Cutaneous T-Cell Lymphoma: A Dermatology Perspective

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Cutaneous Lymphoma Society

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Cutaneous T-Cell Lymphoma: A Son's Perspective

In 2001 I diagnosed my father with CTCL

What is CTCL

- Lymphoma of skin-homing T-cells
  - Rare: 0.3 / 100,000 incidence (new onset)
  - If KU Derm is referral center for 3 million, we should see 9 / year
- Clinical presentation: usually red and scaly
  - Often develops in setting of chronic eczema
  - Bathing-suit area
  - Can masquerade as other things such as morphea
- It's an immunologically confusing T-cell disease
  - Treat with immunosuppressives (steroids, lights)
  - Treat with immune boosters (IL-12, IFN)
  - Treat with immune ???'s (ECP)

When to suspect CTCL

- Chronic rash
- Not sure what it is
- Not going away after a few months
- More severe → get more suspicious

Most CTCL can be controlled

- Don’t panic
- Do take it seriously, or it can progress
- Many non-chemo treatments are available

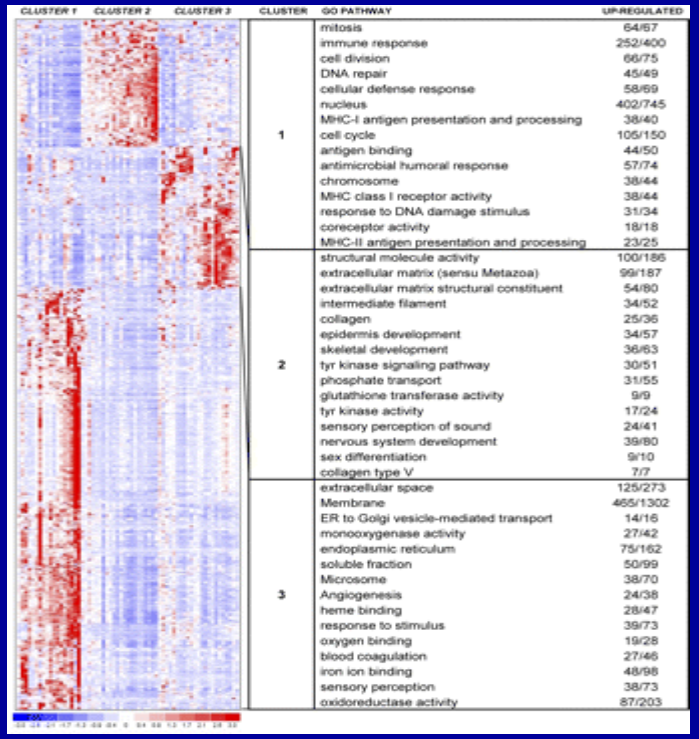
Working up CTCL

- CT with & without contrast to assess LN
- Labs
  - CBC w diff
  - LFT
  - flow CD3, CD4, CD7, CD8, CD15/56, CD4/25

Treatment philosophy

- Stamp out the disease!
  - In theory, aggressive subset emerges via mutation
  - More T-cell burden = more chances for mutation
  - Fewer T-cells = less substrate, less chance for mutation
- CTCL treatment is not yet cut-and-dried
- Doctors and patients need to handle ambiguity
  - Assess treatment responses and risks
  - “Dial” treatments up and down
  - Tailor the treatment to the patient

