Recent diagnostic and therapeutic innovations of T-cell-lymphoma

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Classification of T-cell-Lymphoma

NODAL

- Angioimmunoblastic T-cell Lymphoma
- Peripheral T-cell-Lymphoma
- Anaplastic Large-cell-Lymphoma
- ALK +/-

EXTRANODAL

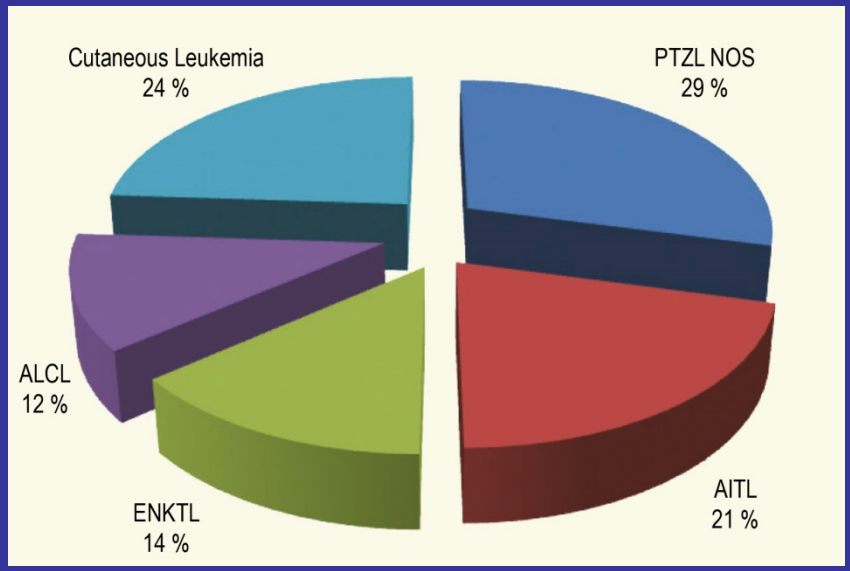
- Extranodal NK/T-cell-Lymphom nasal
- Subcutaneous T-cell-Lymphoma paniculitis
- Enteropathy associated T-Cell-Lymphom
- Hepatosplenic γ/δ T-Cell-Lymphoma

LEUKEMIA

- T-cell-prolymphocytic Leukemia
- Large granular T-cell-Lyeukemia
- Chronic Lymphoproliferative disease of NK-cells
- Aggressive NK-cell-Leukemia
- Adult-T-cell-Leukemia-Lymphoma

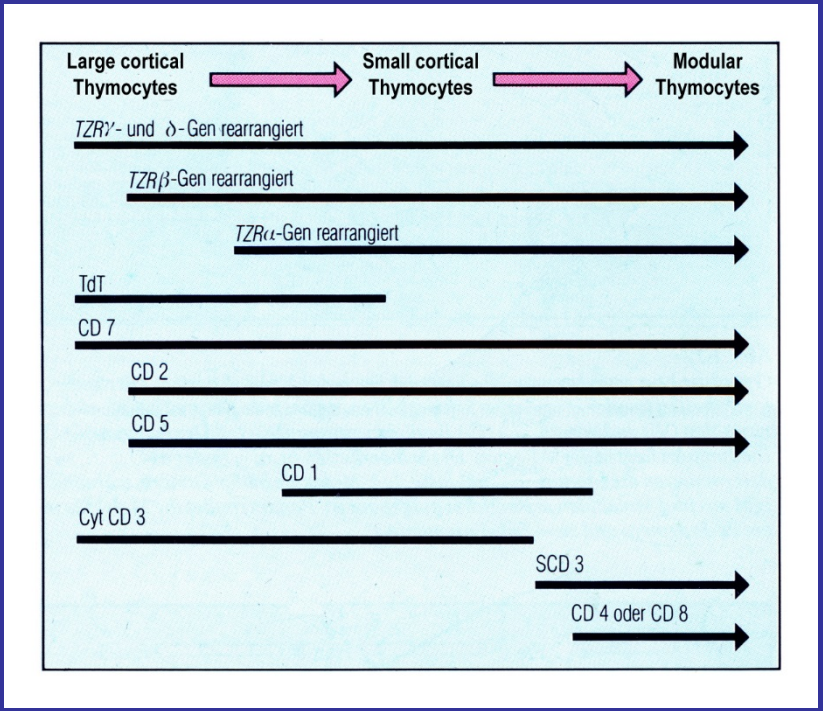
CUTAN

- Mycosis fungoides
- Sézary Syndrome
- Primary cutan CD30 + T-Cell-proliferative disease
- Peripheral cutan T-cell-Lymphoma

