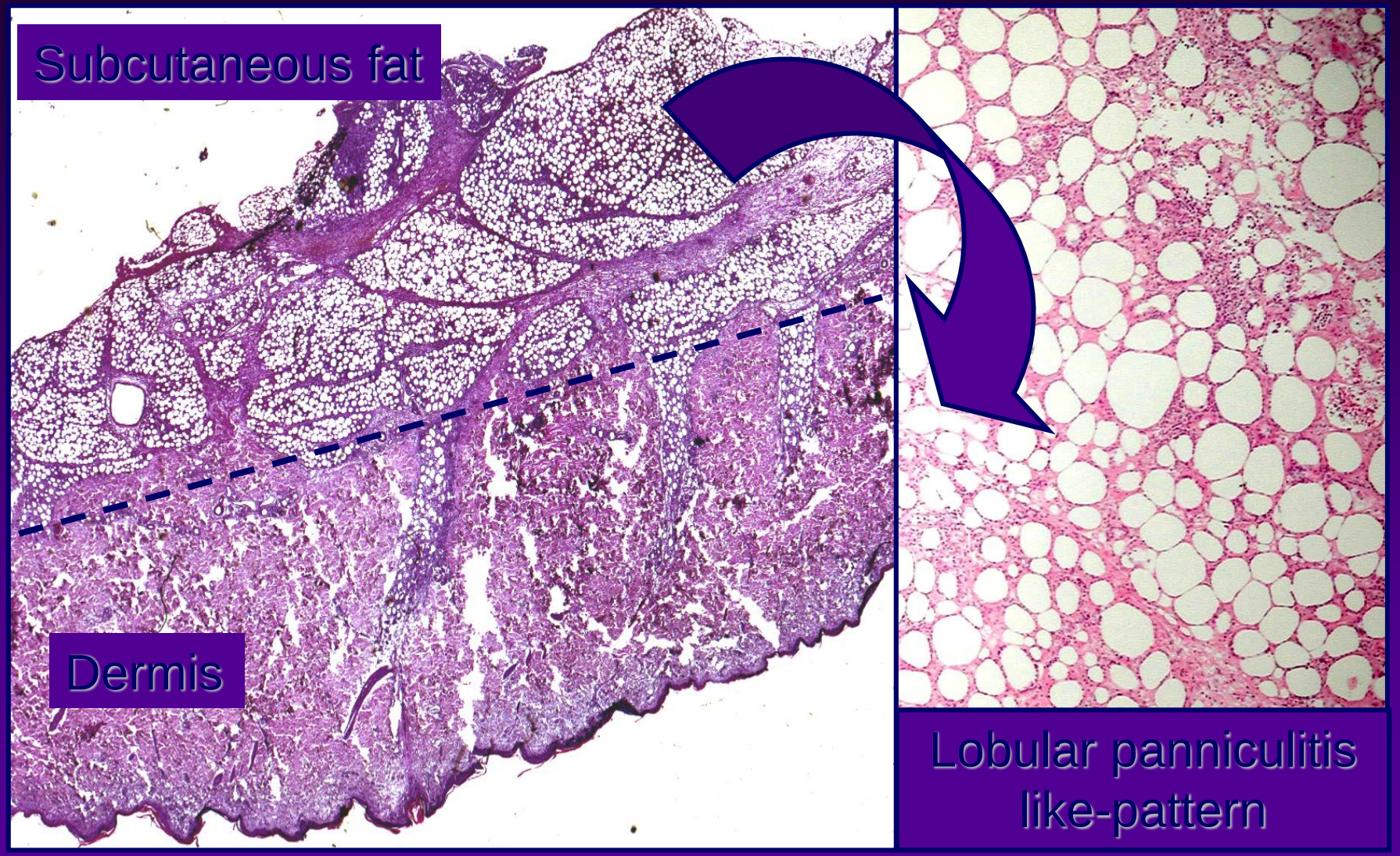
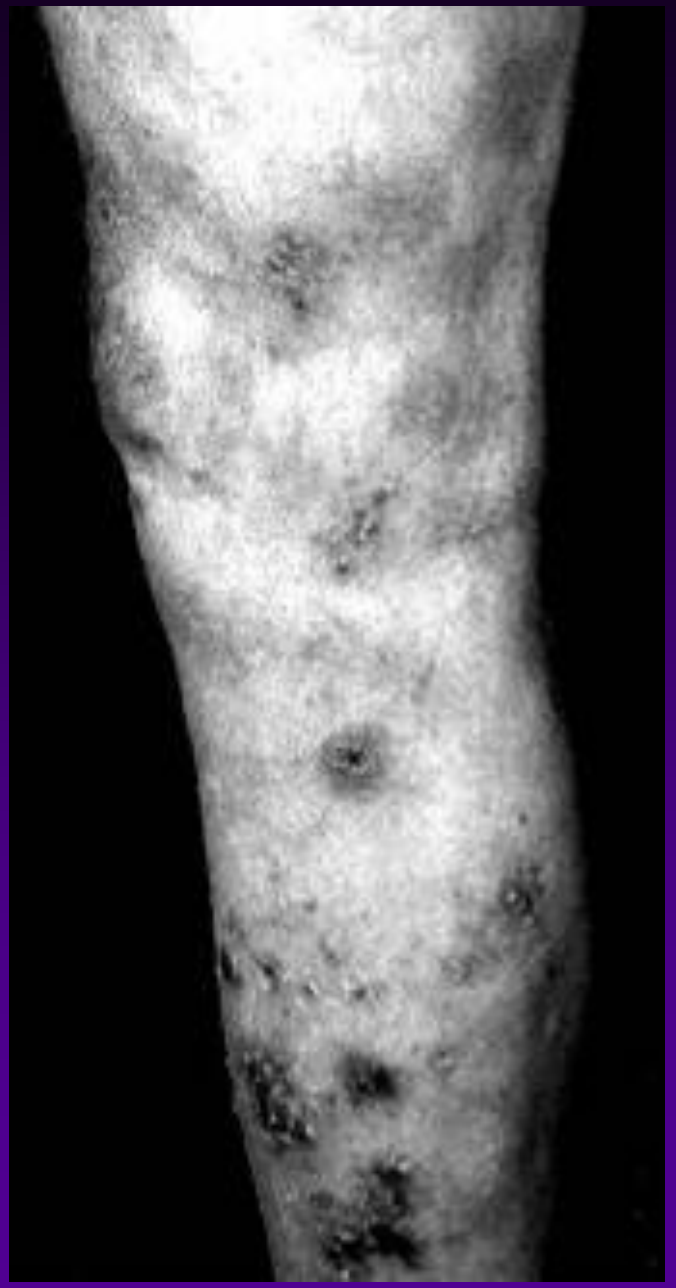
