T/NK lymfoproliferace

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Mature T and NK neoplasms
T-cell prolymphocytic leukemia
T-cell large granular lymphocytic leukemia
Chronic lymphoproliferative disorder of NK cells
Aggressive NK-cell leukemia
Systemic EBV$^+$ T-cell lymphoma of childhood*
Hydroa vacciniforme–like lymphoproliferative disorder*
Adult T-cell leukemia/lymphoma
Extranodal NK-/T-cell lymphoma, nasal type
Enteropathy-associated T-cell lymphoma
Monomorphic epitheliotropic intestinal T-cell lymphoma*
*Indolent T-cell lymphoproliferative disorder of the GI tract**
Hepatosplenic T-cell lymphoma
Subcutaneous panniculitis-like T-cell lymphoma
Mycosis fungoides
Sézary syndrome
Primary cutaneous CD30$^+$ T-cell lymphoproliferative disorders
Lymphomatoid papulosis
Primary cutaneous anaplastic large cell lymphoma
Primary cutaneous γδ T-cell lymphoma
Primary cutaneous CD8$^+$ aggressive epidermotropic cytotoxic T-cell lymphoma
*Primary cutaneous acral CD8$^+$ T-cell lymphoma**
*Primary cutaneous CD4$^+$ small/medium T-cell lymphoproliferative disorder**
Peripheral T-cell lymphoma, NOS
Angioimmunoblastic T-cell lymphoma
*Follicular T-cell lymphoma**
*Nodal peripheral T-cell lymphoma with TFH phenotype**
Anaplastic large-cell lymphoma, ALK$^+$
Anaplastic large-cell lymphoma, ALK$^-$*
*Breast implant–associated anaplastic large-cell lymphoma**

Provisional entities are listed in italics.
*Changes from the 2008 classification.

Swerdlow et al, Blood 2016

Mature T and NK neoplasms	
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Mature T and NK neoplasms	**T-PLL**
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Systemic EBV$^+$ T-cell lymphoma of childhood*	
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Anaplastic large-cell lymphoma, ALK$^+$	**ALCL**
Anaplastic large-cell lymphoma, ALK$^-$*	
*Breast implant–associated anaplastic large-cell lymphoma**	

Algoritmus

- Jaký materiál?
- Klinické projevy?
  - rychlost rozvoje, kožní projevy, hepatosplenomegalie atd.
- Anamnéza, komorbidity?
  - autoimunita, splenektomie, st.p. transplantaci atd.
- Morfologie?
- Dostupnost stanovení klonality TCR?

T-CLPD panel (EuroFlow)

Tube	PacB	PacO	FITC	PE	PerCPCy5.5	PE Cy7	APC	APC H7
LST	**CD20 + CD4**	**CD45**	**CD8 + SmIgλ**	**CD56 + SmIgκ**	**CD5**	**CD19 + TCRγδ**	**CD3**	**CD38**
1	**CD4**	**CD45**	CD7	CD26	**CD3**	CD2	CD28	**CD8**
2	**CD4**	**CD45**	CD27	CCR7	**CD3**	CD45RO	CD45RA	**CD8**
3	**CD4**	**CD45**	CD5	CD25	**CD3**	HLA-DR	TCL1	**CD8**
4	**CD4**	**CD45**	CD57	CD30	**CD3**		CD11c	**CD8**
5	**CD4**	**CD45**	Perforin	Granzyme	**CD3**	CD16	CD94	**CD8**
6	**CD4**	**CD45**		CD279	**CD3**			**CD8**

Panel VFN

- 1. LST zkumavka (bez TCR g/d) – dřeň, uzlina apod.
  - CD3, CD4, CD5, CD8, CD56
- Periferní krev
  - Navíc CD2, CD7
- Při patologii pokračování:

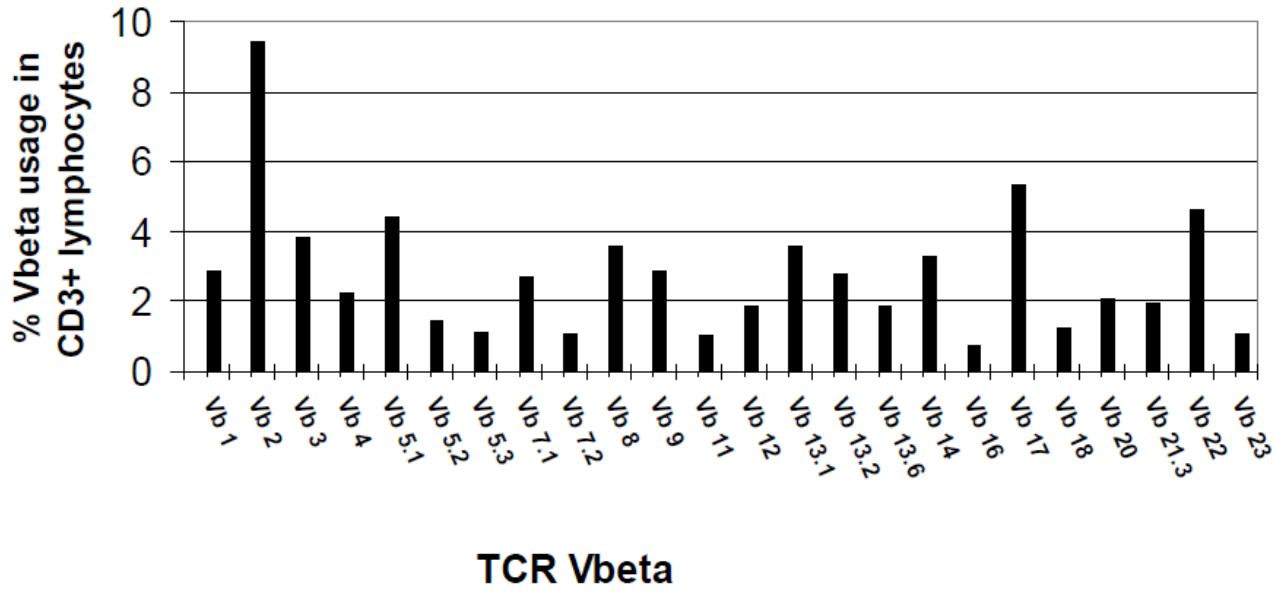
Zk.	PB	KO	FITC	PE	PerCP Cy5-5	PE Cy7	APC	APC Alexa 750
1	**CD4**	**CD45**	CD7	CD26	**CD3**	CD2	CD28	**CD8**
2	**CD4**	**CD45**	CD5	CD25	**CD3**	CD45RO	CD45RA	**CD8**
3	**CD4**	**CD45**	HLA-DR	TCRab	**CD3**	TCRgd	CD27	**CD8**
4	**CD4**	**CD45**	CD57	CD30	**CD3**	CD16	CD11c	**CD8**

Panel VFN

- **Doplnění:**
- Při podezření na T-PLL: cyTCL1
- Při podezření na AITL: CD10, CD279
- Při nejasnostech: TCR klonalita

TCR

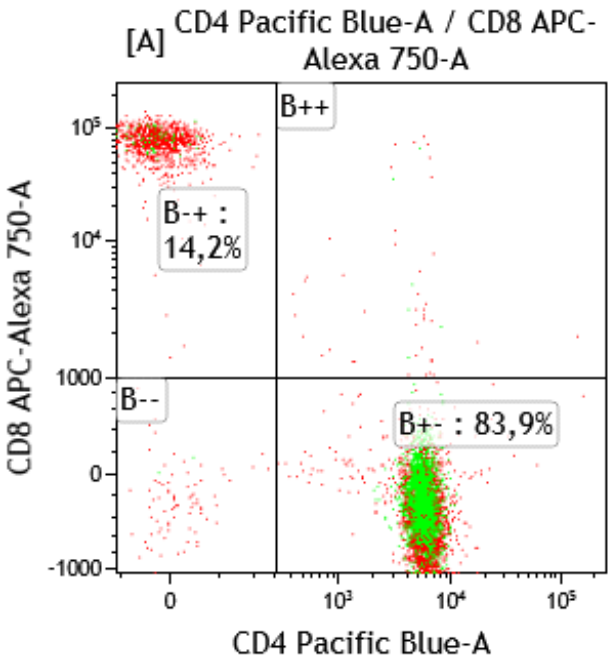
- IOTest Beta Mark TCR Vβ Repertoire Kit (Beckman Coulter), pokrytí asi 70%
- 8 zkumavek se 3 monoklonálními protilátkami
  - FITC, PE, FITC+PE
- Gating: CD4 nebo CD8 nebo CD3 (CD45…)