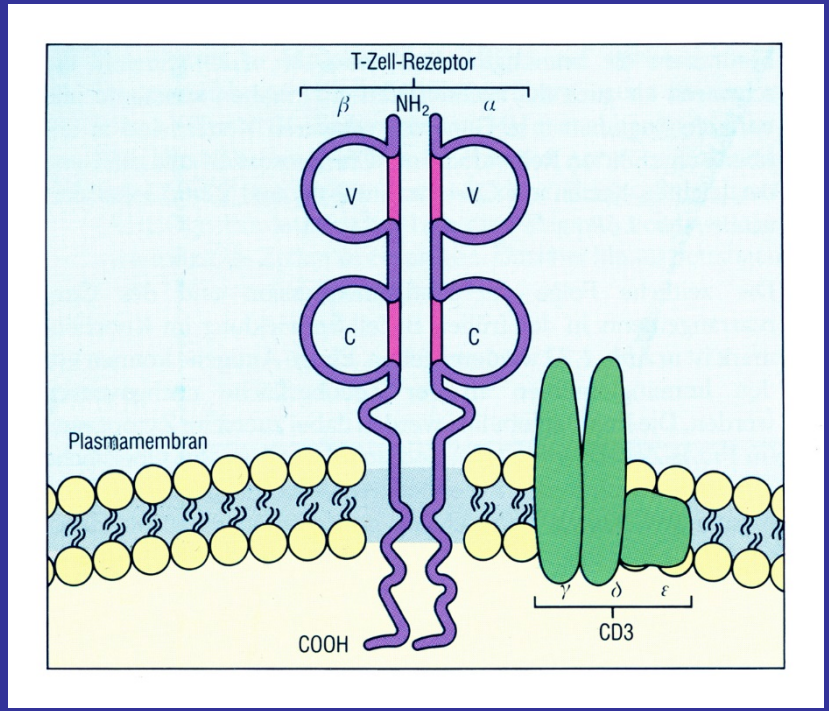


Incidence of T-cell lymphoma entities

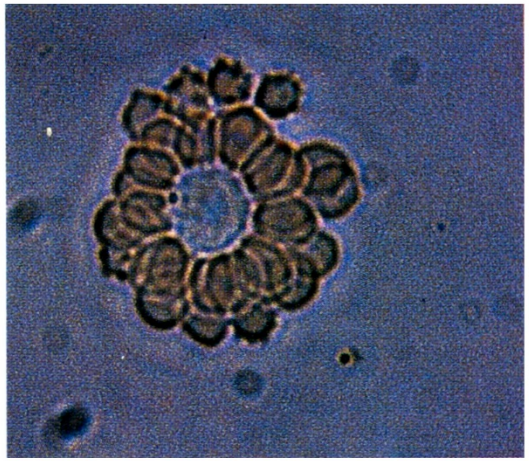
Major characteristic of T-lymphocytes

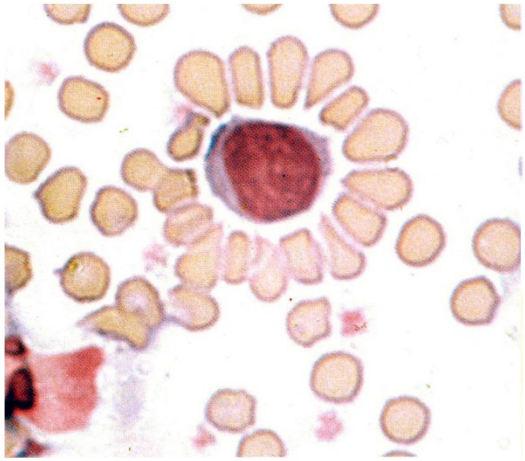


Time dependent gene rearrangement of T-cell receptor and antigen expression



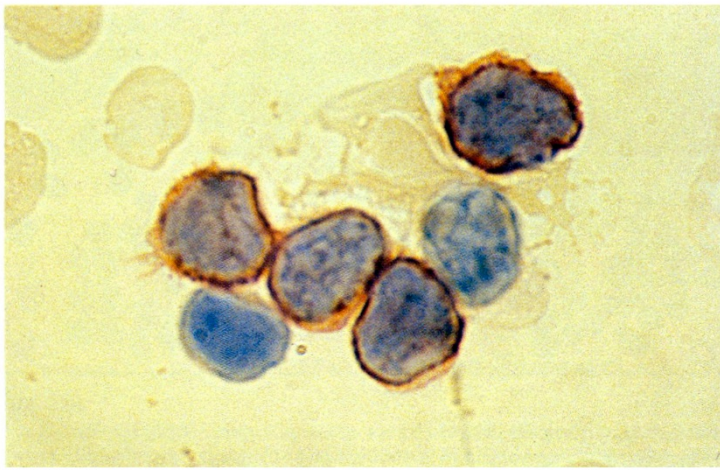
T-cell antigen receptor



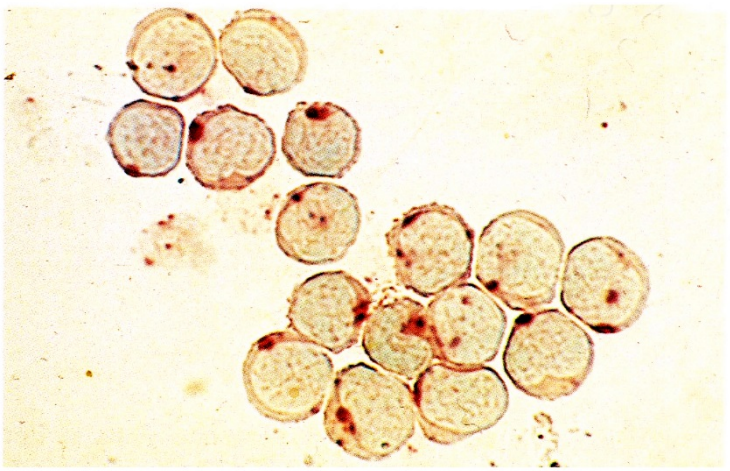


T-lymphocytes:

CD 2 - associated rosette phenomenon

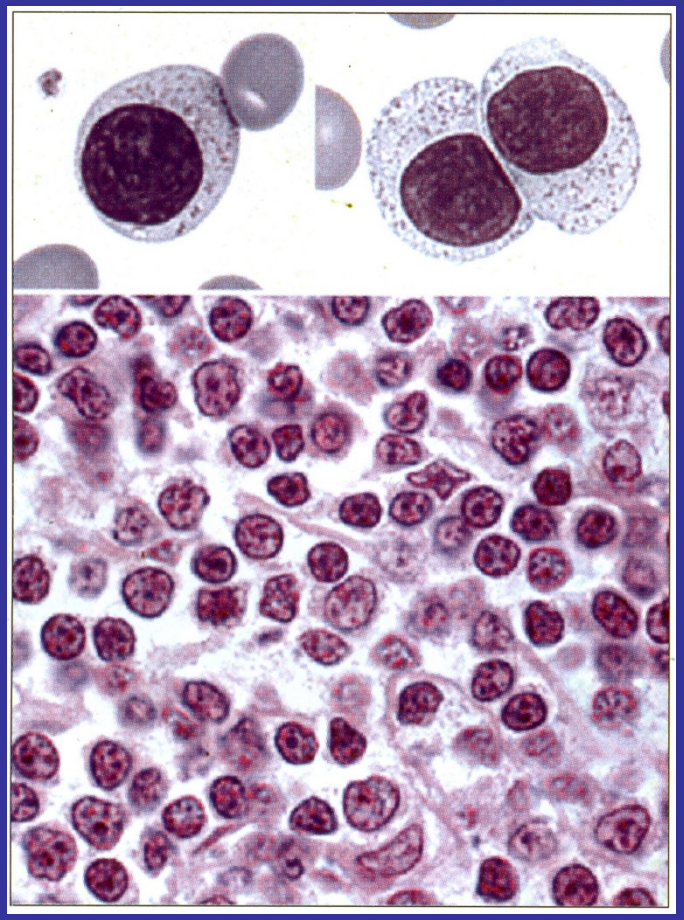


T-lymphocytes: CD 5 - staining with monoclonal antibodies



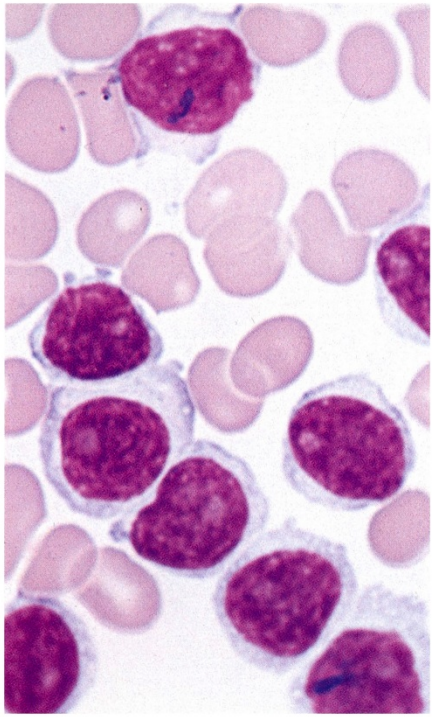
T-lymphocytes: Acid phosphatase reaction within Golgi

Large Granular Lymphocytic Leukemia

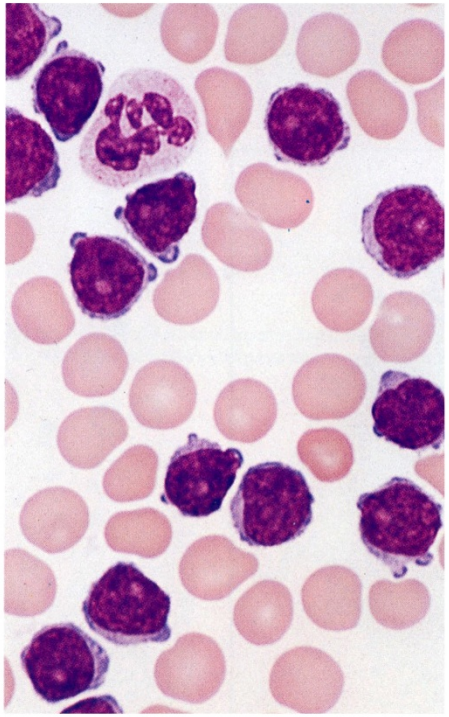


Immunology	CD2	+
	CD3, 8	+/-
	CD16	+
	CD56, 57	-/+

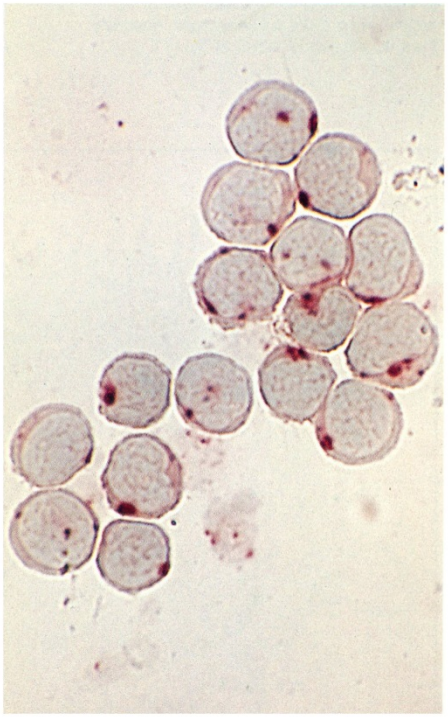
T- and B-cell prolymphocytic Leukemia



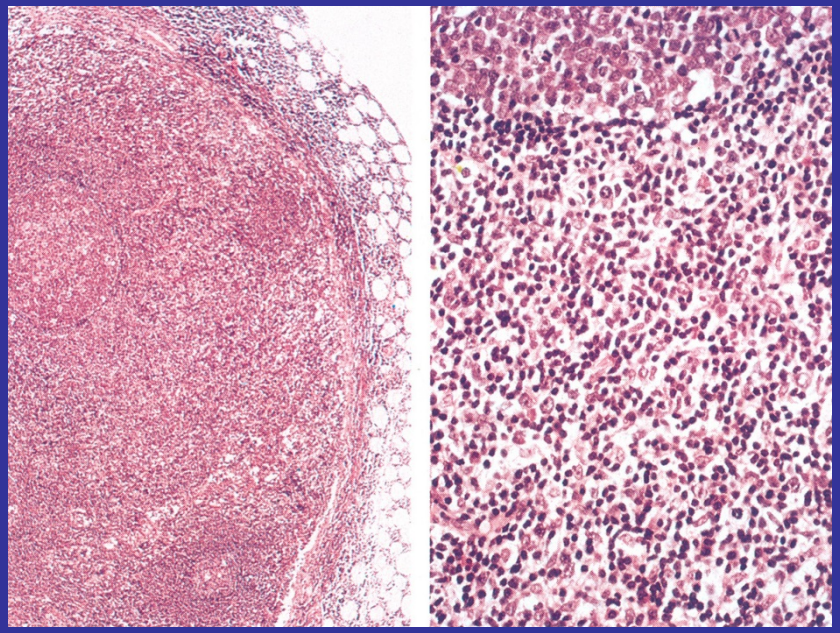
B-cell prolymphocytic leukemia surface Immunglobulin