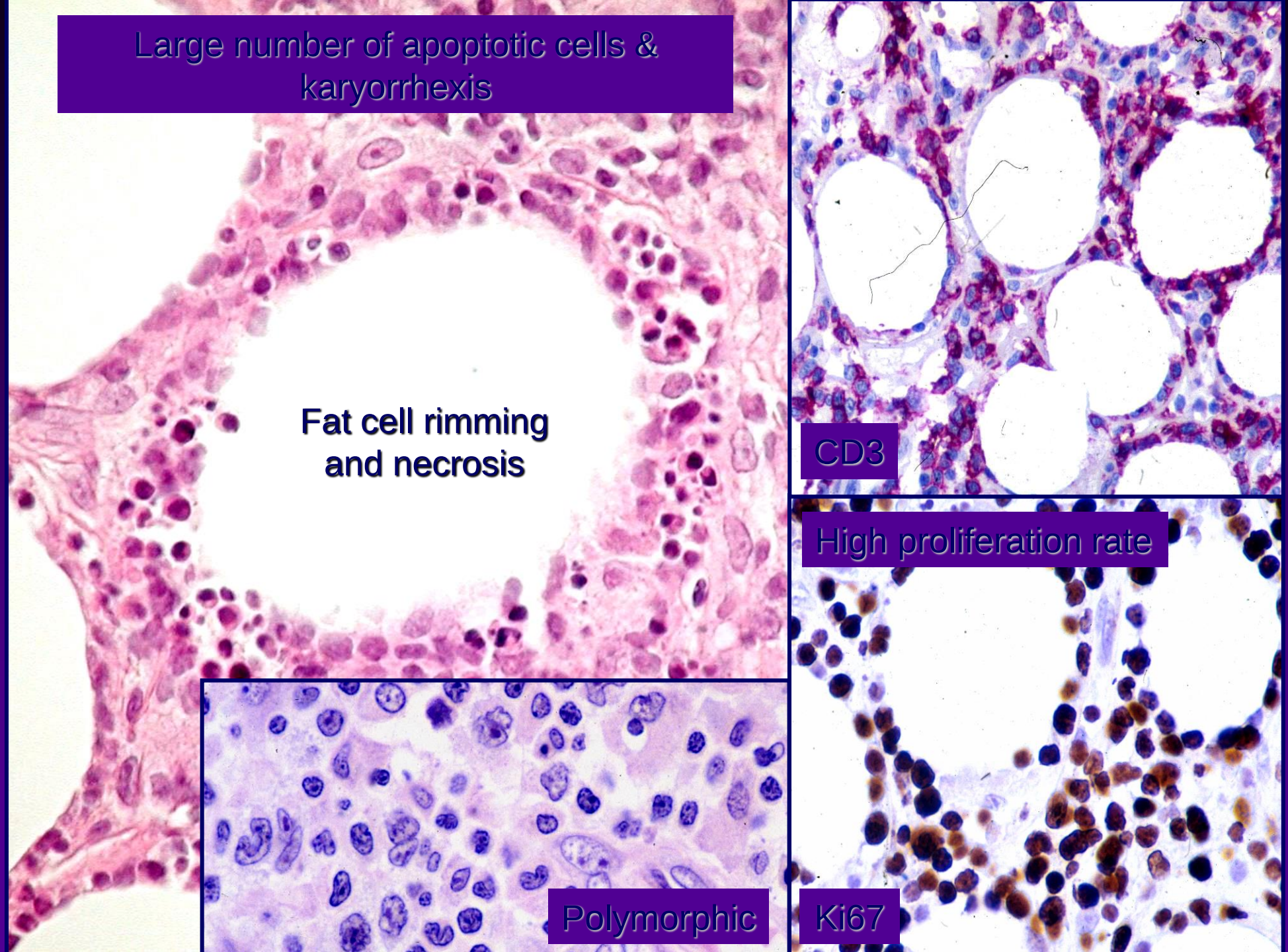
Subcutaneous panniculitis-like TCL