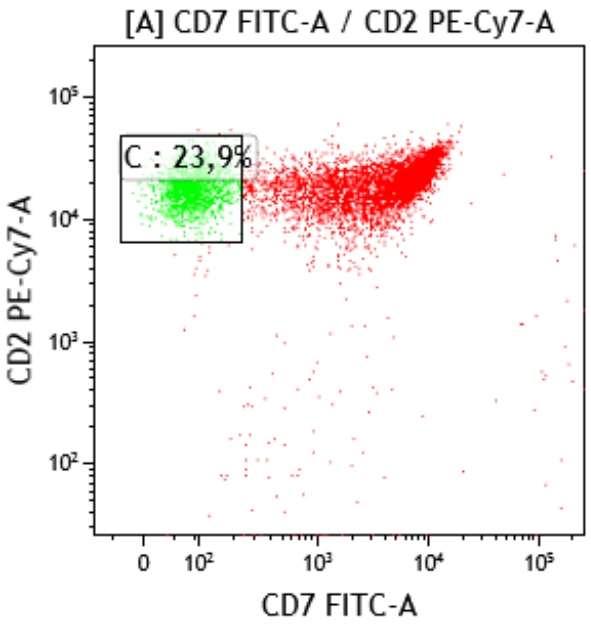


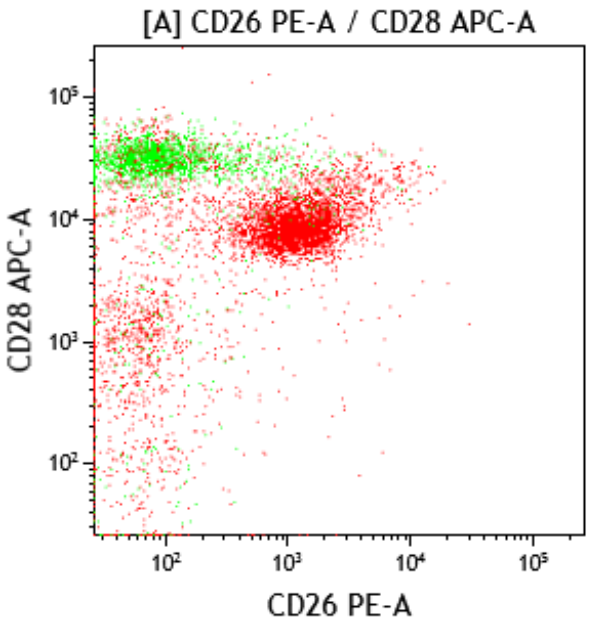
Kazuistika 1

- Muž, 70 let
- Erythrodermie, kožní biopsie: dermatitis
- KO: WBC 8,2x10^9/l, Hgb 120g/l, PLT 200x10^9/l
  - Lymfo 2,7x10^9/l
- **Periferní krev**

Kazuistika 1







Na populaci leukocytů PK tvoří 2,9% T lymfocytů s aberantním fenotypem: CD2+CD3+CD4+CD5+CD7-CD26-CD45RO+TCRalfa,beta+.
Nález svědčí pro přítomnost buněk MF/SS v periferní krvi.

Potvrzeno opakovanou kožní biopsií.

MF/SS

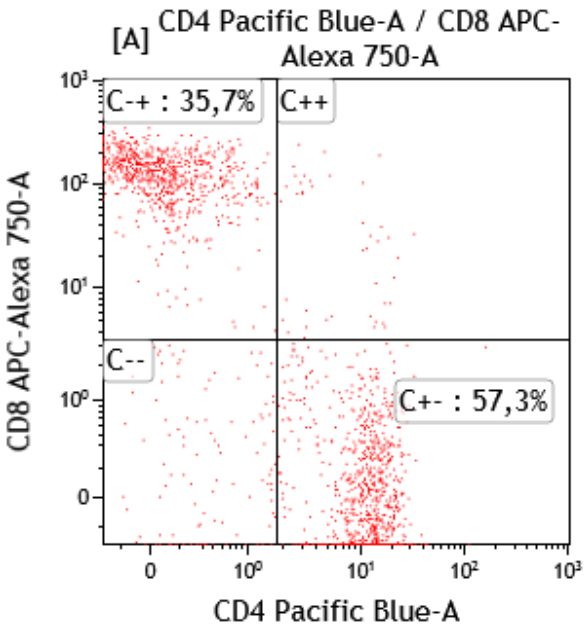
- Mycosis fungoides / Sézaryho syndrom
- Erythrodermie, lymfadenopatie
- MF: 50% primárně kožních T-NHL
- Pozitivní: CD2, CD3, CD4, CD5, CD45RO, CD28
- Negativní: CD7, CD26
- Vzácně CD8+

Kazuistika 2

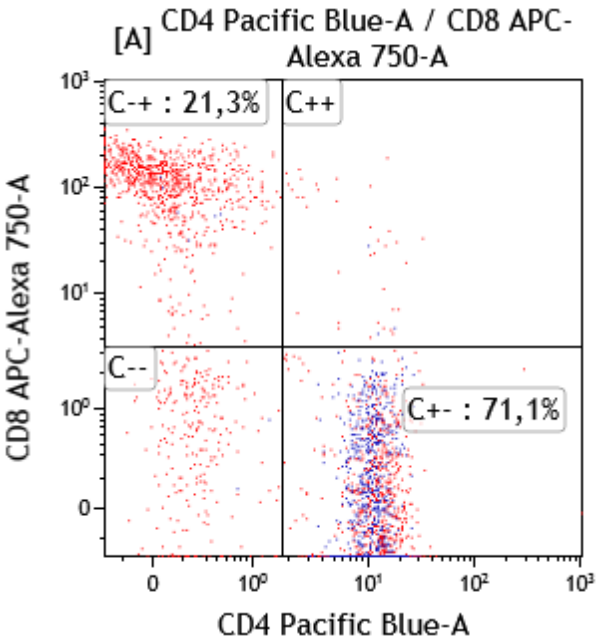
- Muž, 63 let
- Únava, noční pocení, bolesti břicha
- Lymfadenopatie, splenomegalie (20cm)
- Biopsie uzliny: high grade lymfom, bez bližší specifikace
- **Vyšetření kostní dřeně**