Array study: 3 CTCL Clusters



CLUSTER	GO PATHWAY	UP-REGULATED
1	mitosis	64/67
	immune response	252/400
	cell division	66/75
	DNA repair	45/49
	cellular defense response	58/69
	nucleus	402/745
	MHC-I antigen presentation and processing	38/40
	cell cycle	105/150
	antigen binding	44/50
	antimicrobial humoral response	57/74
	chromosome	38/44
	MHC class I receptor activity	38/44
	response to DNA damage stimulus	31/34
	coreceptor activity	18/18
	MHC-II antigen presentation and processing	23/25
2	structural molecule activity	100/186
	extracellular matrix (sensu Metazoa)	99/187
	extracellular matrix structural constituent	54/80
	intermediate filament	34/52
	collagen	25/36
	epidermis development	34/57
	skeletal development	36/63
	tyr kinase signaling pathway	30/51
	phosphate transport	31/55
	glutathione transferase activity	9/9
	tyr kinase activity	17/24
	sensory perception of sound	24/41
	nervous system development	39/80
	sex differentiation	9/10
	collagen type V	7/7
3	extracellular space	125/273
	Membrane	465/1302
	ER to Golgi vesicle-mediated transport	14/16
	monooxygenase activity	27/42
	endoplasmic reticulum	75/162
	soluble fraction	50/99
	Microsome	38/70
	Angiogenesis	24/38
	heme binding	28/47
	response to stimulus	39/73
	oxygen binding	19/28
	blood coagulation	27/46
	iron ion binding	48/98
	sensory perception	38/73
	oxidoreductase activity	87/203

Shin, Monti, Aires, Duvic, Golub, Jones, Kupper. Lesional gene expression profiling in cutaneous T-cell lymphoma reveals natural clusters associated with disease outcome. *Blood* 110(8): 3015-3027 October 15, 2007

Clinical Stage ≠ Cluster

		Cluster		
		1	2	3
Clinical Stage	IA	1.0 [6|4]	1.0 [6|4]	**-1.8 [1|5]**
	IB	**-1.6 [5|10]**	0.7 [11|9]	0.9 [13|10]
	IIB	**1.7 [6|3]**	-0.7 [1|2]	**-1.2 [1|3]**
	III	0.0 [4|4]	**-1.5 [1|4]**	**1.5 [7|4]**

- We don't know everything
- We need to see how things are going, and adjust accordingly

Non-chemo CTCL treatment arsenal

- Topicals
  - Topical steroids
  - Topical calcineurin inhibitors (controversial)
  - Topical retinoids
  - Mustard (compounding pharmacies – talk with COS)
- Lights & rays
  - nbUVB, UVB (safest – but avoid calcineurin inhibitors)
  - PUVA (skin cancer risk)
  - Radiotherapy (if singe lesion)
  - TSEB (generalized thick plaques)
- Oral
  - Bexarotene
  - MTX
  - Vorinostat: histone deacetylase inhibitor used in combo after 2 systemic tx have failed
- Extra corporeal photopheresis (ECP)
- Injectables
  - IFN
  - DAbIL2 / Ontak
  - IL-12
  - CTLA4-Ig
  - Zanolimumab human anti-CD4 monoclonal antibody orphan drug

CTCL treatment: Topicals

- Topical steroids
  - Body: Triamcinolone / Clobetasol
  - Face / groin: Desonide
- Topical calcineurin inhibitors
  - Controversial
  - Less atrophy risk
- Topical retinoids
  - Treat CTCL and prevent atrophy
- Mustard
  - compounding pharmacies – talk with COS

Topical treatment pearls

- Don’t stop treatment until disease signs are gone for at least 6 months
- Typical steroid regimen:
  - 2 weeks BID clobetasol alt w 2 weeks TAC
  - Repeat 3 x (12 weeks total = next visit)
  - Desonide for thin / occluded skin e.g. face, groin
- Intermittent topical retinoid use can help minimize steroid-related atrophy