Clinical features

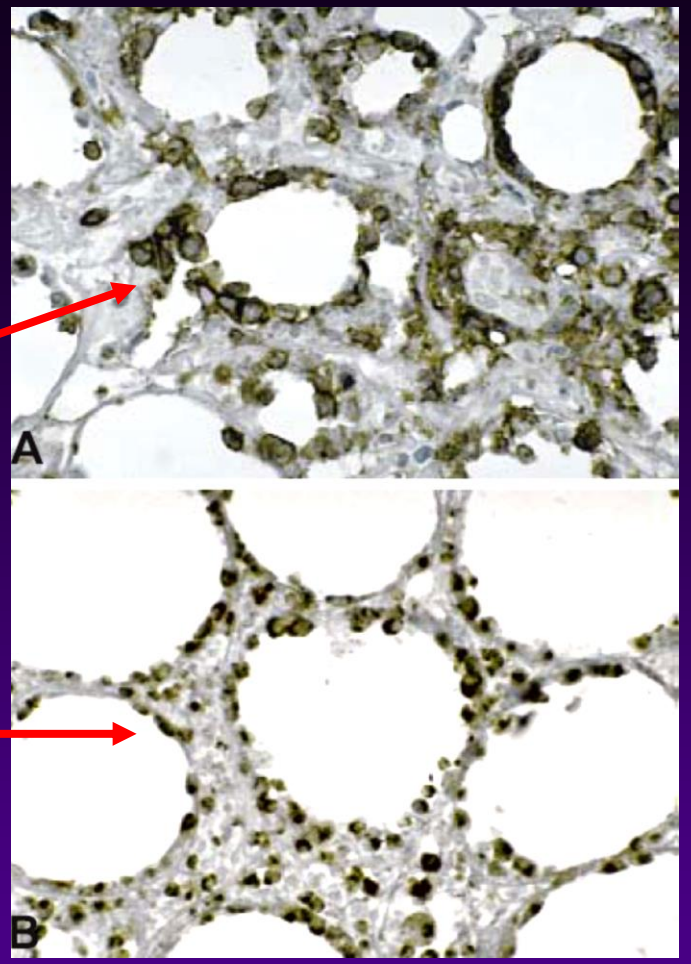
- The median age is around 35 years
- Slight female preponderance
- Clinical symptoms are primarily related to the subcutaneous nodules
- Systemic symptoms in half patients
- The majority of patients have disseminated disease; however, single lesions do occur
- The patients present with typical subcutaneous nodular infiltrates mostly involving the lower extremities and trunk




