

The young side of
LYMPHOMA

gli under 40 a confronto

Reggio Emilia, Hotel Mercure Astoria
2-3 ottobre 2026

**Linfomi cutanei: Il punto di vista
dell'anatomopatologo**

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Anatomia Patologica, Policlinico di Milano – Università di Milano

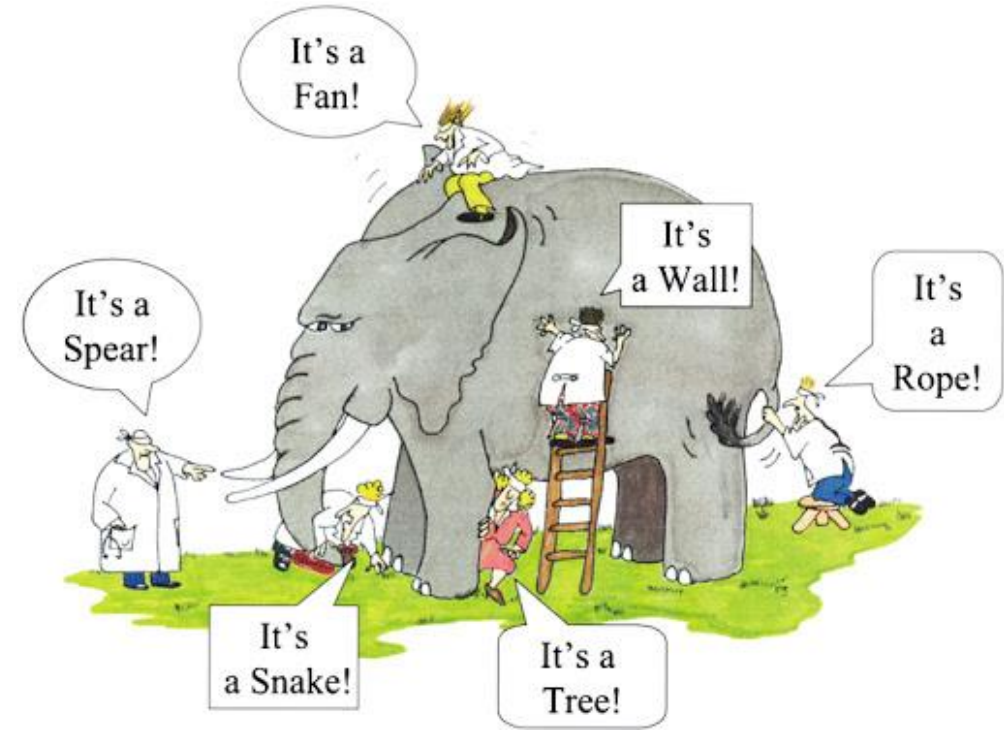


Disclosures of Name Surname

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Recordati Rare Diseases			x				

Approaching cutaneous lymphomas

1. Rare diseases, clonal processes
→ hyperplasia vs lymphoproliferative vs lymphoma
2. Diagnosis
→ pathologist + dermatologist + hematologist
3. Clinical meaning
→ cutaneous vs systemic, indolent vs aggressive



BMJ VOLUME 330 7 MAY 2005

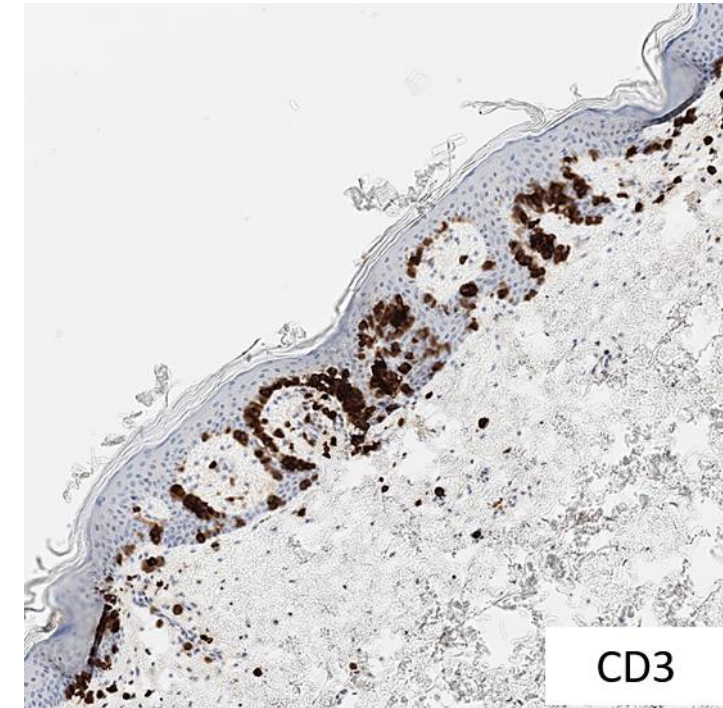
Why clinicians are natural bayesians

Christopher J Gill, Lora Sabin, Christopher H Schmid

Thought you didn't understand bayesian statistics? Read on and find out why doctors are expert in applying the theory, whether they realise it or not

Mycosis fungoides (MF) is

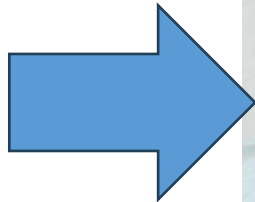
- a primary cutaneous T-cell lymphoma
- clinically characterized by the sequential evolution of patches, plaques, and tumours
- pathologically comprising infiltrates of clonal small to medium-sized mature T cells with hyperconvoluted nuclei, which are epith

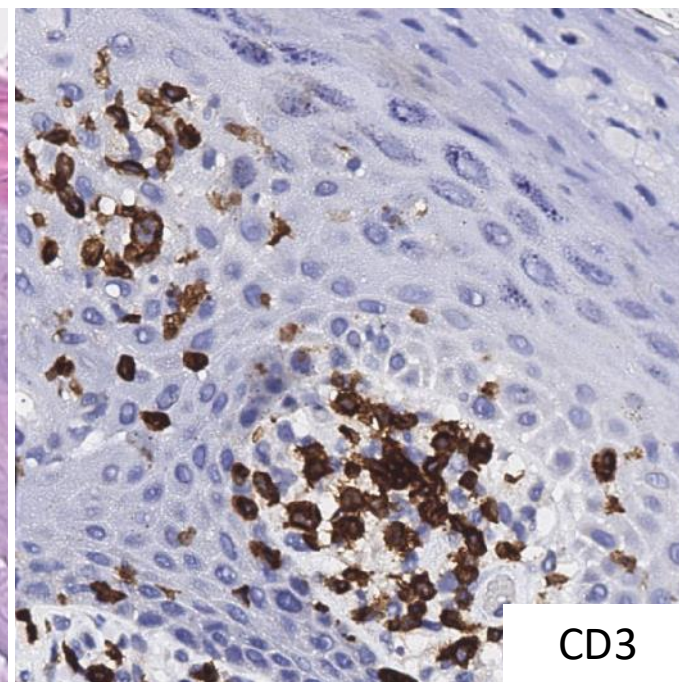


Diseases don't read books!

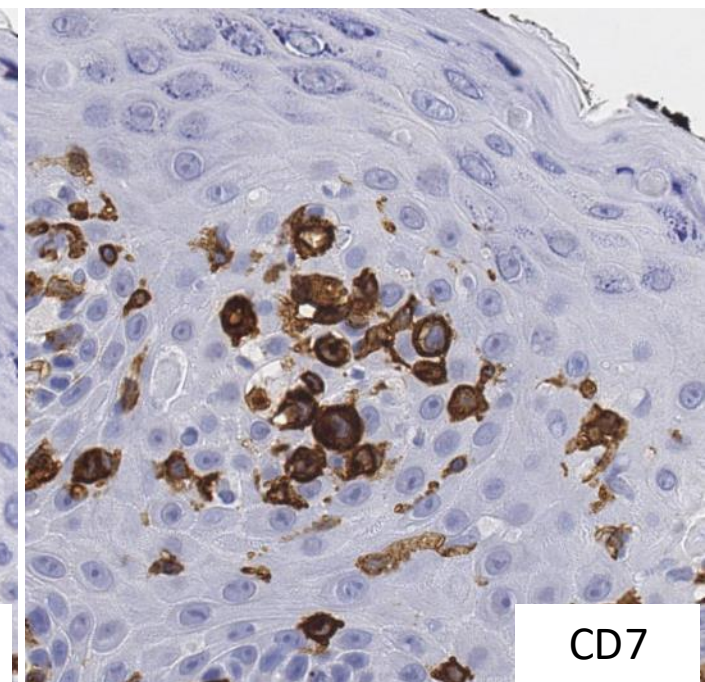
Case outline

- Male, 58 y.o.; unremarkable past history
- Since last 3 years, erythematous lesions with fine desquamation, interpreted as psoriasis with erythrodermic features
- December 2021: suspicion of mycosis fungoides; blood cell count within limits; clinical and radiological staging negative
- referred to our Institution in March 2022