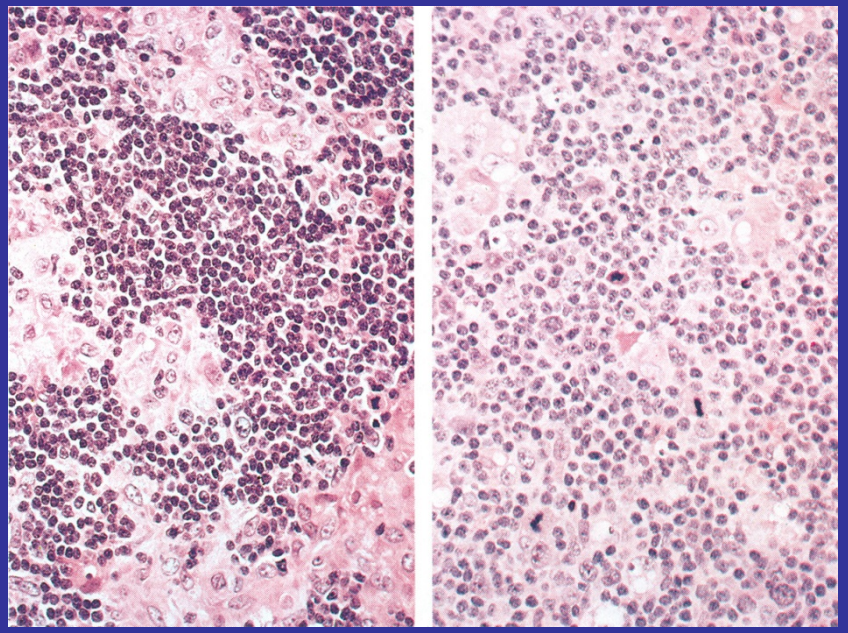
T-cell prolymphocytic leukemia without Immunglobulin



T-cell prolymphocytic leukemia with acid phosphatase within Golgi



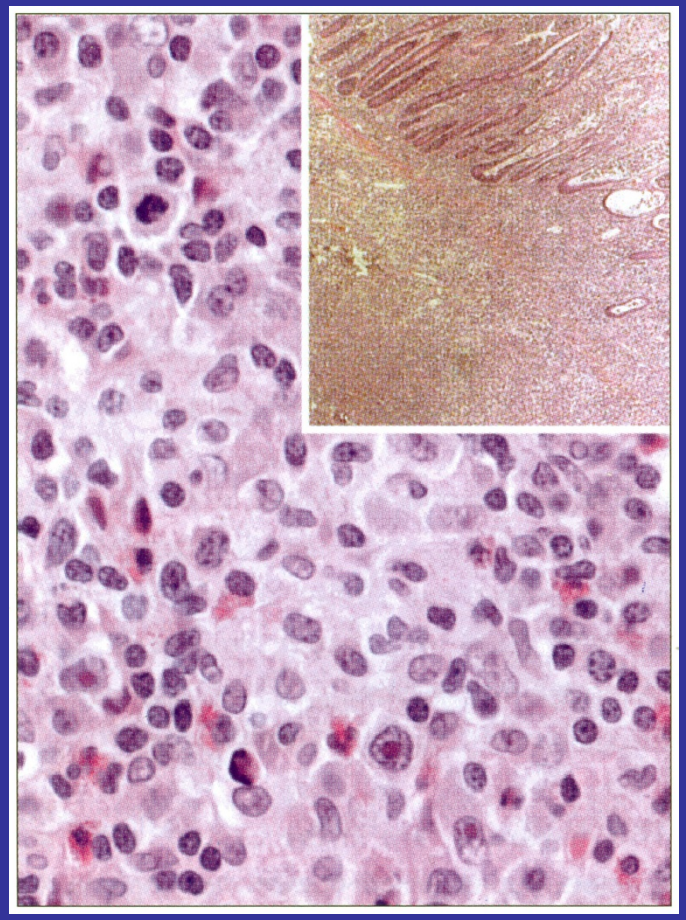
T-Zone Lymphoma



Lymphoepitheloide Lymphoma
(Lennert-Lymphoma)

Infiltration by different size lymphocytes with giant cells mimieking Reed-Sternberg.
Lymphokin-associated epitheloid cells.

Intestinal T-Cell-Lymphoma

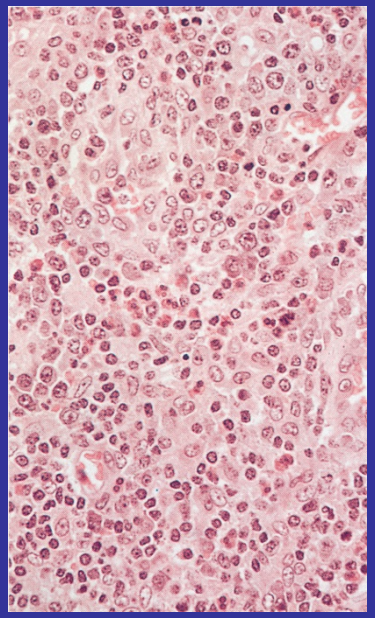


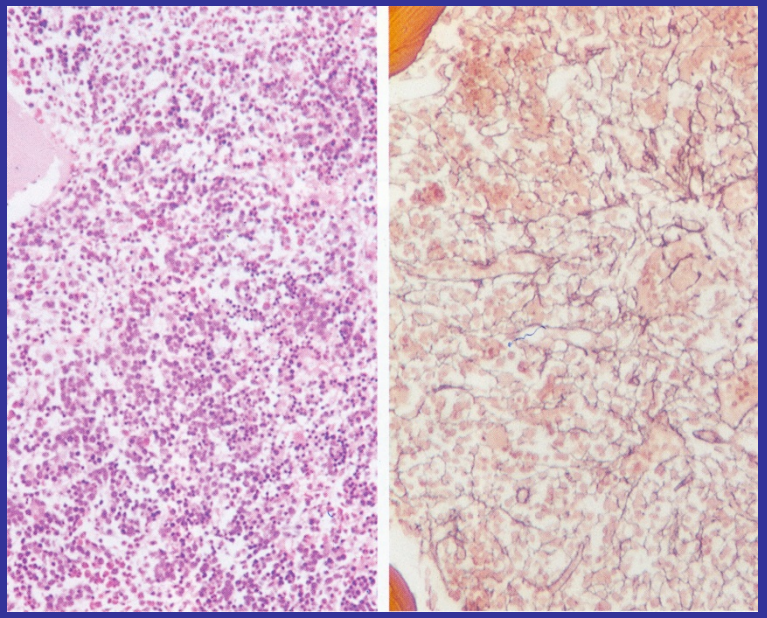
Histology:

Small lymphocytes to large bizarre cells

Aggressive course, often with intestinal perforation.