Kazuistika 2

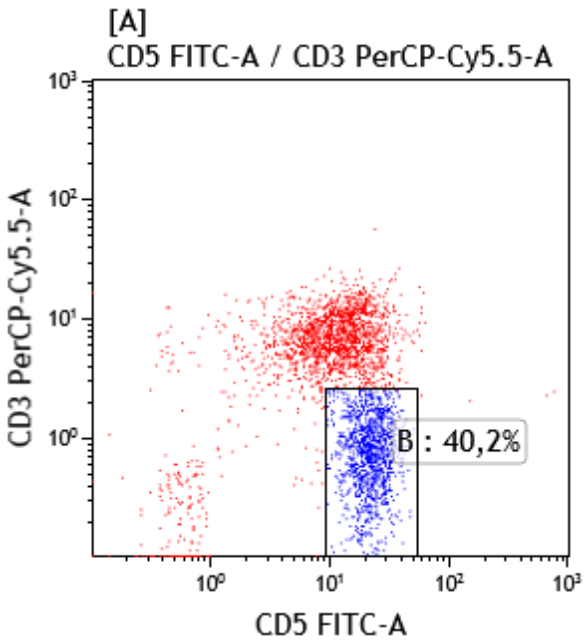
Gate CD3+



Lymfogate



Lymfogate



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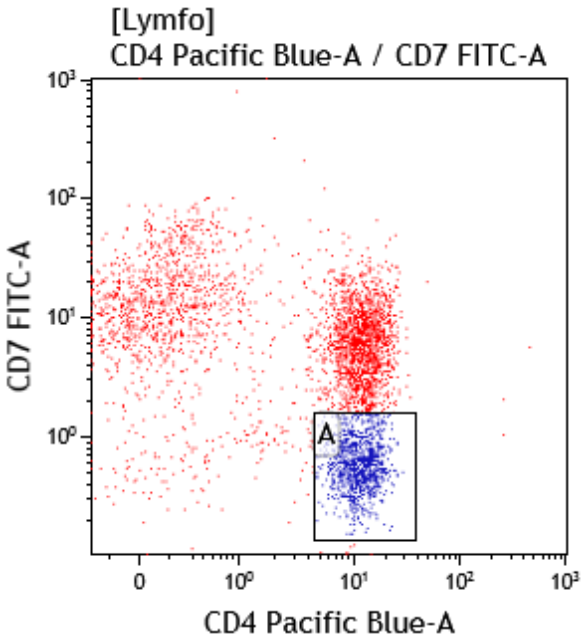
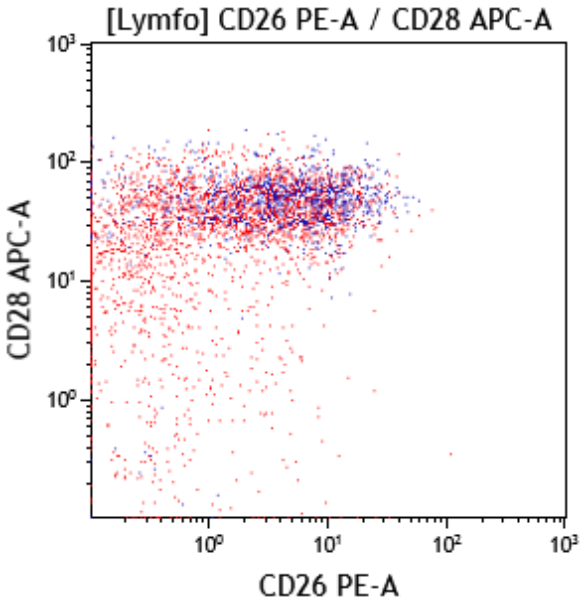
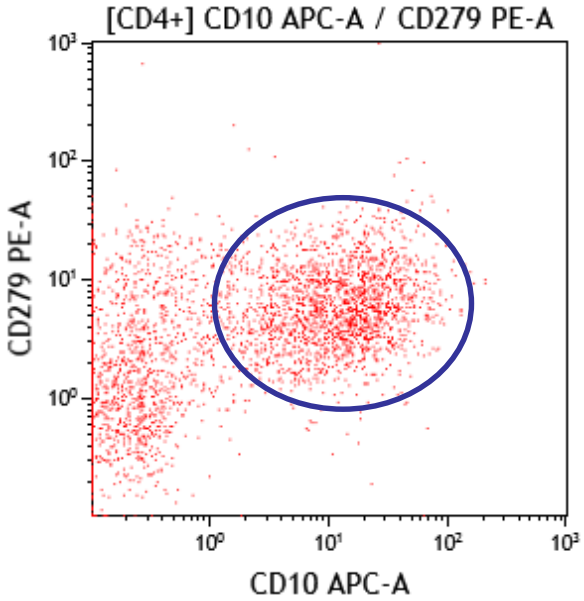