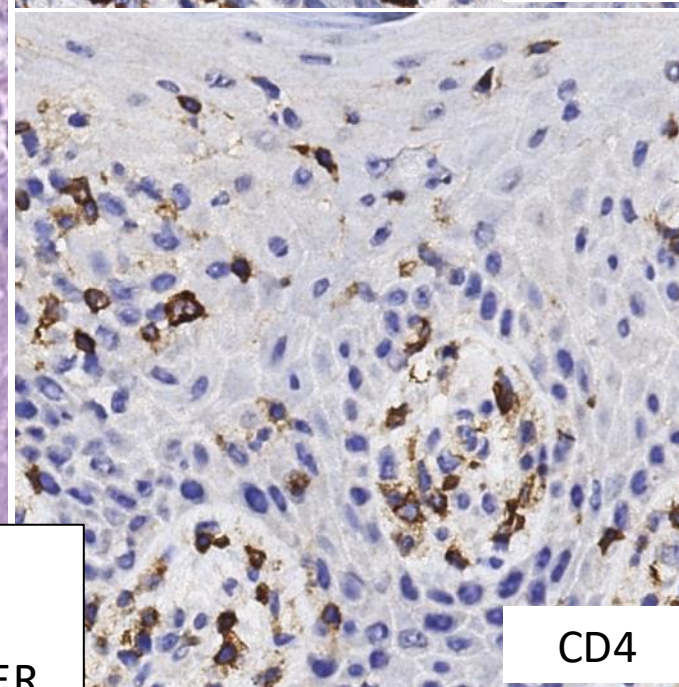




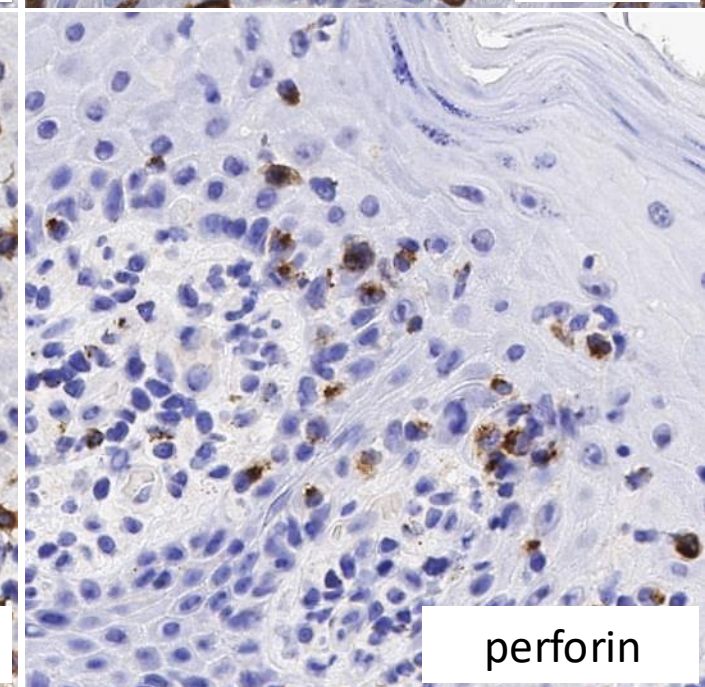
CD3



CD7

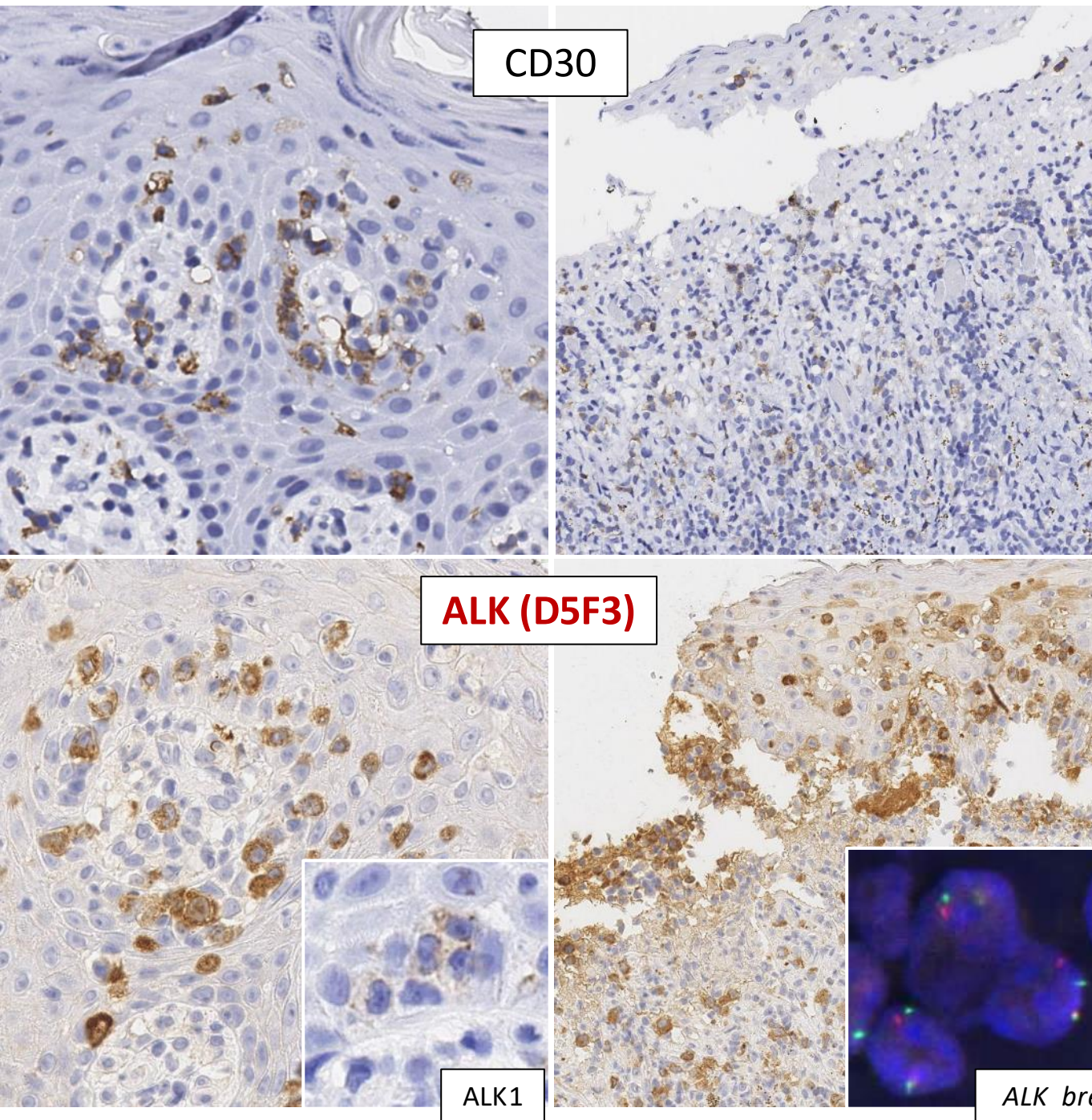


CD4



perforin

CD2+/-, CD3-/+ , CD5-, CD7+, BetaF1+
CD4+dim, granzymeB+, perforin+
Negative: CD8, TCRdelta, CD56, CD45RA, Tbet, PD1 and EBER



Molecular features

- **ALK rearrangement** (FISH, break apart probe)
- RNAseq failed to identify partner

Staging → skin limited disease

- CT, PET: no adenopathies nor organs involvement
- bone marrow biopsy negative

Vote your diagnosis:

1. Mycosis fungoides

→ **clinical pattern and epitheliotropic, BUT unusual morphology and phenotype**

2. Primary cutaneous CD8+ aggressive epidermotropic cytotoxic T-cell lymphoma («Berti's»)

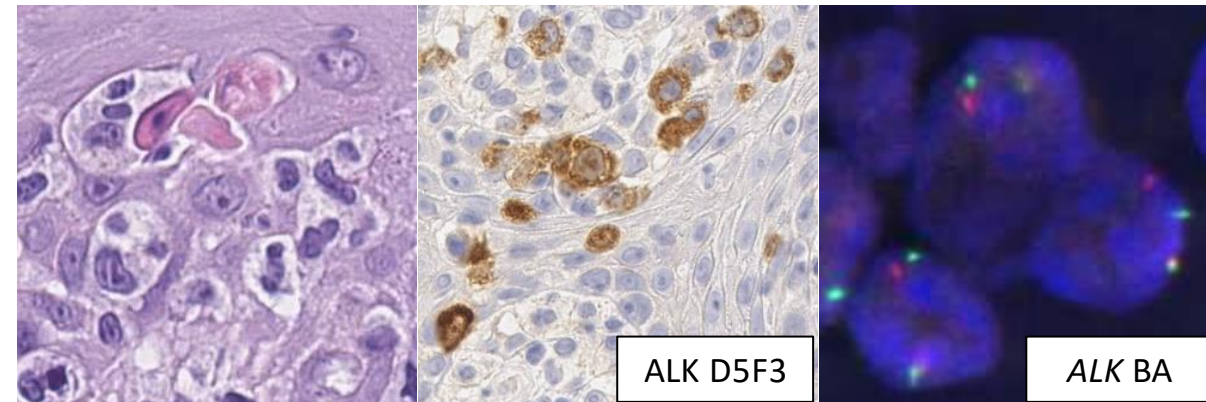
→ **indeed cytotoxic, BUT CD4-positive, and ALK+...**

