

Cutaneous Lymphoma

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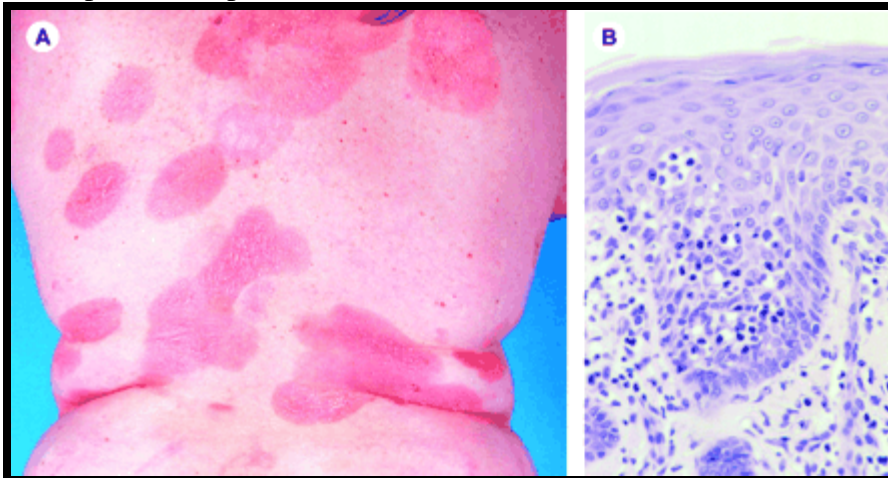
WHO-EORTC CLASSIFICATION OF CUTANEOUS LYMPHOMAS WITH PRIMARY CUTANEOUS MANIFESTATIONS (2005)

1. Addresses differences with WHO classification (2008) for all lymphomas
2. Uses Dutch/Austrian frequency and survival data
3. 1:100,000 annual incidence (#2 after GI tract)

CUTANEOUS T-CELL AND NK-CELL LYMPHOMAS (CD3)

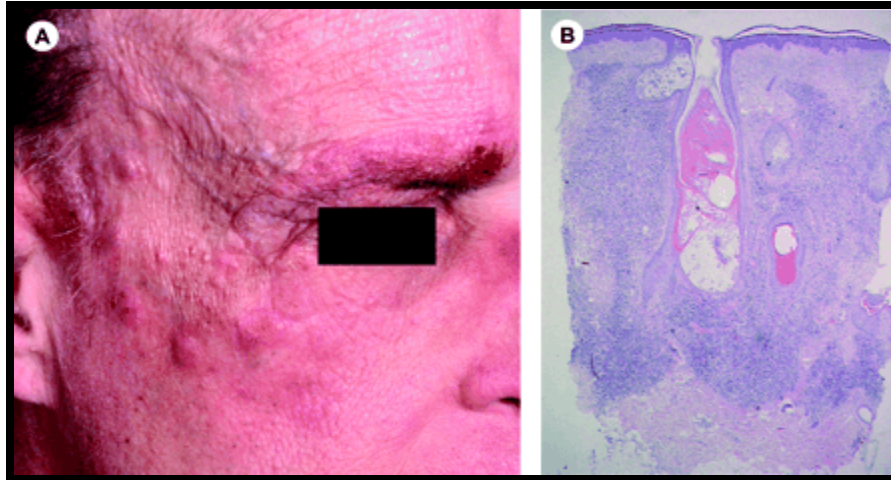
Mycosis fungoides

1. 50% of all primary cutaneous lymphomas—
 - a. Important to stage patient <10% BSA; Tumor, Systemic
2. Reserve term for classical "Alibert-Bazin" type--(patch/plaque/tumor progression)—other tumors have epidermotropism.



3. Older, buttock, slow progression—if present with tumors, not MF
4. Histology
 - a. Epidermotropism
 - i. Pearls on a string (basalis)
 - ii. Pautrier's microabscesses—often not present; may low upward scatter with progression to tumor stage
 - b. CD3+, CD4+CD7-CD8- (most common)
 - i. CD3-panT; CD4-Thelper, CD8
 - ii. Loss of Antigen (CD7, CD26); Gain (CD2,CD3,CD5)
 - c. Clonality—usually present—same clone at different sites (useful for diagnostics)
 - d. 10q and abnormalities in p15, p16, and p53 tumor suppressor genes.
5. Transformation
 - a. >30% large cells (blasts)—can be CD30+ or neg—doesn't matter
 - b. Gain cytotoxic proteins--T-cell intracellular antigen-1 [TIA-1], granzyme B

6. MF variants and subtypes
 - a. Folliculotropic MF—adult men, like tumor stage MF—treat deeper (electron beam)
 - i. vs follicular mucinosis (alopecia mucinosa)-difficult
 - ii. clonality not helpful