V kostní dřeni tvoří 4,6% patologická populace CD3 negativních T-lymfocytů, které exprimují: CD4, CD2, CD7 (část.), CD5, CD28, CD26, CD45RO, HLADR, CD27, CD279, CD10.
Angioimunoblastický T-lymfom (AITL).

AITL

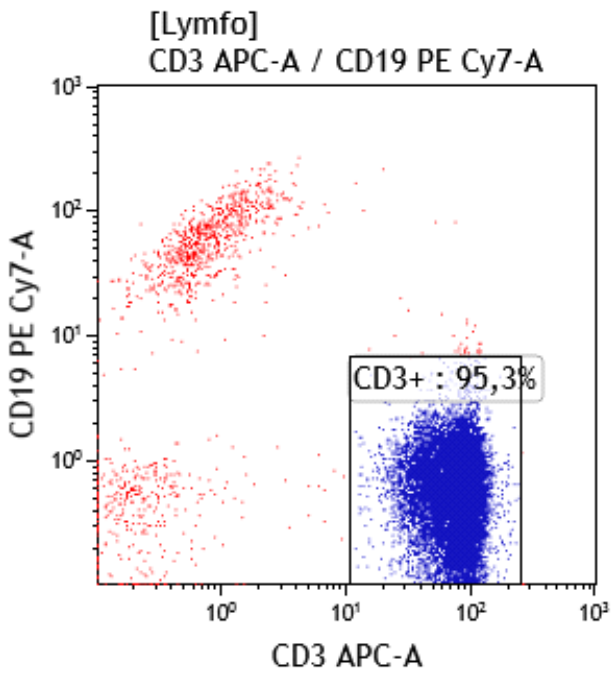
- Angioimunoblastický T-lymfom
- Tvoří 1-2% všech NHL
- Agresivní klinický průběh (medián OS < 3 roky)
- Exprimuje pan-T-lymfocytární znaky (CD3, CD2, CD5)
- CD4+ (většina)
- CD10+
- CD279+ (PD-1)