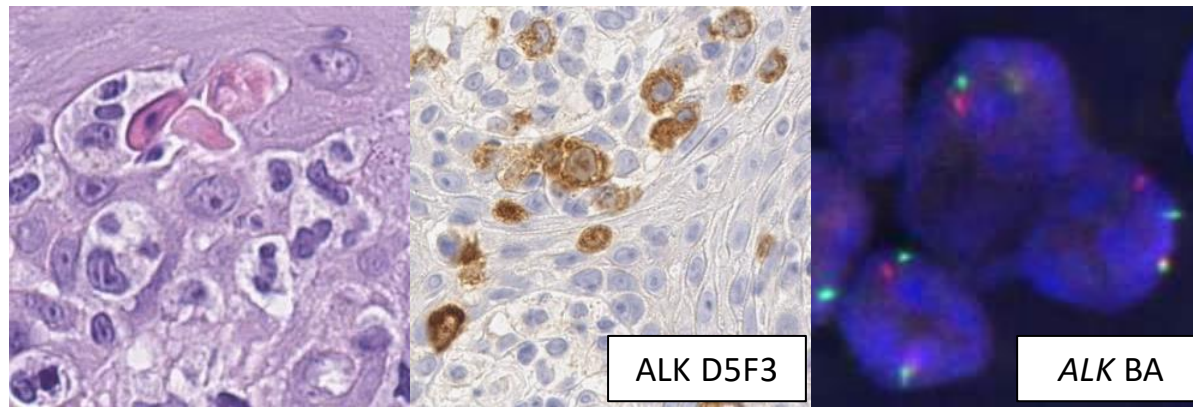
3. ALK+ anaplastic large cell lymphoma, both primary cutaneous or nodal / systemic

→ **pleomorphic / anaplastic and (dim) CD30+, BUT very unusual pattern**

4. Primary cutaneous peripheral T-cell lymphoma, NOS

→ **waste basket...**





Proposed diagnosis

Epidermotropic, cytotoxic, ALK-positive cutaneous T-cell lymphoma

→ **MF-type pattern**

Virchows Archiv (2024) 485:417–425

<https://doi.org/10.1007/s00428-024-03832-6>

Primary cutaneous, epidermotropic mycosis fungoides-like presentation: critical appraisal and description of two novel cases, broadening the spectrum of ALK+ T-cell lymphoma

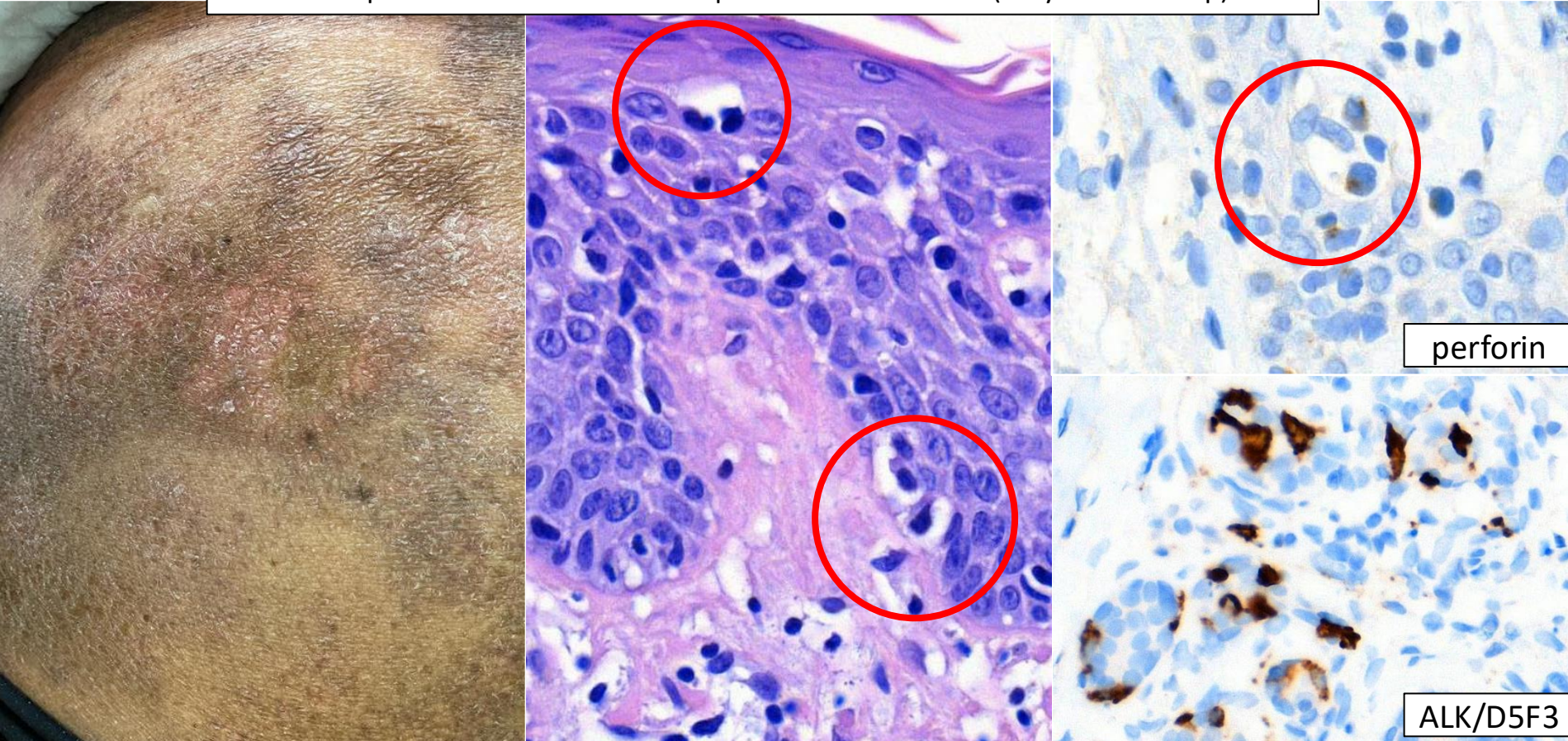
Giorgio Alberto Croci^{1,2}  · Lorena Appio³ · Caterina Cecchetti³ · Silvia Tabano^{1,4} · Silvia Alberti-Violetti^{1,5} · Emilio Berti⁵ · Daoud Rahal⁶ · Francesca Cavallaro⁷ · Francesco Onida⁸ · Dario Tomasini⁹ · Elisabetta Todisco³

MF-like, ALK+

Case 2

→ 65 y.o. patient with a 15-year history of MF + stage I nodal ALK+ ALCL

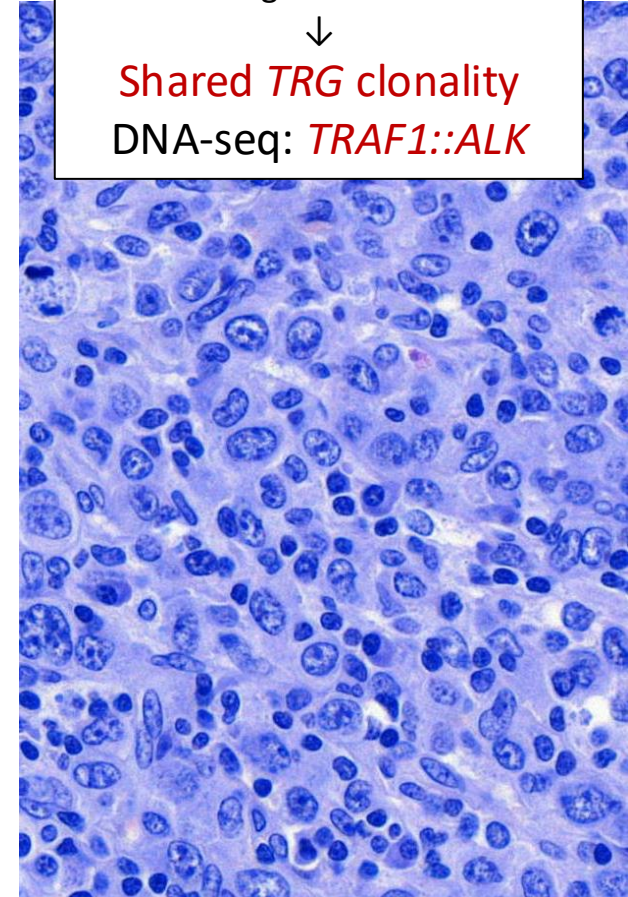
SKIN: poikiloderma vasculare atrophicans variant of MF (18-year follow up)



LN: stage I ALK+ ALCL



Shared *TRG* clonality
DNA-seq: *TRAF1::ALK*



Prognosis and therapy (n = 7)

Follow up and prognosis

- very limited experience; **generally, mycosis fungoides-like**, longstanding course (4-20 yrs)
- limited stage nodal involvement has been observed (II B stage sec. EORTC)

Therapy

Literature

- skin-directed (MF-type); 1 patient treated with chemotherapy and anti-CD30, followed by allo-ASCT

Current case

- acitretin (psoriasis); three lines of CT + anti-CD30, with CR, followed by relapses;
- fourth line, **crizotinib**: CR but followed by relapse and sepsis