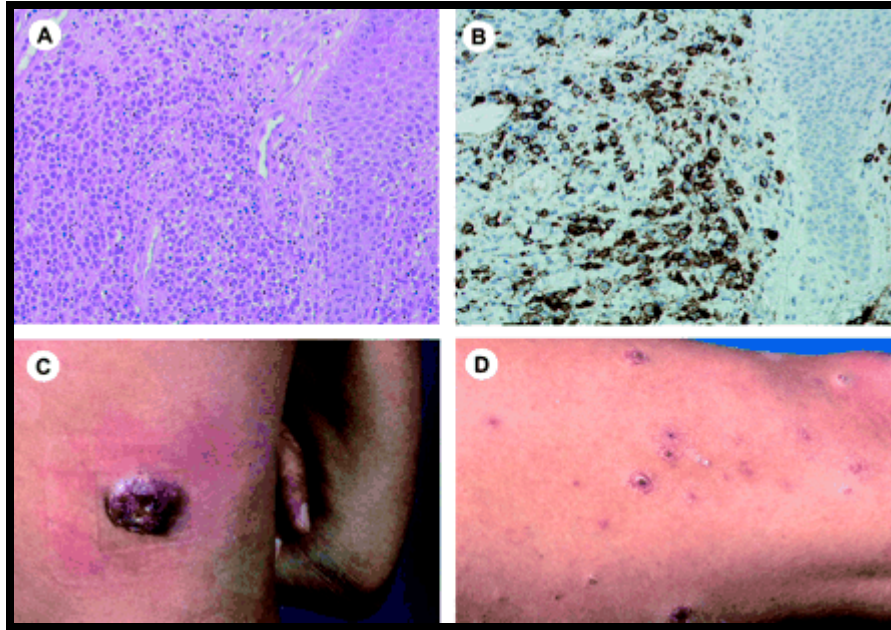
- b. Pagetoid reticulosis
 - i. Large epidermotropic cells (localized type (Woringer-Kolopp type) localized (hand/arm)—(not disseminated Ketrin-Goodman type)
 - ii. CD4+ or CD8+.
- c. Granulomatous slack skin—rare, CD4+/-granulomatous/epidermotropic, specific clinical
- d. Sézary syndrome—diagnose with flow cytometry and clonality studies
 - i. Absolute Sézary cell count of least 1000 cells/mm³
 - ii. CD4/CD8 ratio > 10
 - iii. Loss of CD2, CD3, CD4, CD5 or CD7

Other T-cell Lymphomas

Primary cutaneous CD30+ lymphoproliferative disorders—30% of all lymphoma—most of remaining after MF

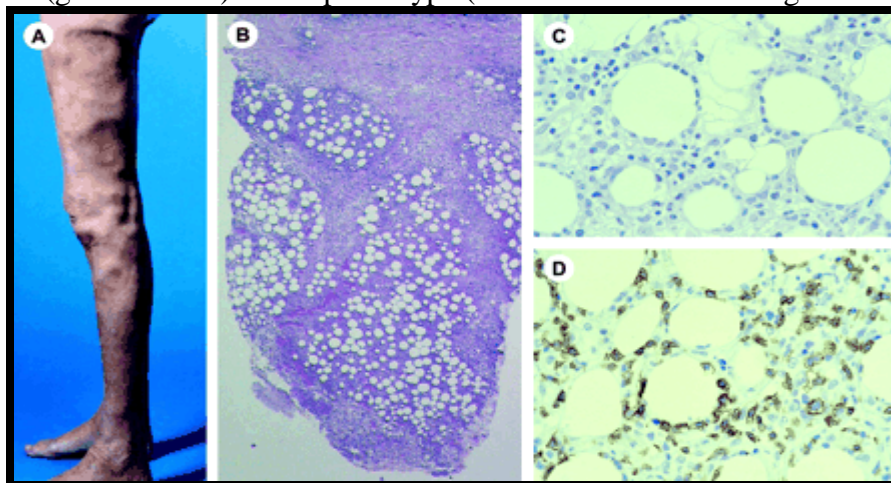
1. Primary cutaneous anaplastic large cell lymphoma vs Lymphomatoid papulosis (LyP)
 - a. Clinical and histologic distinction
 - b. CD4+, CD30+ (Concept: Any large hematopoietic cell can be CD30+)
 - c. No anaplastic lymphoma kinase (ALK) (2;5)(p23;q35) translocation—seen in systemic anaplastic;
 - d. No CD15 (Hodgkin's)

- e. LyP—Histology (Willemze A and B—older classification)
- i. Type A—Reed-Sternberg-like (owl eyes) (CD30+)
 - ii. Type B—MF like—cerebriform—CD30 negative
 - iii. Type C—Monotonous large cluster of CD30+ cells--rare



Subcutaneous panniculitis-like T-cell lymphoma

1. Legs, careful with diagnosis of LE profundus
2. Histo—septal and lobular—“rimming” or adipocytes helpful
3. Two clinical variants
 - a. $\alpha\beta^+$ T-cell phenotype (75%)—indolent
 - i. Gene rearrangement important in diagnostics
 - ii. $CD8^+$
 - iii. Subcutaneous only (no dermal/epidermal)
 - iv. $\gamma\delta$ (gamma/delta) T-cell phenotype (25%--now has own designation—see below)



Cutaneous γ/δ (Gamma/delta) T-cell lymphoma (provisional)

1. Aggressive—not useful to classify as primary cutaneous or systemic; hemophagocytic syndrome
2. CD56+ plus cytotoxic proteins (TIA-1, granzyme B, perforin)
3. TCR gamma rearrangement (not beta)
4. Can involve all levels of skin (epidermis/dermis/subcutis)—may affect prognosis—?subcutaneous only worse?