Angioimmunoblastic T-Cell-Lymphoma



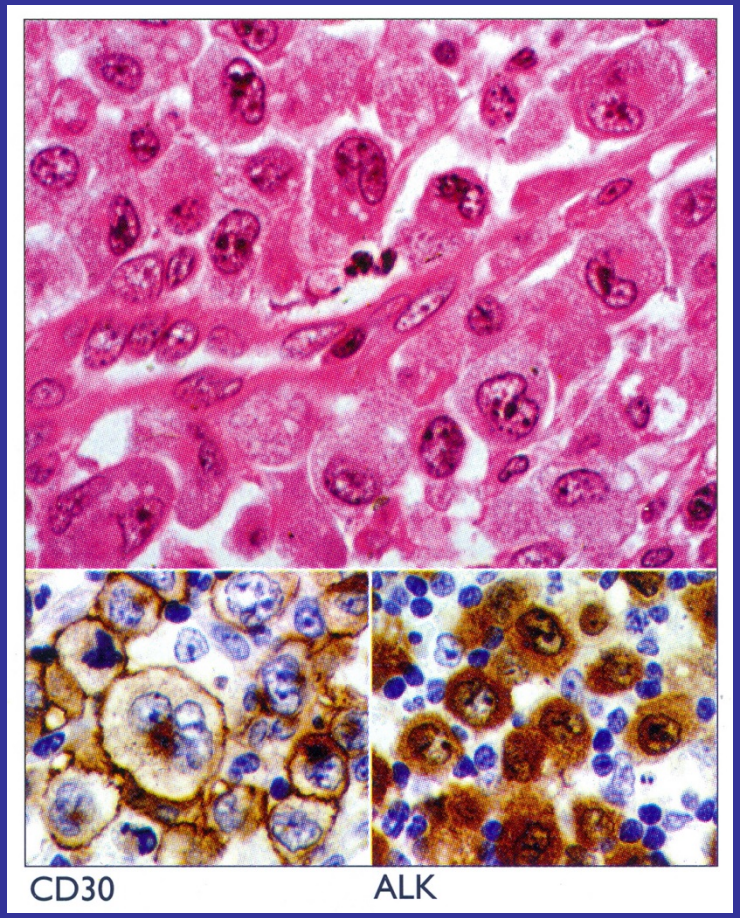


Angioimmunoblastic Lymphadenopathy: Polymorphic lymphocytic infiltration + immunoblaste and plasmacells.

Complete destruction of structure and proliferation of postcapillary venules with endothelial components.

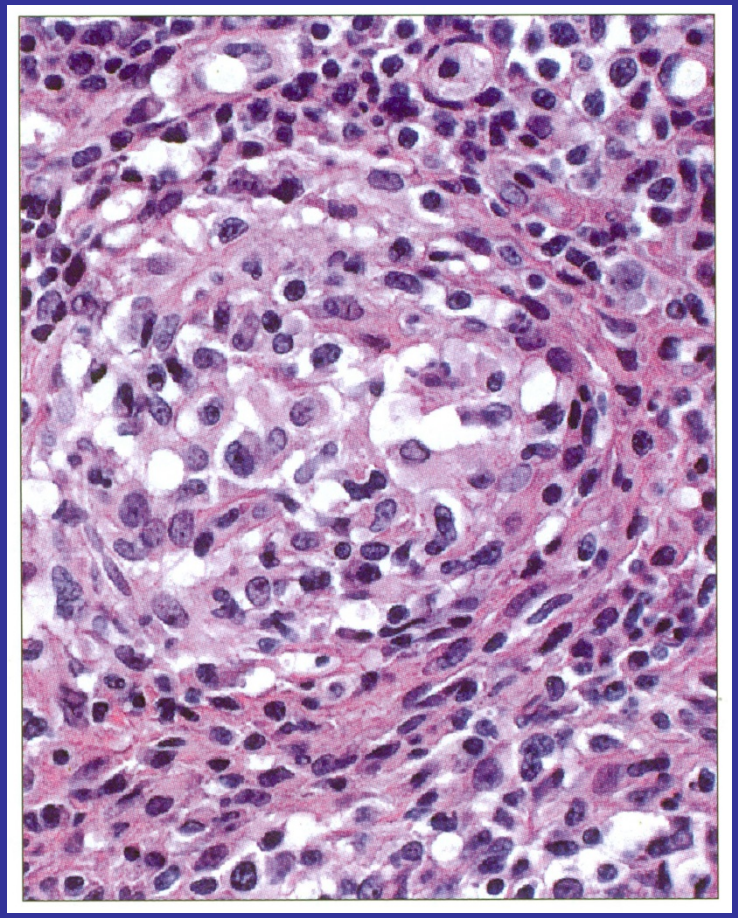
Systemic disease with fever, weight loss polyclonal hypergammaglobulinemia.

Anaplastic Large-Cell-Lymphoma



Immunology	T or null phenotype CD30 + EMA +/- ALK +/-
Genetics	t(2;5), causing fusion of *ALK* and *NPM* genes, in majority of cases

Angiocentric T-Cell-Lymphoma



Extranodal lymphoma, nasal-type or midline lymphoma.

Tendency to invade the walls of blood vessels; Polymorphic lymphocytes.

Immunology	CD2, 56	+
	CD3	-/+
	CD5, 7	+/-
	CD4 or 8	+/-

Primary Therapy of T-Cell NHL

1. Combined chemotherapy CHOP
2. Consolidation by HDCT + antologous transplantation in patients with CR
3. Intensification of primary chemotherapy by adding of Etoposide

Results of autologous Transplantation in T-Cell

Autor	n	Alter	Konditionie-rung	DFS/EFS/ PFS	OS	Tx-Rate	TRM	Follow-Up (Monate)
Rodriguez [15]	26	44	BEAM	53% (3 Jahre)	73% (3 Jahre)	73%	5%	35
Corradini [16]	62	43	Mitoxantron/ Melphalan oder BEAM	30% (12 Jahre)	34% (12 Jahre)	71%	0	76
Mercadal [17]	41	47	BEAM/BEAC	30% (4 Jahre)	39% (4 Jahre)	41%	n. d.	38
Reimer [19]	83	47	HD-Cyclo-phospha-mid/TBI	36% (3 Jahre)	48% (3 Jahre)	66%	4%	33
D´Amore [19]	160	57	BEAM	49% (3 Jahre)	51% (5 Jahre)	71%	4%	61

Primary Therapy of T-Cell-Lymphoma

Involved field radiotherapy in stage I – II of patients with extranodal disease, ENKT (nasal).