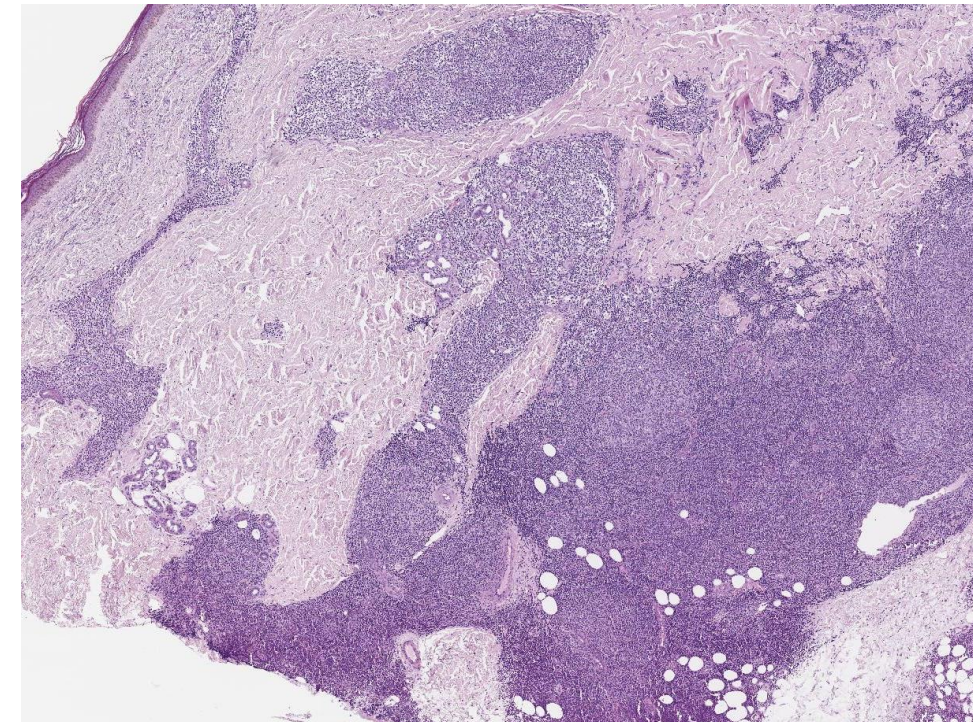
Abdulla FR et al. *J Cutan Pathol*. 2013;40(3):348-350
Quintanilla-Martinez L et al. *Am J Clin Pathol*. 2013;139(4):491-514
Wehkamp U et al. *J Cutan Pathol*. 2015;42(11):870-877
Barbe J et al. *Int J Dermatol*. 2020;60(4):e146-e147

And now
for something
completely different...



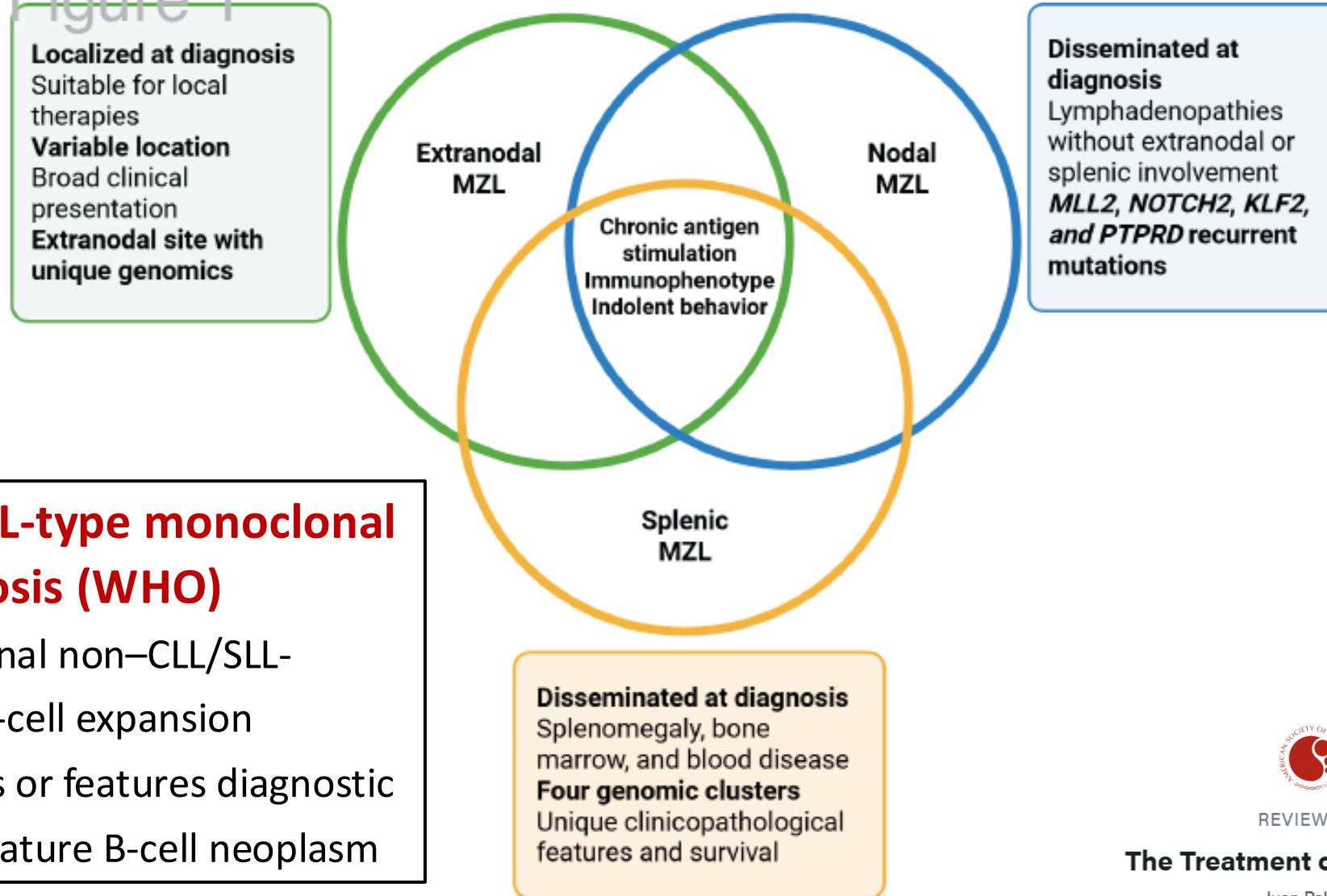
Primary cutaneous marginal zone lymphoma

- an **indolent cutaneous B-cell lymphoma**
composed of neoplastic small B cells, plasma cells, and a variable number of reactive T cells;
- **no evidence of extracutaneous disease at the time of diagnosis**
- exclusion of other cutaneous lymphomas