Extranodal NK/T-cell lymphoma, nasal type

1. Asia/Latin America, adults
2. Not useful to separate from “nasal”
3. Histology—Angiodestructive
4. CD56+, EBV+

Primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma (provisional)

1. CD8 plus cytotoxic proteins (TIA-1, granzyme B, perforin)
2. Think of this when see pagetoid reticulosis

Primary cutaneous CD4+ small/medium-sized pleomorphic T-cell lymphoma (provisional)

1. May have been called “Tumor stage MF” in prior years
2. Upper body
3. Fairly good prognosis—excise or XRT.

Adult T-cell leukemia/lymphoma

- a. HTLV-1,
- b. Acute (systemic) vs “smoldering” skin only—tx smoldering like MF
- c. CD4+, ++CD25 (board question)

Primary cutaneous peripheral T-cell lymphoma, unspecified—Trash can for unclassifiable lymphomas.

CUTANEOUS B-CELL LYMPHOMAS (CD20, CD79a)**Primary cutaneous marginal zone B-cell lymphoma**

1. Clinical—multiple lesions, trunk/arms, ulceration
 - a. Helps in distinguishing from cutaneous lymphoid hyperplasia (aka Pseudolymphoma)—both have 100% survival-??
 - b. *Borrelia burgdorferi* association in Europe
2. Marginal zone—edge of follicle (centrocyte)—formerly called “immunocytoma”
3. Plasma cells—“light chain restriction”—only kappa or lambda (Normal 2:1 κ : γ)
4. Don’t get same translocation as other MALT lymphomas—get t(14;18)(q32;q21) (IGH and MLT genes) and t(3;14)(p14.1;q32) (IGH and FOXP1)

Primary cutaneous follicle center lymphoma

1. Clinical—Scalp/trunk—single lesion—good prognosis with XRT
2. Histo—Follicles with epidermal sparing—can have blasts (Centroblasts, Immunoblasts)
3. bcl-6—no macrophages in follicles (“tangible”)
4. No bcl-2 or t(14;18) translocation, as seen in systemic.

Primary cutaneous diffuse large B-cell lymphoma, leg type

1. Elderly—bad prognosis
2. Diffuse, large cells (centroblasts)
3. bcl-2 positive; no t(14;18)

Intravascular large B-cell lymphoma

1. Usually systemic—rare cutaneous only—can look “angiomatous”
2. CD20+ cells in vessels

Primary cutaneous diffuse large B-cell lymphoma, other—Trash can

PRECURSOR HEMATOLOGIC NEOPLASM

CD4+/CD56+ hematodermic neoplasm (formerly blastic NK-cell lymphoma but not an NK cell)

1. Plasmacytoid dendritic cell—cell of origin
2. 50% marrow involvement—differentiated from myelomonocytic leukemia
3. EBV negative
4. Treat like leukemia

OTHER

Cutaneous Lymphoid Hyperplasia (CLH) (Pseudolymphoma)

1. Single or multiple lesions—old bite—consider complete excision.
2. B-cells (CD20) and T-cells (CD3)
3. CD21 highlights germinal centers (follicular dendritic cells)
4. CD10 and bcl-6 highlight ONLY germinal centers (Follicular lymphoma highlights beyond)
5. Can show clonality

Leukemia cutis—histology plus IHC studies

1. CD34—hits many cells
2. tDt--Can hit other lymphomas
3. Myeloperoxidase—anything myeloid (neutrophils, etc)

Flow Cytometry—Consider this as a diagnostic tool when you have EQUIVOCAL biopsy results and a cellular infiltrate.

1. Able to test many more antigens—better sensitivity/specificity
2. Able to look at 2 or more antigens at once (co-expression)
3. 4mm punch—mince and place in RPMI media (tissue culture media which can be obtained from the flow lab. Also, sending the biopsy fresh immediately to the lab also works.

CONCEPTS:

- 1. Clonality≠Malignancy**
- 2. Antigens: Can have loss of gain of antigens in malignancy—used in diagnostics (i.e. CD4+CD7- in MF).**
- 3. CD30 is expressed by many large cells (blasts)—not specific—can be associated with reactive (B9) processes.**
- 4. Don't overdiagnose MF—don't scare patients.**
- 5. Don't let the pathologist spend too much time working up an aggressive looking process.**
- 6. If it isn't acting benign (pseudolymphoma), it might be malignant.**
- 7. Primary cutaneous B-cell lymphoma is quite rare—much more common to have secondary involvement of skin by systemic lymphoma. Send the patient to an oncologist as soon as you suspect a B-cell lymphoma for a pan-man-scan.**

References

Willemze R et al. WHO-EORTC classification for cutaneous lymphomas. *Blood*, 15 May 2005, Vol. 105, No. 10, pp. 3768-3785.