Large number of apoptotic cells & karyorrhexis
Fat cell rimming and necrosis
CD3
High proliferation rate
Polymorphic
Ki67

Immunophenotype:

βF1	+
CD2	+
CD3	+
CD4	-
CD8	+
CD56	-
TIA 1	+
Granzyme B	+
Perforin	+



Genotype:

- Monoclonal rearrangement of TCR genes. SPLTCL cells express α/β TCRs.
- EBV negative.
- No specific cytogenetic abnormalities

Clinics:

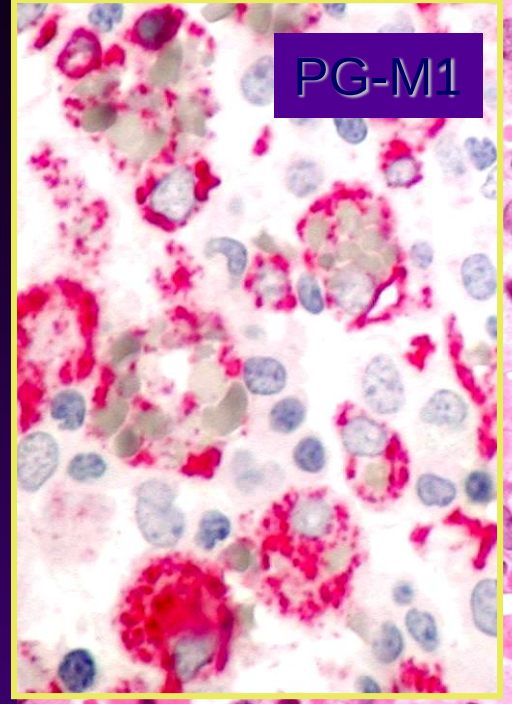
Involvement of organs rare

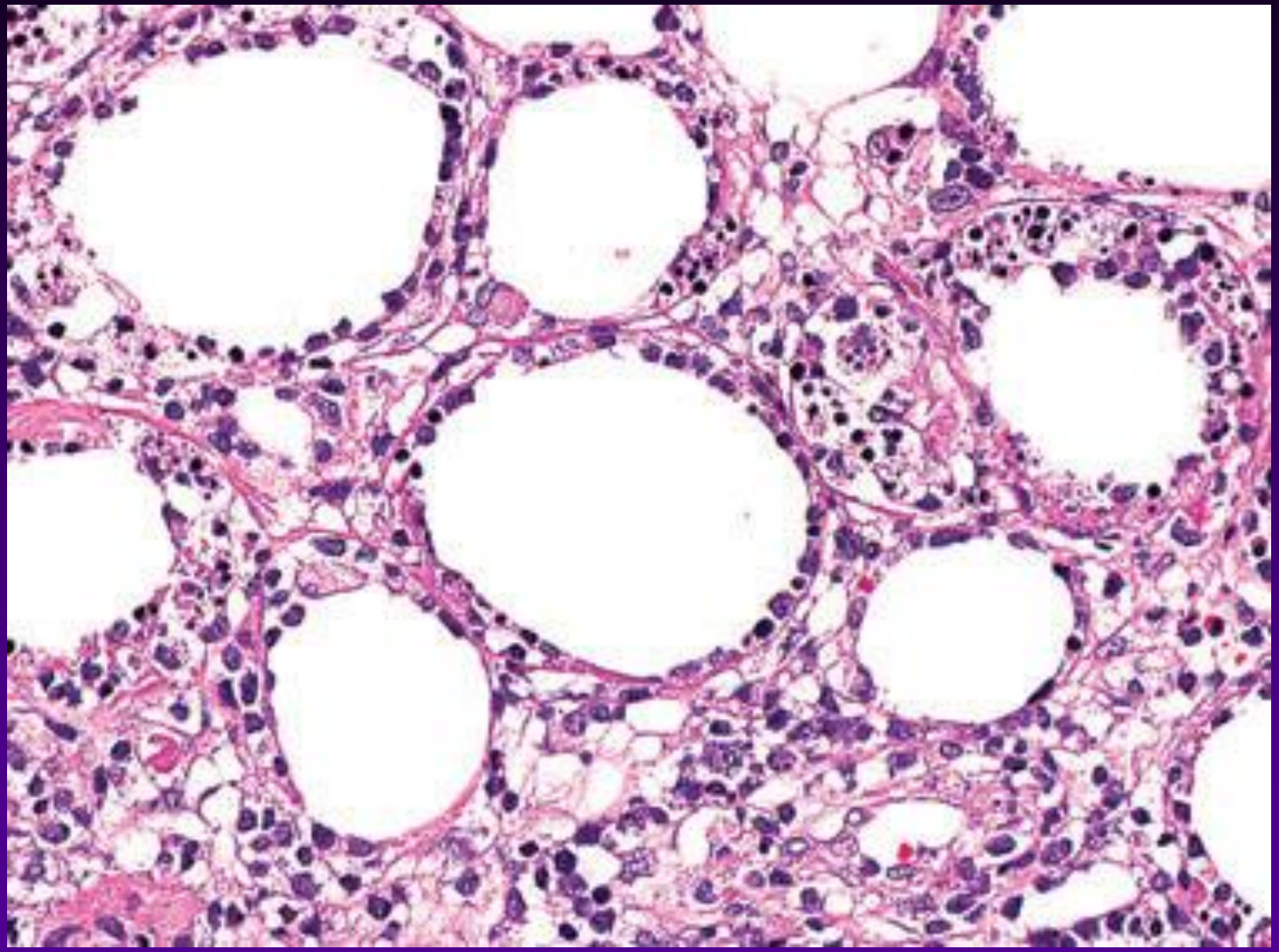
5-year-survival: >80%

Treatment conservative (cyclosporine, chlorambucil, prednisone)

Haemophagocytic syndrome possible and associated with worse prognosis

Distinction from cutaneous γ/δ T-cell lymphoma is basic!





Knowles

- An additional distinctive feature is the presence of large polyhedral macrophages with abundant eosinophilic cytoplasm unaccompanied by other inflammatory cells exhibiting a single-cell pattern of infiltration amidst a mucinous dermis and within the septa of the fat.

Differential diagnosis

- Cutaneous γδ T-cell lymphoma
  - Commonly involves dermis and epidermis
  - May show epidermal ulceration
- In contrast, tumour cells in subcutaneous lymphoma with a γδTCR phenotype express CD56, CD2 and CD3, but are negative for CD4, CD8 and βF1

Differential Diagnosis

- Gamma-Delta T cell lymphoma; in which:
  - Ulcerative lesion
  - Hemophagocytic syndrome is frequent
  - 50% of pts have elevated liver enzymes and leukopenia
  - Involvement of epidermis and dermis as well as subcutaneous fat
  - Absence of CD4, CD8, and BF1
  - Granzyme M and CD56 are positive
  - Worse prognosis: about 1 year median survival

Knowles

- The clinical presentation and light microscopic findings are essentially identical although constitutional symptoms, more pronounced cytopenias, and features of HPS would be more commonly observed n the setting of gamma delta T-cell lymphoma

Differential Diagnosis

- **Lupus panniculitis**

- Both SCPTCL and SLE:
  - Predilection for thigh and proximal arm
  - Both can wax and wane

Knowles:

- Both share: lymphocytic infiltration of the fat lobule, lymphoid atypia, erythrocyte phagocytosis, variable CD5 and CD7 deletion, increased numbers of CD8 lymphocytes,
  and clonality