The spectrum of marginal zone

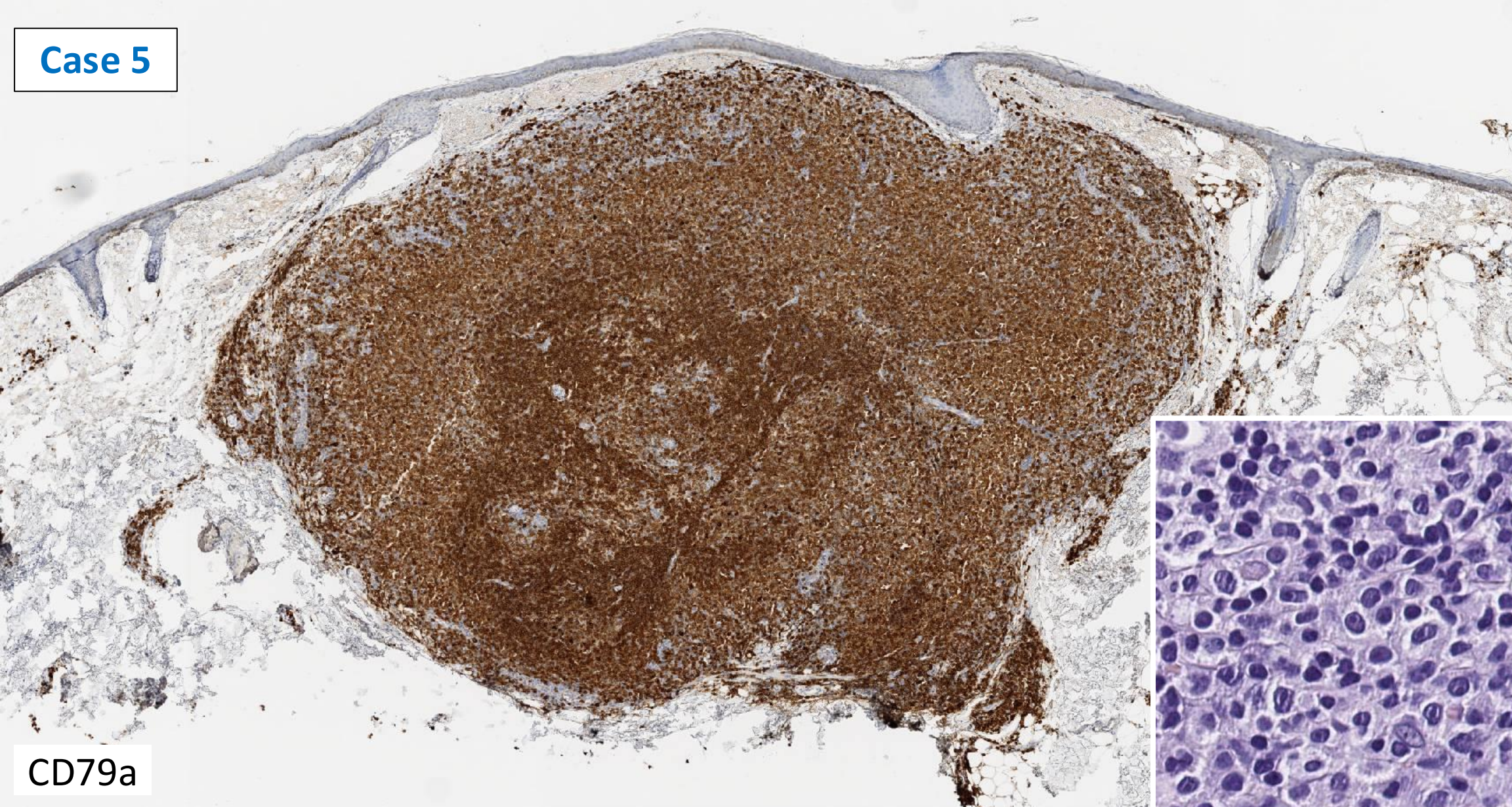
Figure 1



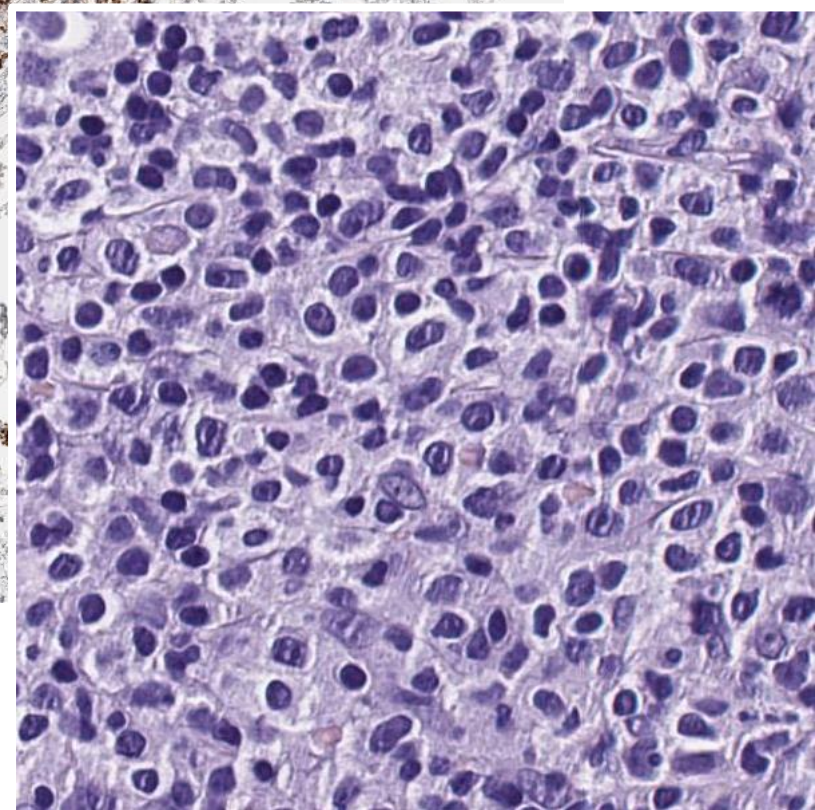
+ non-CLL/SLL-type monoclonal B-lymphocytosis (WHO)

- any monoclonal non-CLL/SLL-phenotype B-cell expansion
- no symptoms or features diagnostic of another mature B-cell neoplasm

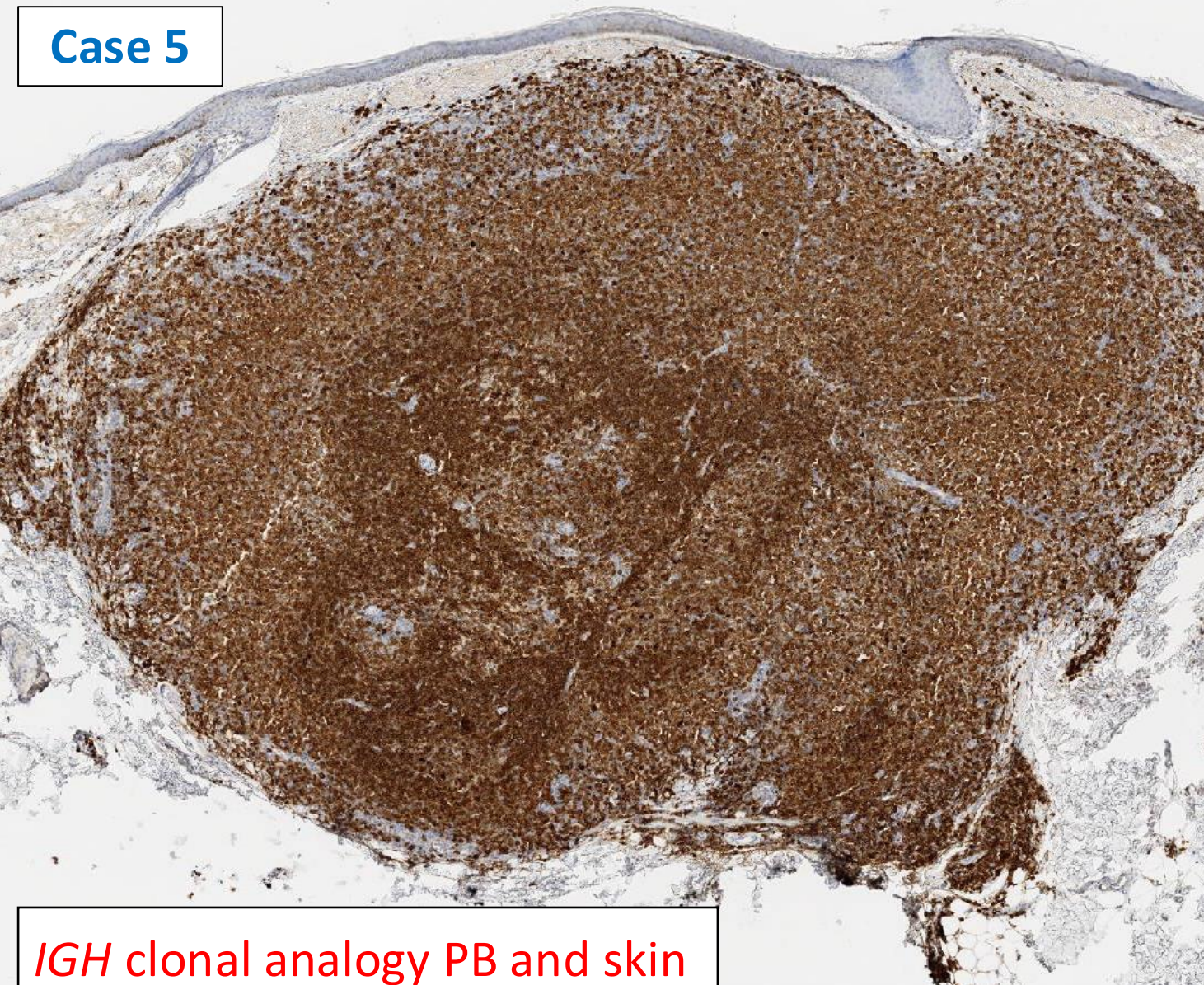
Case 5



CD79a



Case 5



F, 72 y.o., acnes-like manifestation

- PB Ly normal range/ μ L;
- no splenomegaly, nor adenopathies
- **BM 1% MZL-like monocytic B-cells**

***IGH* clonal analogy PB and skin**



Vote your diagnosis and strategy:

1. Extranodal MZL, stage IV

→ **chemo-immunotherapy**

2. Extranodal MZL, stage IV

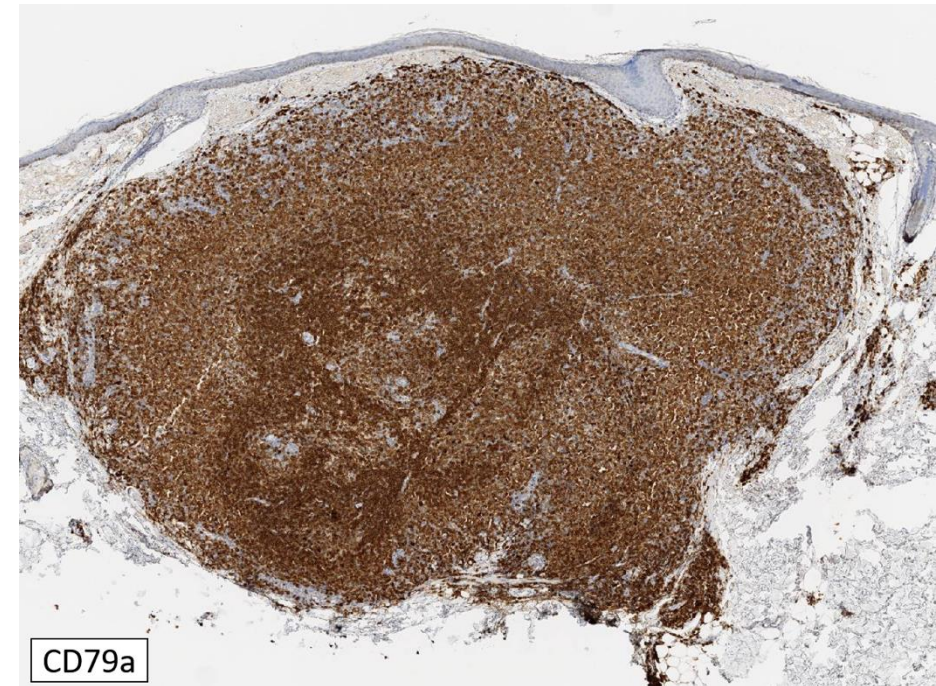
→ **wait and see**

3. Primary cutaneous MZL + monoclonal B-cell lymphocytosis, MZL-type

→ **skin directed therapy**

4. Splenic MZL with cutaneous involvement

→ **chemo-immunotherapy**



What is already known about this topic?