Combined chemo-radiotherapy in ENKTL assosiated with excess glycoproteinproduction.
Cisplatinum based chemotherapy or asparaginase based chemotherapy.

SMILE-Protocol:

Dexa, MTX, Ifo, LASP,
Etoposide
For time beeing most
effective chemotherapy

Targeted Therapy of T-Cell-Lymphoma

Anti-CD30 monoclonal antibody conjugated with Monomethyl-Auristatin

Brentuximab Vedotin

Potent therapeutic agent for CD30 + Lymphomas:

Hodgkin Lymphoma
Anaplasic Large-Cell-Lymphoma

Response	86 %
CR	57 %
PFS	13,3 months

Targeted Therapy of T-Cell-Lymphoma

Histodeacetylase Inhibitor

Romidepsin

Response Rate	25 %
Complete Remission	15 %

Salvage Therapy of T-Cell-Lymphoma

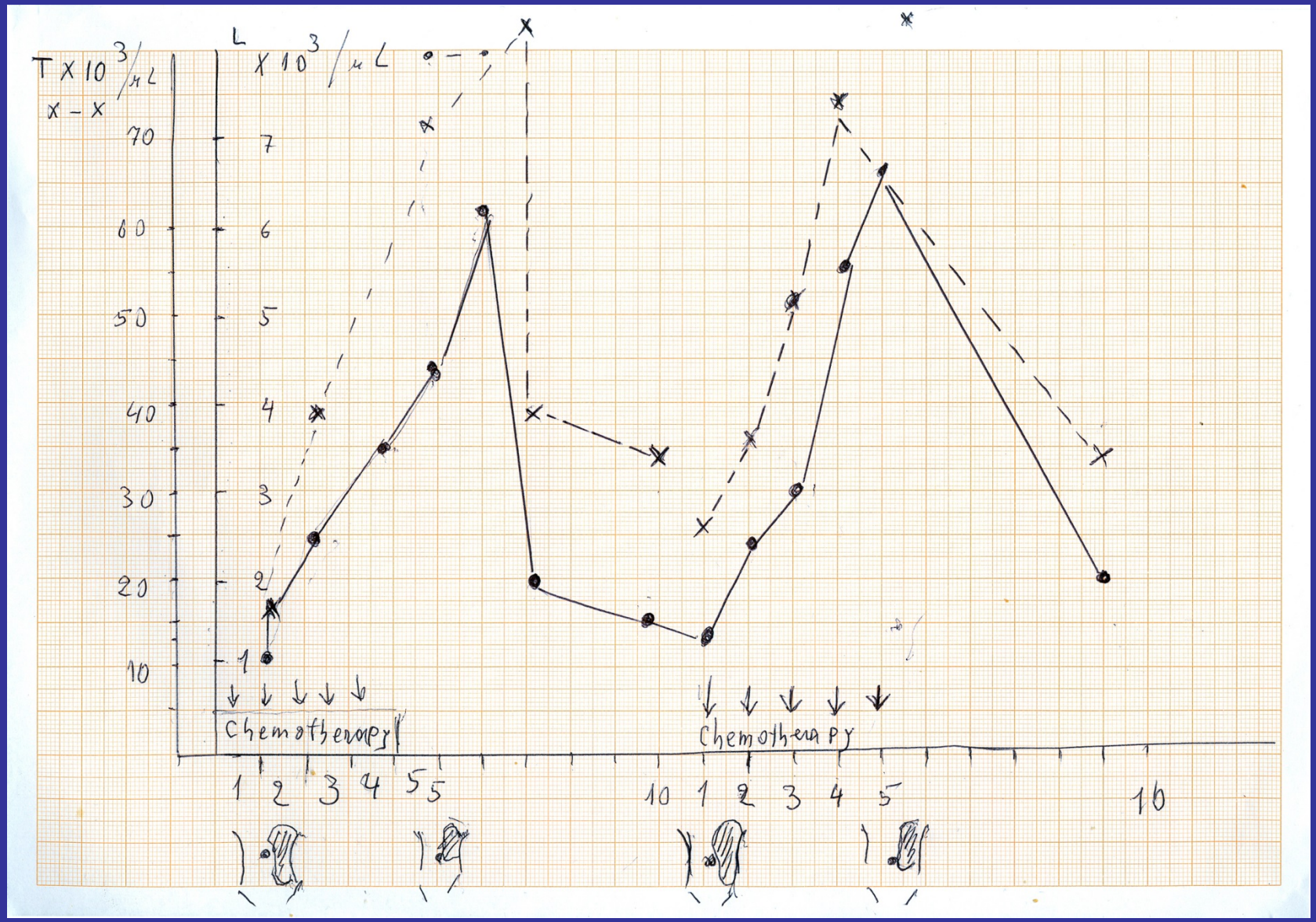
Allogen B. M. Transplantation

Graft-versus-Lymphoma

Retrospektive Studien (* an Tag 100, ** nach 3 Jahren, *** nach 1 Jahr)								
Autor	n	Alter	Vorherige autoSZT	Anteil RIC	DFS/EFS/ PFS	OS	TRM/ NRM	Follow-Up (Monate)
Le Gouill [23]	77	36	25%	26%	53% (5 Jahre)	57% (5 Jahre)	21%*	43
Kyriakou [24]	45	48	33%	45%	53% (3 Jahre)	64% (3 Jahre)	18%*	29
Jacobsen [25]	52	46	21%	40%	30% (3 Jahre)	41% (3 Jahre)	27%**	49
Dodero [26]	52	47	52%	100%	40% (5 Jahre)	50% (5 Jahre)	12%	67
Kanakry [27]	44	51	9%	54%	40% (3 Jahre)	43% (3 Jahre)	9%***	47
Smith [28]	126	38	n. d.	36%	37% (3 Jahre)	46% (3 Jahre)	34%**	49
Prospektive Studien								
Autor	n	Alter	Vorherige autoSZT	Anteil RIC	DFS/EFS/ PFS	OS	TRM/ NRM	Follow-Up (Monate)
Corradini [29]	17	41	47%	100%	64% (3 Jahre)	81% (3 Jahre)	6%	28
Wulf [30]	10	45	20%	100%	60% (7 Monate)	70% (7 Monate)	30%	7