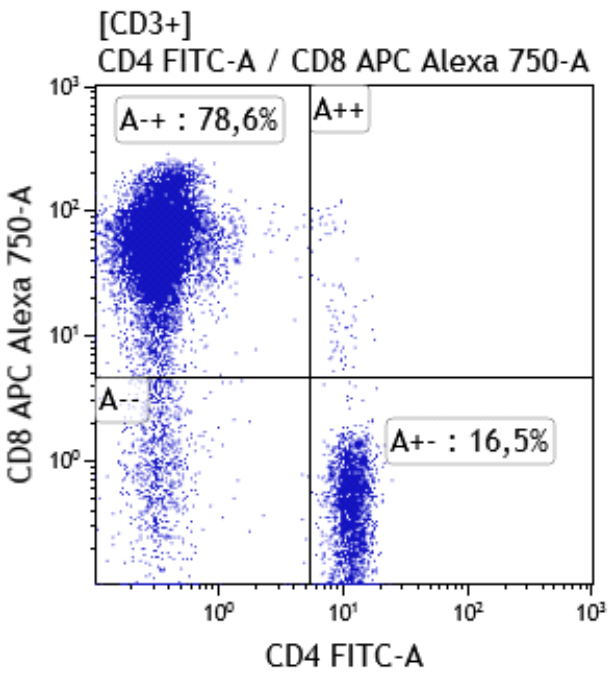
Kazuistika 3

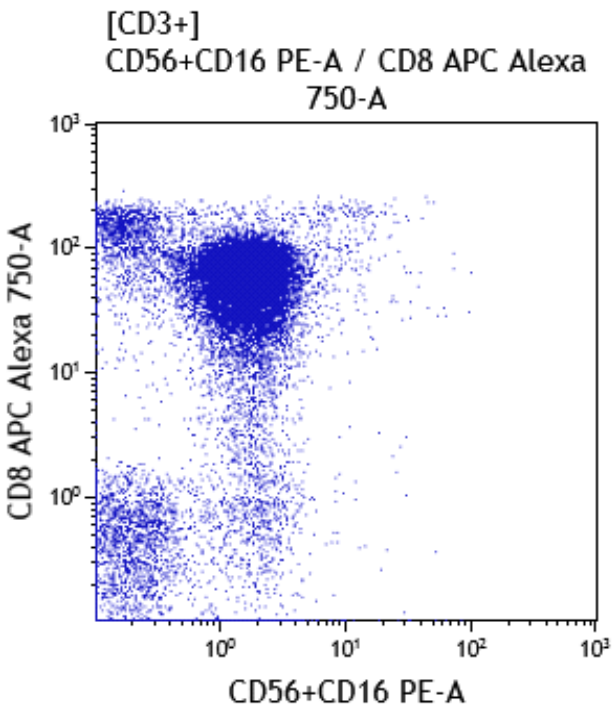
- Muž, 80 let
- WBC $7x10^9/l$, Hgb 103g/l, PLT $331x10^9/l$
- Lymfocyty 60%
- Lymfadenopatie

- **Periferní krev**

Kazuistika 3







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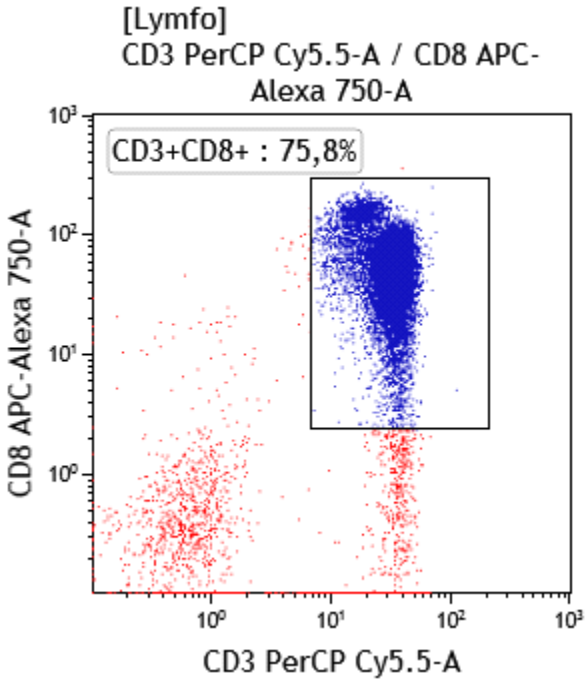