- In recent classifications several cutaneous malignant lymphomas were reclassified as cutaneous lymphoproliferative disorders (LPDs).
- These include primary cutaneous CD4⁺ small/medium T-cell LPD (PCSM-TCLPD), primary cutaneous acral CD8⁺ T-cell LPD (acral CD8⁺ TCLPD) and primary cutaneous marginal zone lymphoma/LPD (PCMZL/LPD).
- Recommendations for the management and treatment of cutaneous LPDs are lacking.

PCMZL/LPD

Physical examination of skin and peripheral lymph nodes
Complete blood count, differential, lactate dehydrogenase
immunoelectrophoresis

Borrelia testing (serology; *Borrelia* DNA on tissue sections)^a

Computed tomography of the neck, chest, abdomen, pelvis

- «It was agreed that **further studies are required** to more accurately define risk factors for progressive disease, which may be helpful to decide in which patients CT scans are required»
- **Bone marrow not recommended, nor flow cytometry on PB**

Case 5

Acnes-like cutaneous MZL

+ MZL-type monoclonal B-lymphocytosis



Arch Dermatol. 2012;148(7):824-831.

Cutaneous B-Cell Neoplasms Mimicking Granulomatous Rosacea or Rhinophyma

Aviv Barzilai, MD, MSc; Hana Feuerman, MD; Pietro Quaglino, MD; Michael David, MD; Meora Feinmesser, MD; Marisa Halpern, MD; Edit Feldberg, MD; Carlo Tomasini, MD; Hilla Tabibian-Keissar, PhD; Ninette Amarilgio, PhD; Emilia Hodak, MD

12 patients (F>M), with B-LPD presenting with a facial eruption mimicking rosacea or rhinophyma:

- **6 pcMZL**
- 4 pcFCCL
- 2 skin involvement in CLL

In the **setting of preexisting rosacea**, or as a new eruption.

Case 7

Localized plaque

MZL-MBL

PB Ly 1760/ μ L

BMB 5%

IGH analogy skin/PB



Case 4

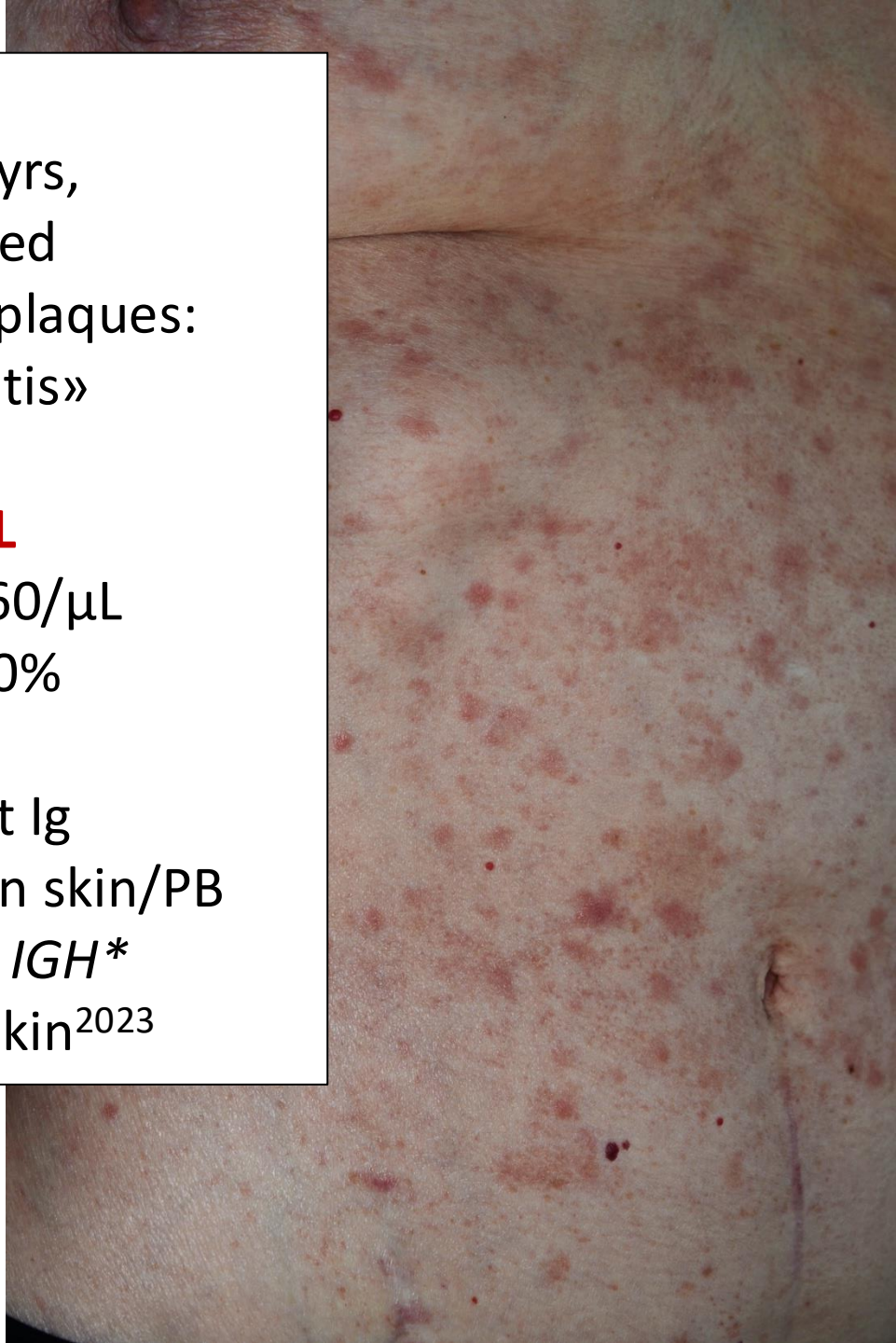
Since 13 yrs,
generalized
patches/plaques:
«dermatitis»

MZL-MBL

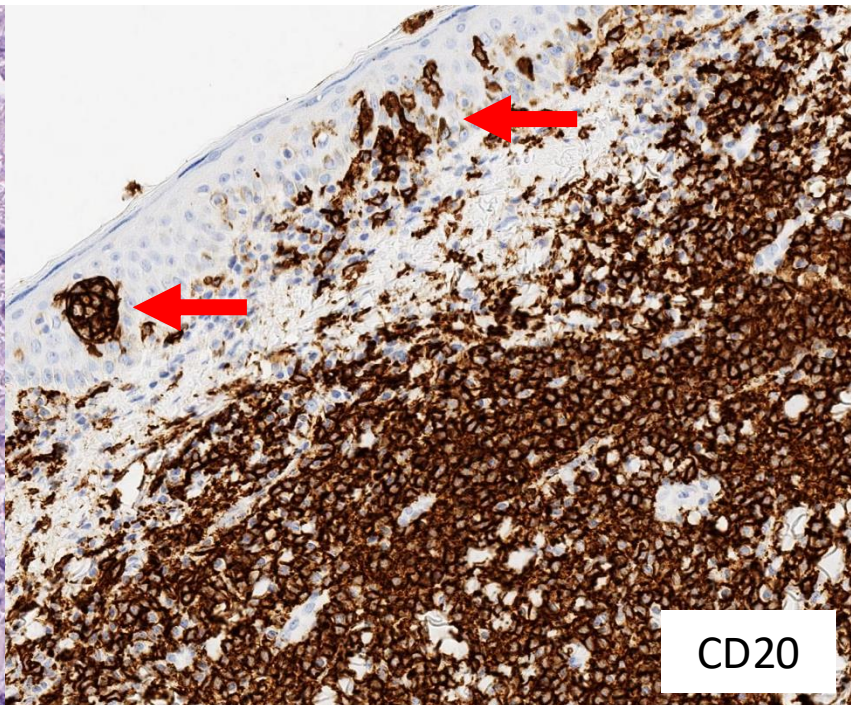
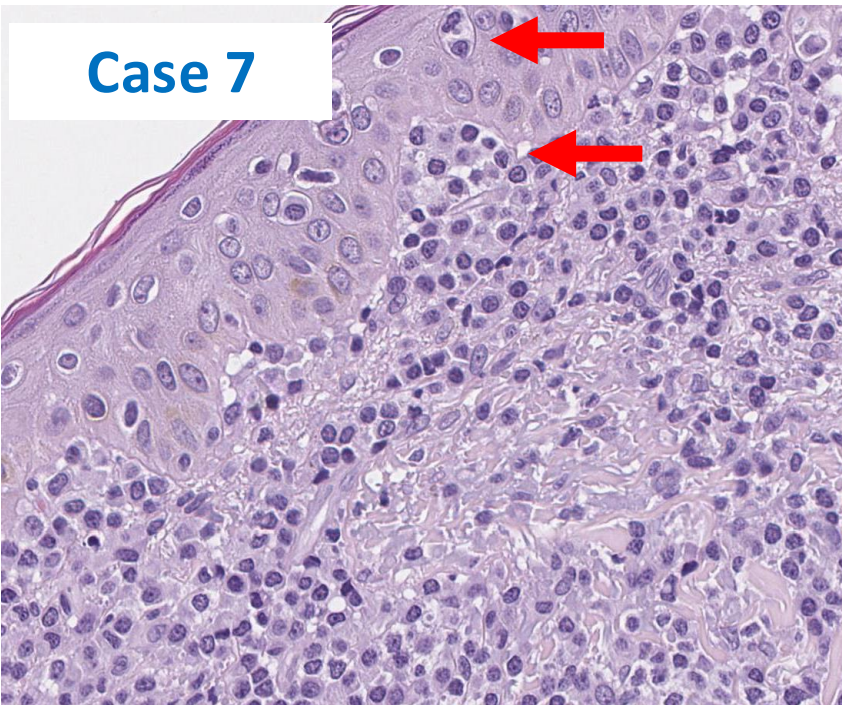
PB Ly 2360/ μ L