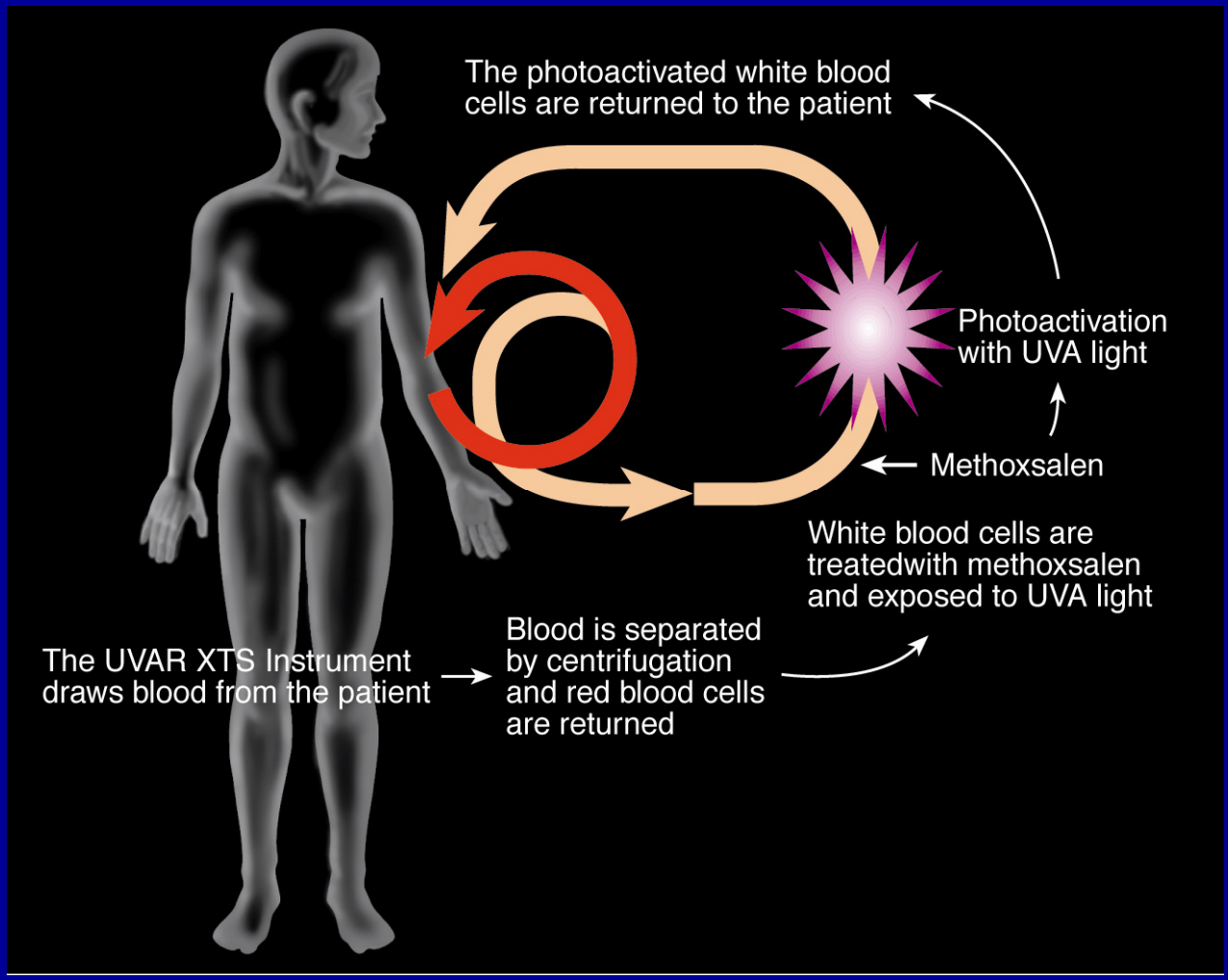
CTCL Treatment: Rays

- nbUVB, UVB
  - Safest
  - Check for photosensitizing medicines
  - Avoid calcineurin inhibitors
- PUVA
  - Skin cancer risk
- Radiotherapy
  - Typically for focal lesions
- Total Skin Electron Beam