Case Report

- 38 Y. ♂ with severe condition due to anemia-leucocytopenia and thrombocytopenia.
- Clinical investigation: Remarkable splenomegaly
- Peripherel. Hematology: Leucocyte 2.100; Hgb 8,2; Eryth. 2,8; Thrombocyte 31.000
- Bone marrow. First examination. Hyperplastic cythropoesic and non specific elevation of lymphocytes.
- Therapy: Hydroxy urea without effect.
- Revision of bone marrow and hematopathologic examination of liver biopsie: Sinosoidal lymphocytic infiltration within bone marrow as well as within hepatic parenclym most likely compatible with hepato-splenic lymphoma.
- Extended molecular investigations $\gamma\delta$: Clonility of T-Cell Receptor-Gene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Chemotherapy
Chemotherapy
1 2 3 4 5 5
10 1 2 3 4 5
10

Hepatosplenic Lymphoma

Splenectomy in Summer 2014

24 hours after splenectomy:

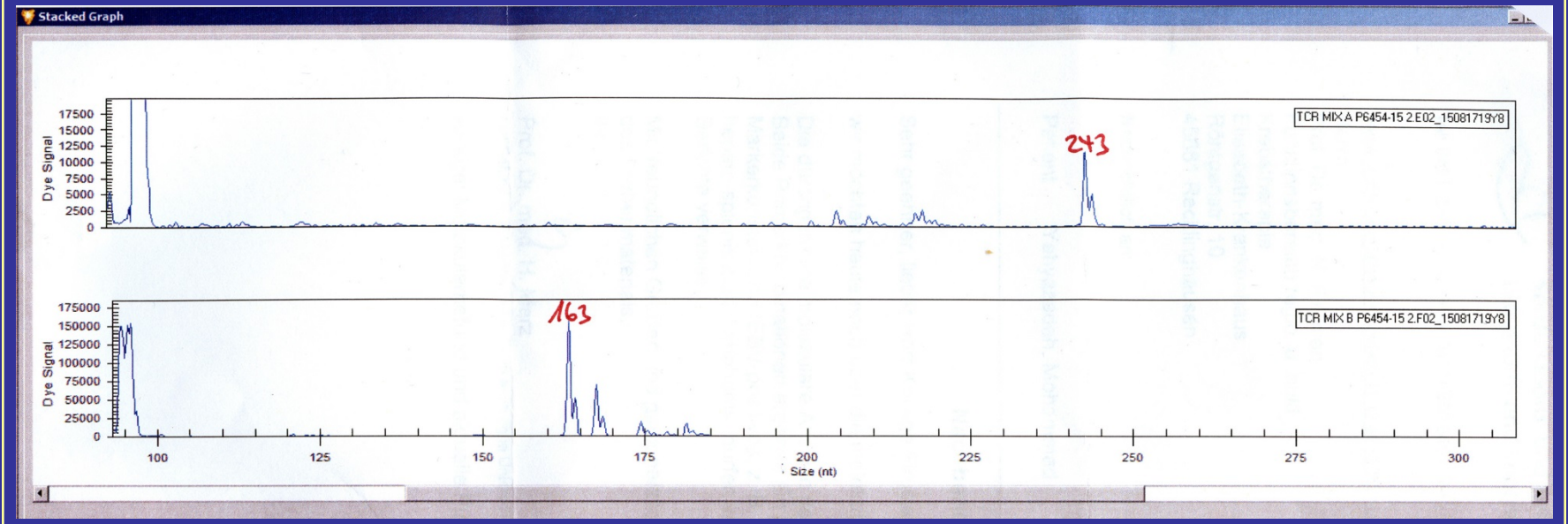
Remark elevation of thrombocytes with maximum in a range of 600,000 and improvment of general condition

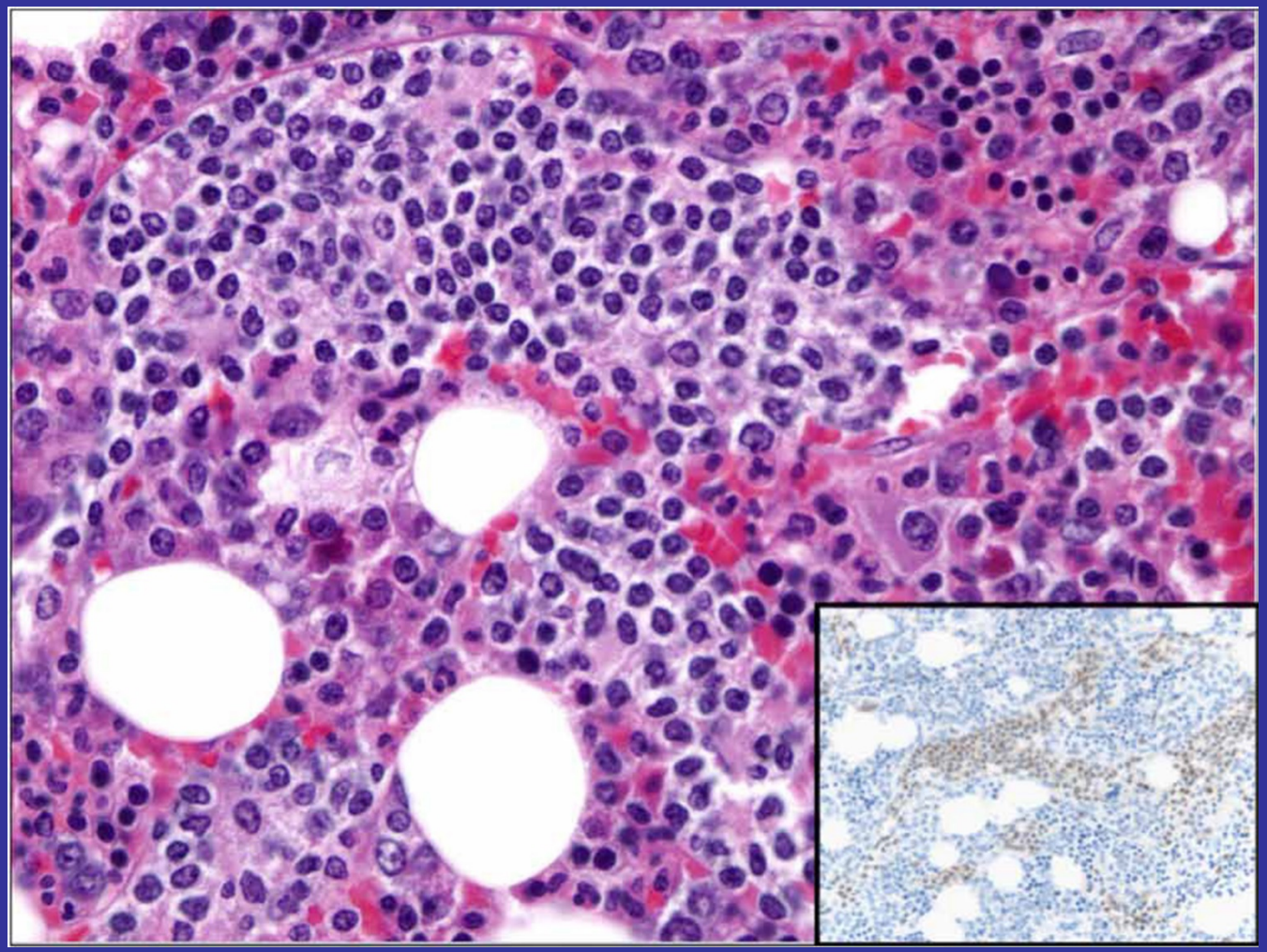
maintenance: Cyclophosphamide,
Etoposide,
Methylprednisole.