BMB 9-10%

Divergent Ig
restriction skin/PB
Different *IGH**
skin²⁰¹⁵/skin²⁰²³

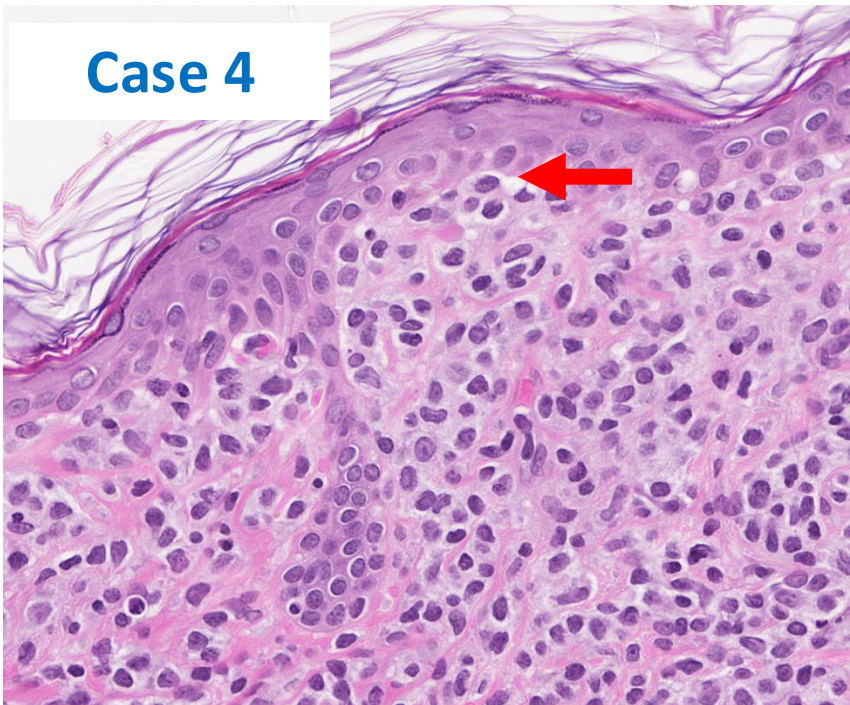


Case 7



CD20

Case 4



Am J Dermatopathol • Volume 38, Number 2, February 2016
Epidermotropic B-Cell Lymphoma: A Unique Subset of CXCR3-Positive Marginal Zone Lymphoma

- «diffuse skin rash»
- BM/PB+ in 4/5 detailed cases
- None, died of disease

TABLE 1. Summary of Cases of Epidermotropic B-Cell Lymphoma Involving the Skin Reported in the English Literature to Date (Including Our Cases)

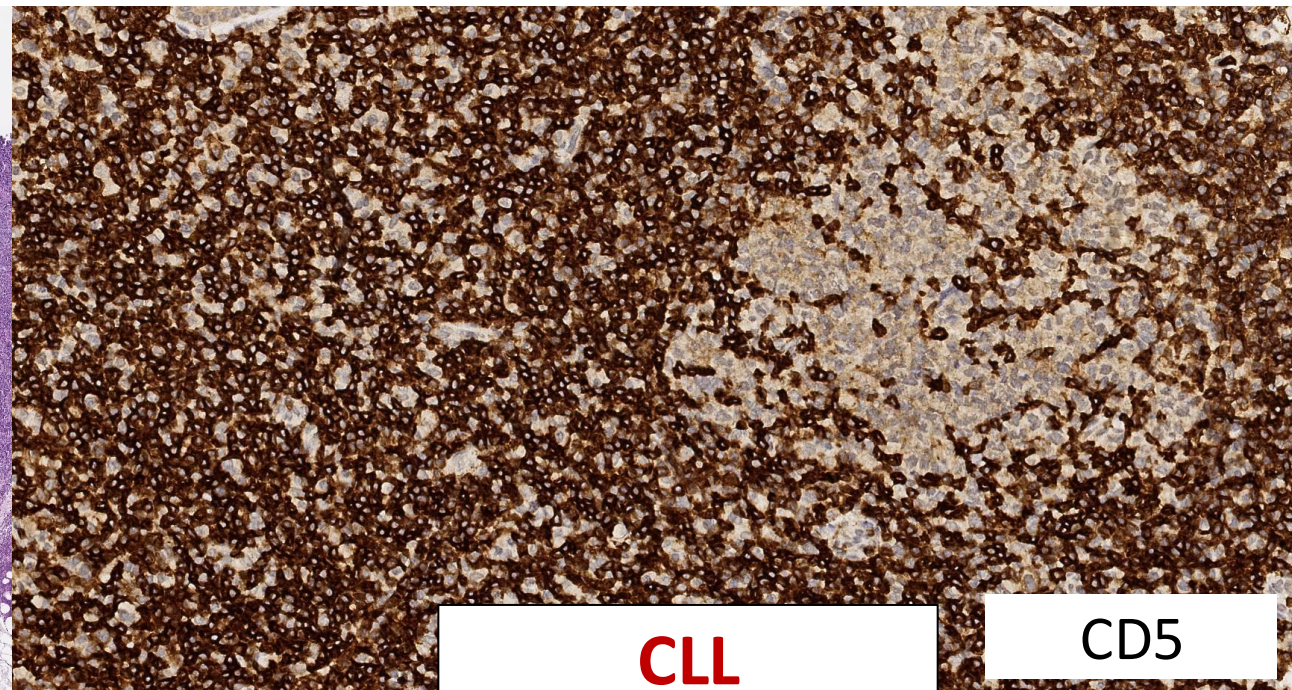
Reference	Age (yrs)/ Sex	Nature of the Skin Disease	Duration of Skin Disease Before Diagnosis	Symptoms	Extracutaneous Involvement	Therapy	Outcome
Chui et al ⁹	70/M	Disseminated, trunk and prox. limbs	7 mo	Pruritic	BM	CHOP	Alive
Pavlović et al ¹⁰	56/M	Disseminated, trunk and arms	1.5 yrs	Pruritic	Unknown	PUVA and subcutaneous interferon- α	Alive
Chiang et al ¹¹	57/M	Disseminated, chest, abdomen, and thighs	5 yrs	Pruritic	BM, spleen, PB, splenic Lymph nodes	UVB	Alive
Lee et al ¹²	80/M	Disseminated, trunk and lower limbs	2 wks	Asymptomatic	Unknown	None	Alive
Gómez-de la Fuente et al ¹³	68/M	Disseminated, abdomen, trunk and limbs	1 yr	Asymptomatic	BM, PB, Spleen	R-CHOP	Died of viral hepatitis
Present	51/M	Disseminated, trunk	7 mo	Pruritic	BM	Chemotherapy	Alive
Present	74/F	Abdomen and cheek	Unknown	Asymptomatic	None	Unknown	Alive

BM, bone marrow; CHOP, cyclophosphamide, hydroxyl doxorubicin, vincristine, prednisone; F, female; M, male; PB, peripheral blood; PUVA, psoralen plus ultraviolet phototherapy; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; UVB, ultraviolet B phototherapy.