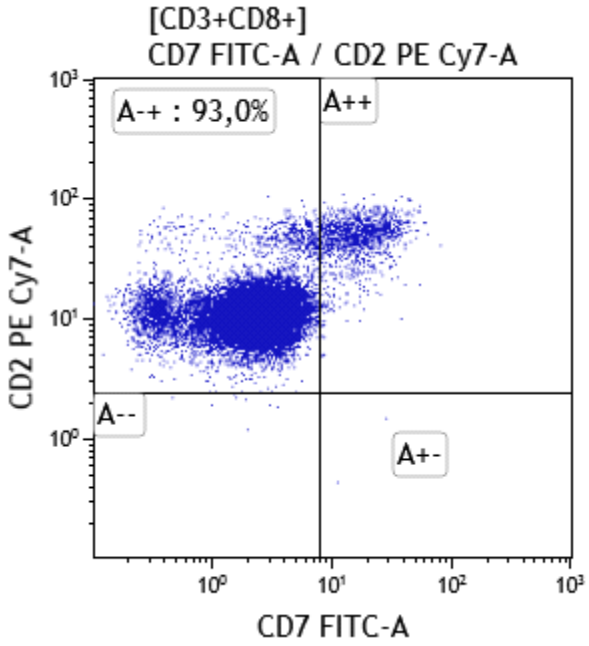

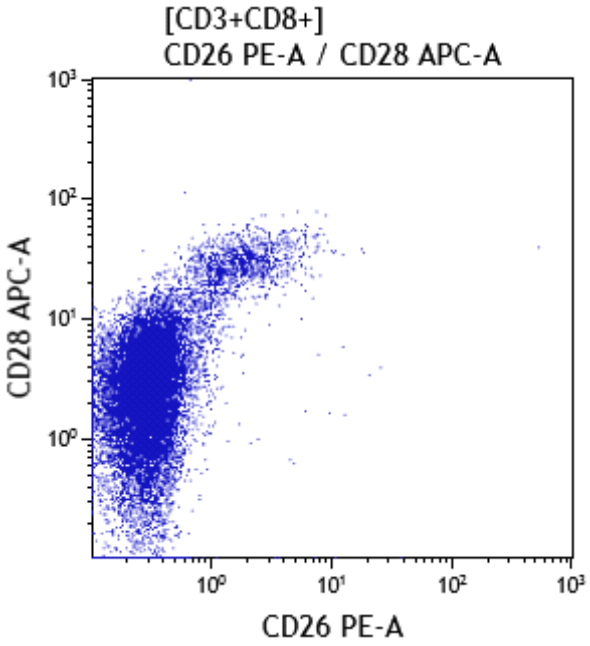

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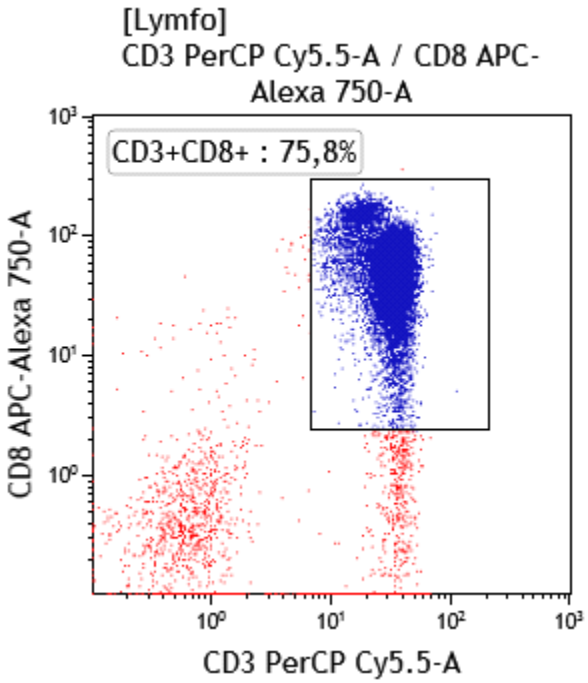