Case 2

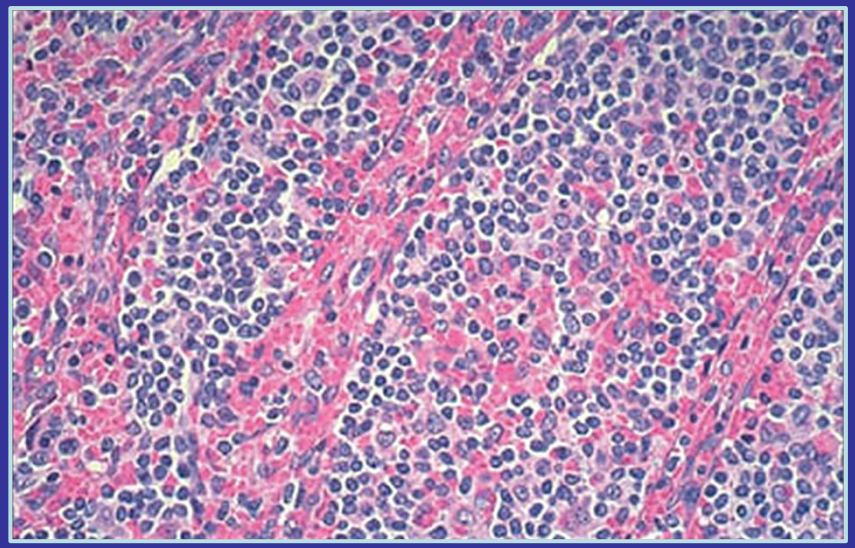
- 38 Y. ♂ with fever since 4 weeks associated with severe condition. There were no evidence for septicemia or virusinfektion.
- Peripherel. Hematology: Leucocyte 2.100; Hgb 9,5; Eryth. 2,5; Thrombocyte 55.000
- Clinical investigation: Lymphodenopathy Ø
  Hepatosplenomegaly ++
- Bone marrow examination: Inconclusive. Revision of bone marrow + Liver biopsie:
  - Remarkable sinosoidal lymphocytic infiltration
  - Consistent with hepatosplenic T-Cell-Lymphoma

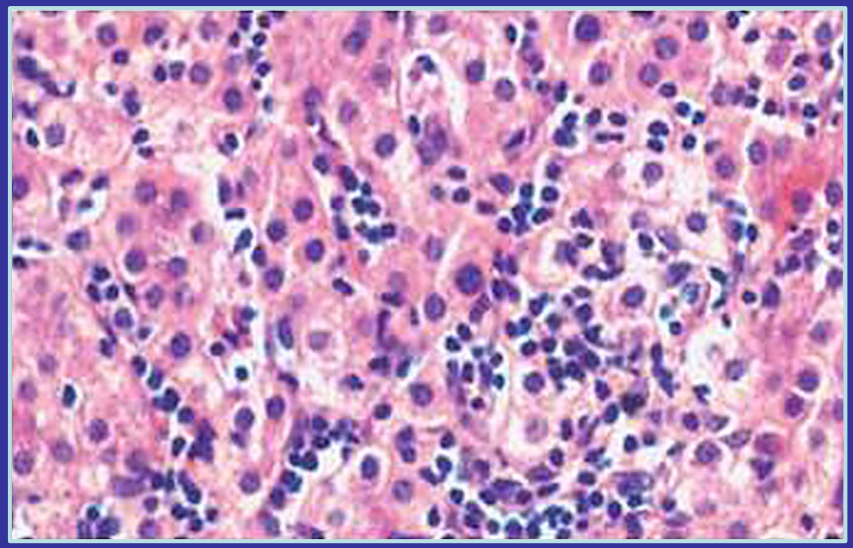
Confirmation of γδ-hepatosplenic T-Cell-Lymphoma by TCR-Gene Analysis





A Bone marrow biopsy shows prominent distinctly intrasinusoidal infiltrate of medium-sized T lymphocytes, highlighted by immunostain for CD3 (inset), which is characteristic of hepatosplenic T-cell lymphoma.





B Sinusoidal lymphocytic infiltration of liver associated with hepatosplenic T-Cell-Lymphoma.

Summery

Peripheral T/NK-cell-lymphomas comprise a heterogenous group of rare mature lymphoid neoplasmas.

With the exception of anaplastic-large-cell-lymphoma (ALCL) expressing ALK-kinase PTCL show an agressive clinical coure and have a worse prognosis.

Adoped from the treatment of B-cell-lymphoma, CHOP or Chop-like regimens are most common used for first-line therapy, however autolog and allogen transplantation have to be considered.

Radiotherapy is essential in patients with early extranodal NK/T-cell-lymphoma (ENKT).
Bretuximab-Vedolin for relapsing and refractory ALCT.