Case 6

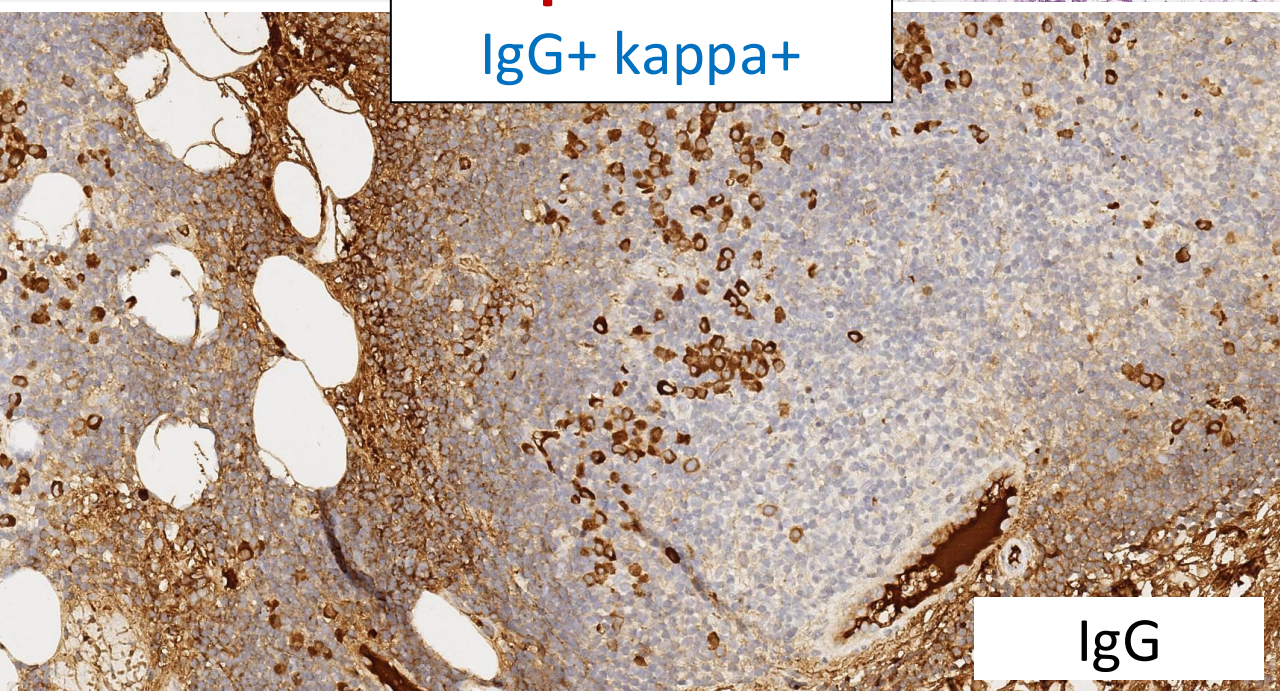


pcMZL
IgG+ kappa+

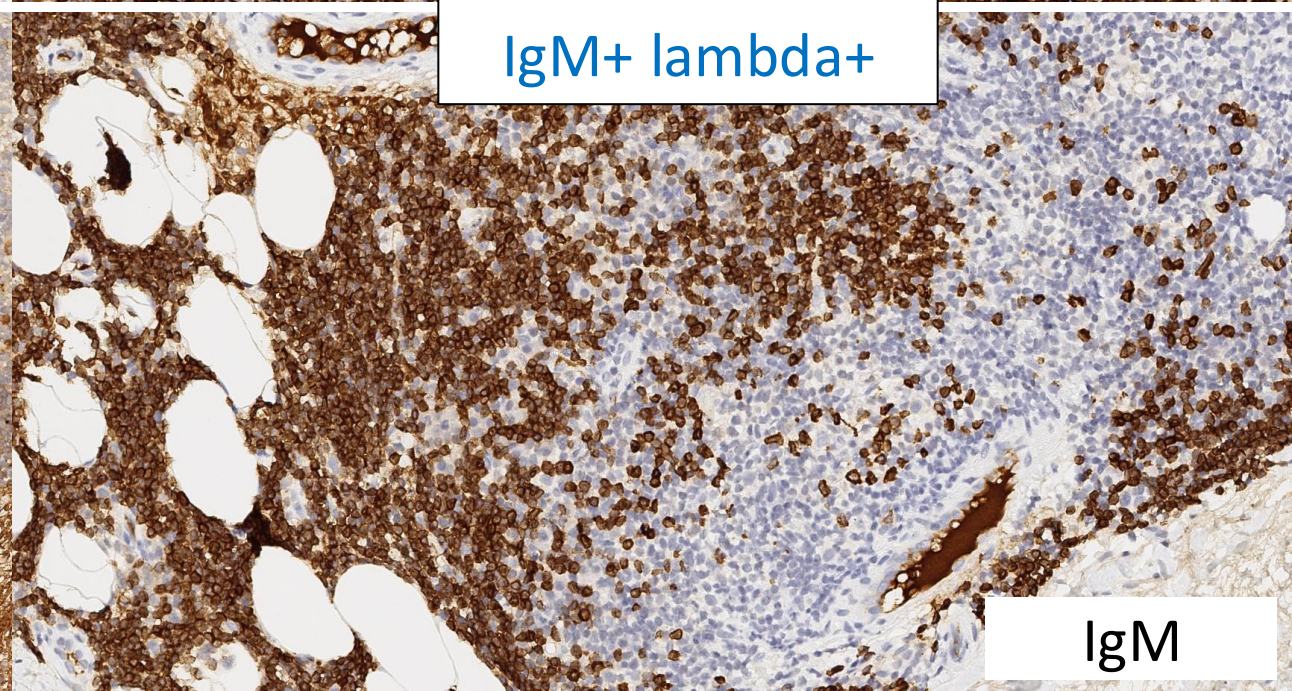


CLL
IgM+ lambda+

CD5



IgG



IgM



Case 6

Insect bite-like

CLL

PB Ly 4560/ μ L; BMB 30%

Lymph nodes > 15 mm

Topical steroid and wait and see



Lymphomatoid exaggerated insect bite-like reaction?

Therapy and follow up: Milano-Paris series (n=7)

Therapy

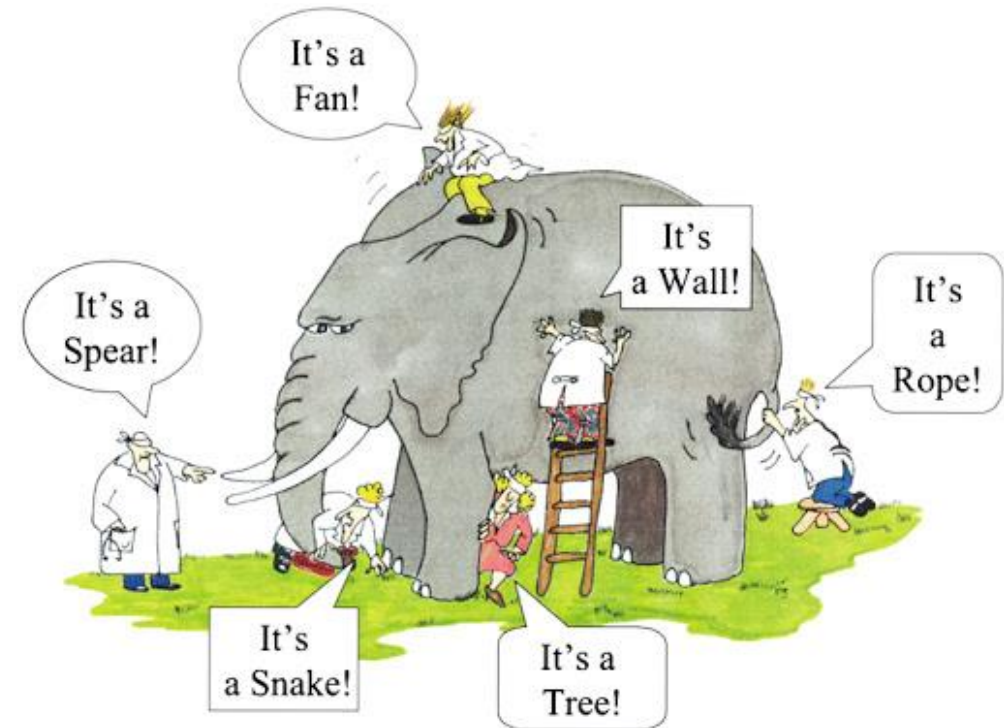
- 3 patients, **chemo-immunotherapy** (1 rituximab, 2 rituximab + chloraminophene) as first therapeutic choice, achieving partial or complete remission (2 PR, 1 CR)
- 4 patients, **local therapy** (3 steroid, 1 radiotherapy), achieving PR; 1 patient further started on rituximab + bendamustine, followed by PR and watchful waiting

Follow up

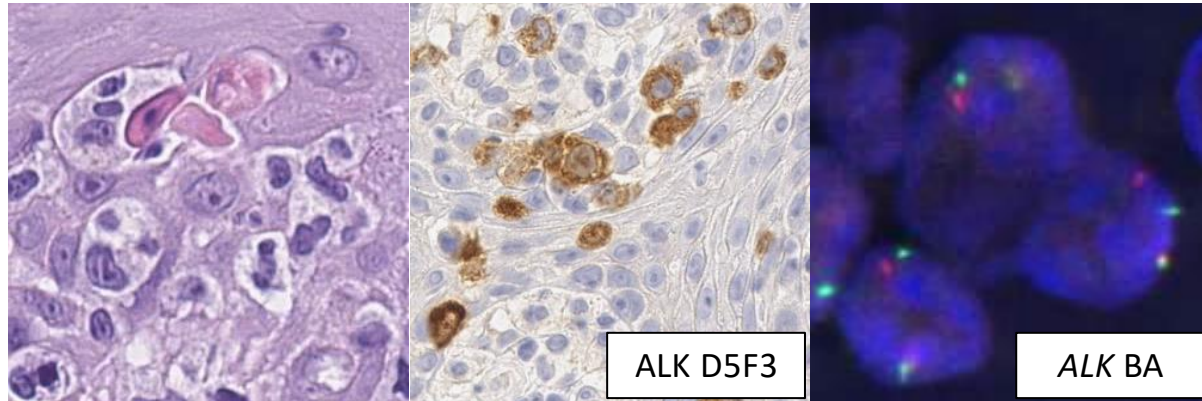
- **chronic-indolent course in all patients** (median follow up 4.5, range 2.5-13 years)
- **relapse / persistence of skin lesions**, no evidence of disease progression.

Find the pattern!

1. Clonal processes: **blurred borders (pattern)**
→ hyperplasia vs lymphoproliferative vs lymphoma
2. Diagnosis: **clinic-pathologic pattern!**
→ pathologist + dermatologist + hematologist
3. Clinical meaning: **see and wait (the pattern)**
→ cutaneous vs systemic, indolent vs aggressive:
rely on what you see, along time and space



Acknowledgments



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