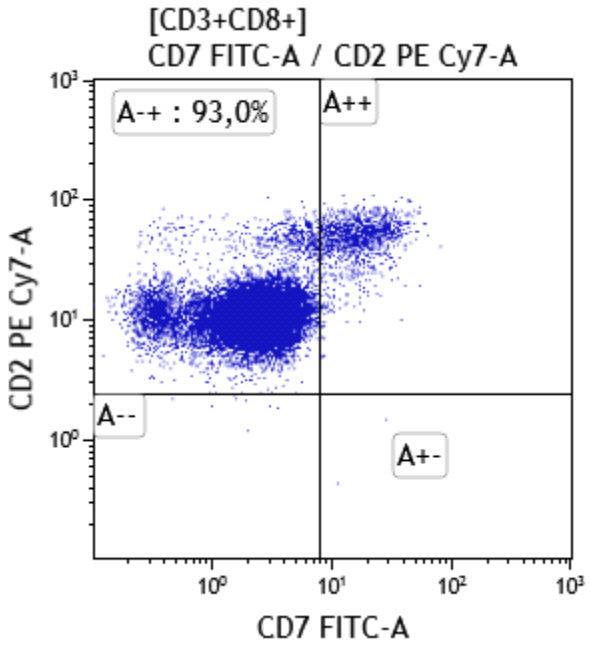

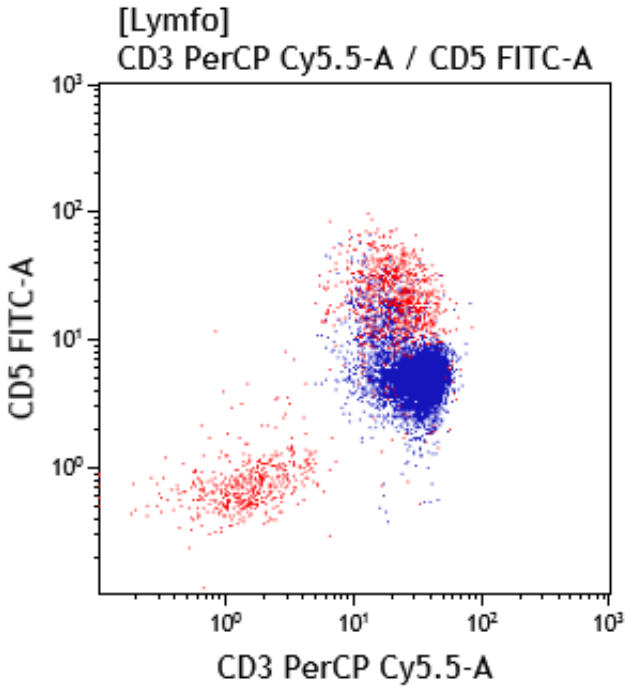

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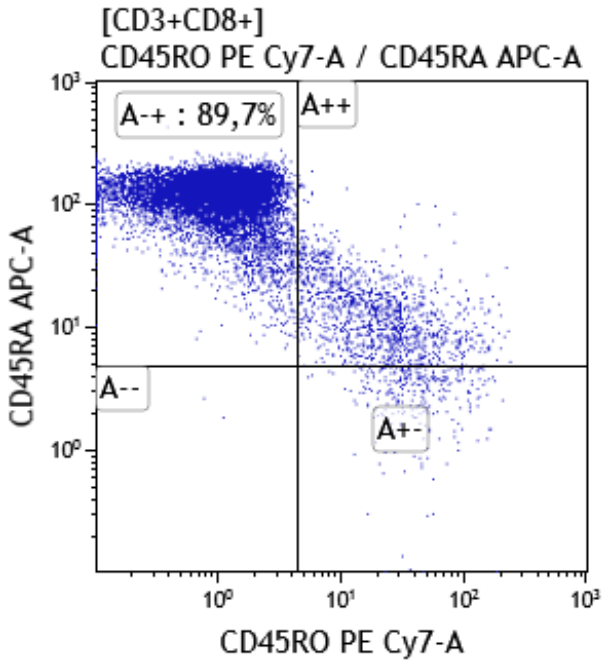

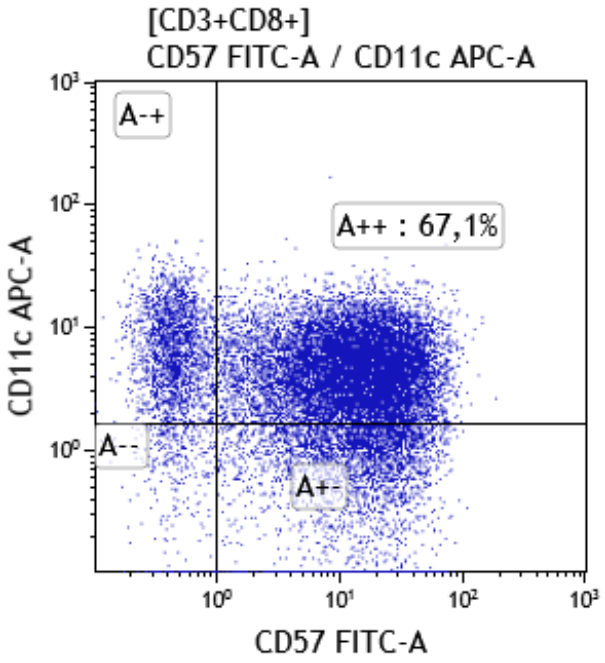

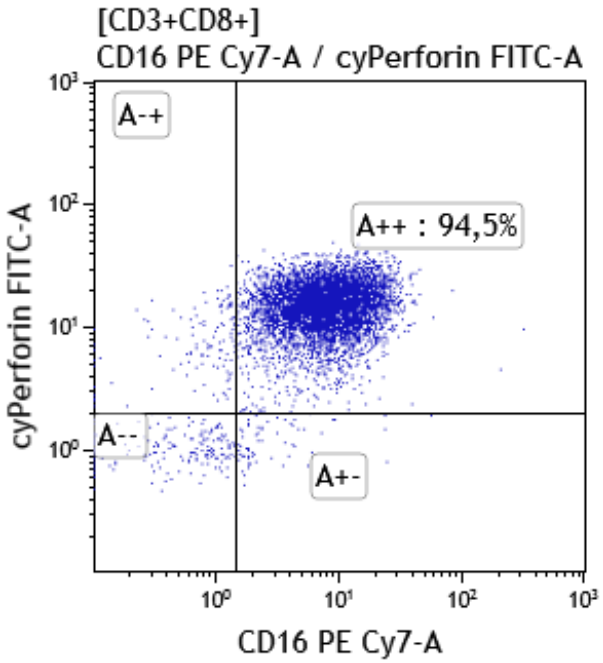

Na populaci leukocytů PK tvoří patologické T-lymfocyty 40% a exprimují CD3, CD2, $CD5^{dim}$, CD11c, CD16, CD45RA, CD56, CD57; negativní CD7. Nález svědčí pro T-LGLL.

T-LGLL

- Leukémie z velkých granulární T-lymfocytů
- Přetrvávající (>6 měs.) elevace velkých granulárních lymfocytů v PK bez jasné příčiny
- CD3+CD8+ (vzácně CD4+)
- 80% CD16+ a CD57+
- Abnormální exprese CD5, CD7
- CD11c+, CD45RA+

Závěr

- Diagnostika T/NK lymfoproliferací je komplexní, nestačí pouze imunofenotypizace
- Dif. dg. zvažovat dle kliniky, vyšetřovaného materiálu, dalších vyšetření…
- Rozsah dg. panelu zvážit dle pracoviště, primárně se zaměřit na vyš. PK
  - T-LGLL, MF/SS, PTCL-NOS, T-PLL
  - CD2, CD3, CD4, CD5, CD7, CD8, CD16, CD56

Děkuji za pozornost