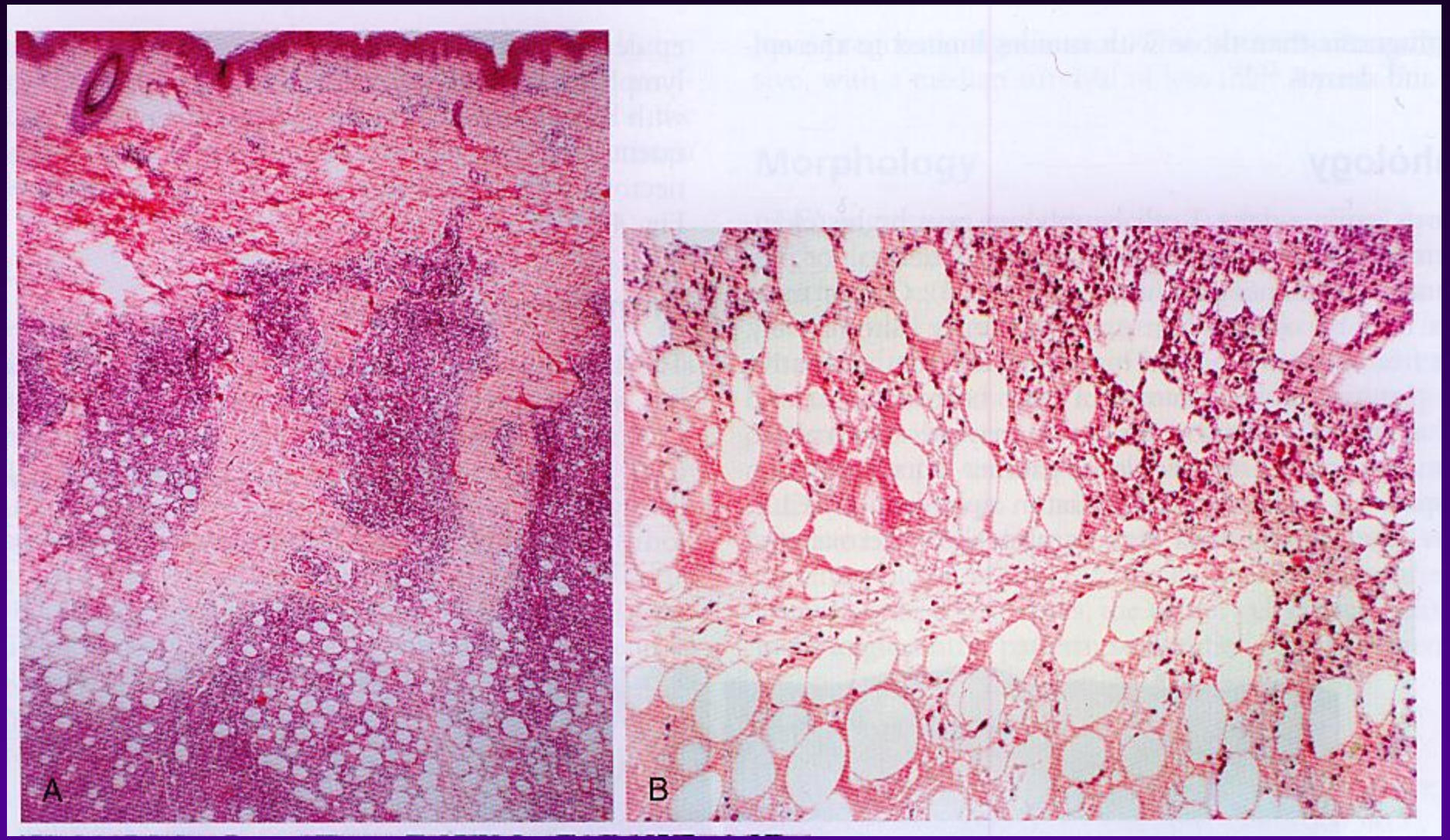
- However, distinguishing clinical features from panniculitic T-cell lymphoma include:
  - Lack of any constitutional symptoms, the tendency for spontaneous resolution, and the absence of cytopenia while light microscopically the density of infiltration, cytologic atypia, and erythrocyte phagocytosis is less and necrosis is typically absent in SLE

- With respect to lupus profundus, this condition also presents with waxing and waning plaques and nodules involving the proximal extremities; however, either there are overlying skin changes diagnostic of lupus erythematosus or the patient has a known history of lupus erythematosus

Differential Diagnosis
Lupus profundus

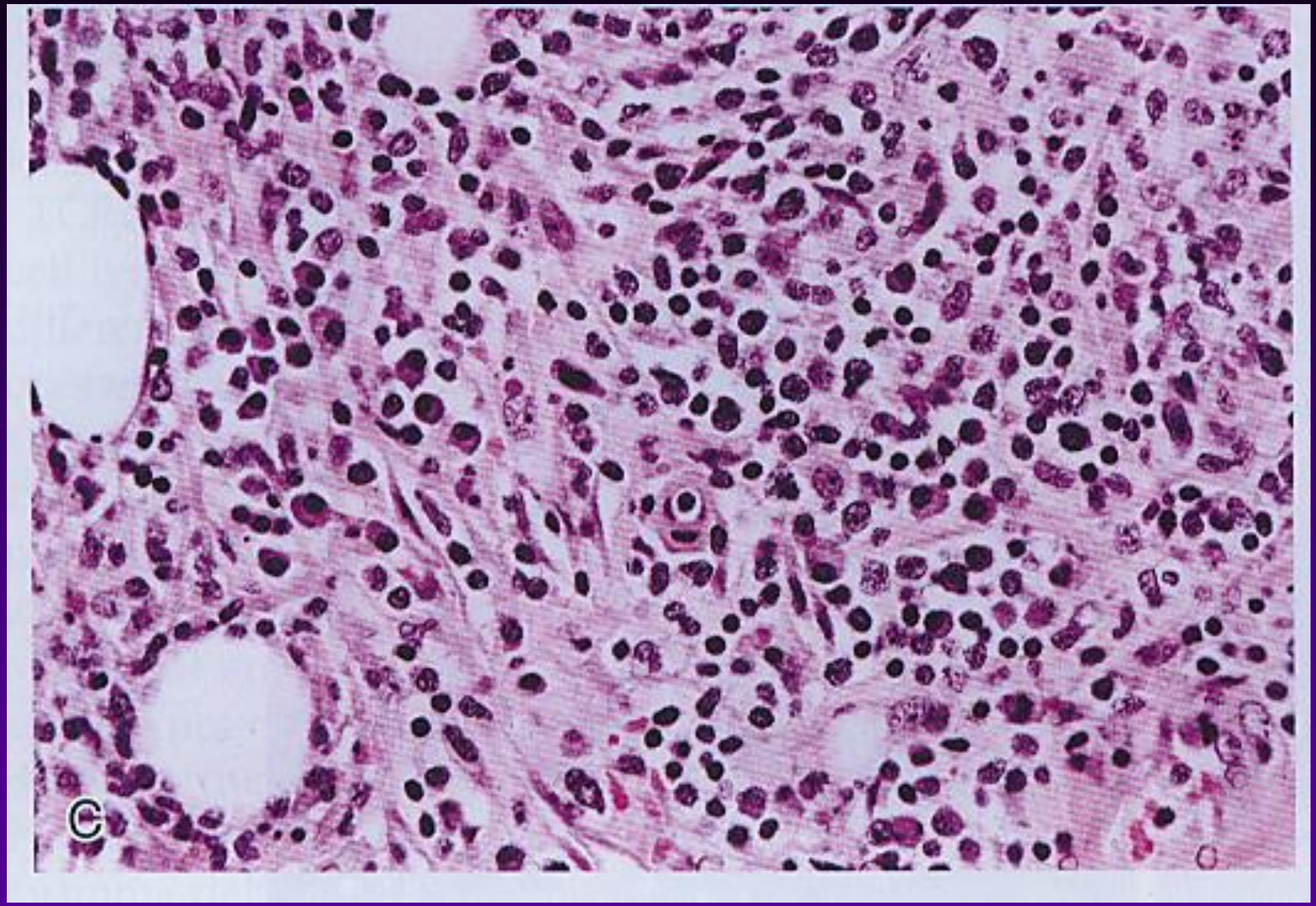
Table 40-3 Differentiation between Subcutaneous Panniculitis-Like T-Cell Lymphoma and Lupus Profundus

Feature	Lupus Profundus	Subcutaneous Lymphoma
Diffuse infiltration of fat lobules by atypical medium-sized lymphocytes	+	+
Fat necrosis	+	+
Histocytes containing cellular debris	+	+
Lymphoid follicles	+	–
Eosinophilic hyaline change of fat ("honeycomb")	+	–
Hyaluronic acid deposition ("mucin")	+	–
Epidermal changes (atrophy, vacuolar interface change, follicular plugs)	+	–
Erythrophagocytosis	–	+
Rimming of adipocytes by atypical T cells	–	+
CD8	+	+
CD56	–	–
CD30	–	–


A
B

- Useful discriminating light microscopic features include an
  - atrophying interface dermatitis
  - plasmacellular infiltration
  - germinal centers within the fat
  - positive lupus band test
  - the absence of red cell phagocytosis
  - dominance of CD4 lymphocytes over those of the CD8 subset

- Lymphocytic vasculitis, plasma cell infiltrate: typical of Lupus profundus is not seen in SPTC


C

Differential Diagnosis

- Extranodal NK/T cell lymphoma, nasal type: CD56+
  - CD3-, but cytoplasmic CD3 is +
  - ISH for EBV (EBER) is positive
  - Angioinvasion and filling of the fat lobules rather than rimming of the adipocyte spaces are more common

- If CD30+, CD4+ and CD8- ➔ ALCL: dermal involvement