CTCL Treatment: Oral

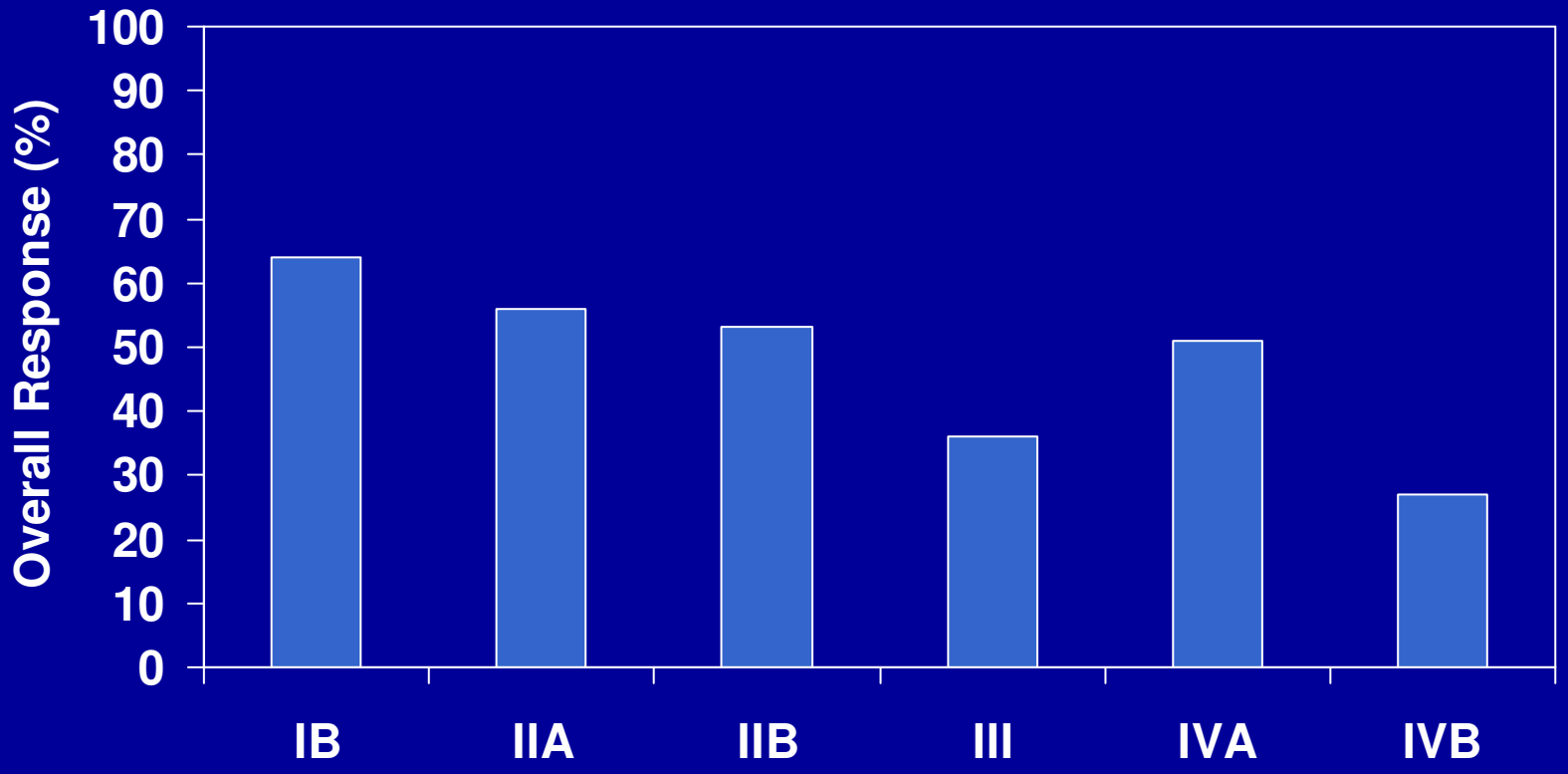
- Bexarotene
  - follow labs every 3 months (lipids, CBC, LFT)
  - thyroid (central so test free T4)
  - Treat or pre-empt hypertriglyceridemia
    - Gemfibrozil (Lopid) can raise serum Bexarotine
    - Fish oil, “south beach diet”
- MTX
  - Liver, lung toxicity
  - Follow labs
- Vorinostat
  - histone deacetylase inhibitor
  - used in combo after 2 systemic tx have failed

Extra-corporeal photopheresis



"Giving the blood a suntan"

Response to Photopheresis



Zic JA The Treatment of Cutaneous T-cell Lymphoma with Photopheresis. Dermatol Ther 2003; 16(4): 337-346

Biologic response modifiers

- Anti-CD25 (ONTAK)
  - Used when clonal T-cells are CD25+
- CTLA4-Ig
  - deplete tolerogenic T-cells
- IL-12 or IFN
  - boost Th1 anti-clone response
- Zanolimumab
  - human anti-CD4 monoclonal antibody
  - orphan drug (call Congress re NIH)

QUESTIONS?

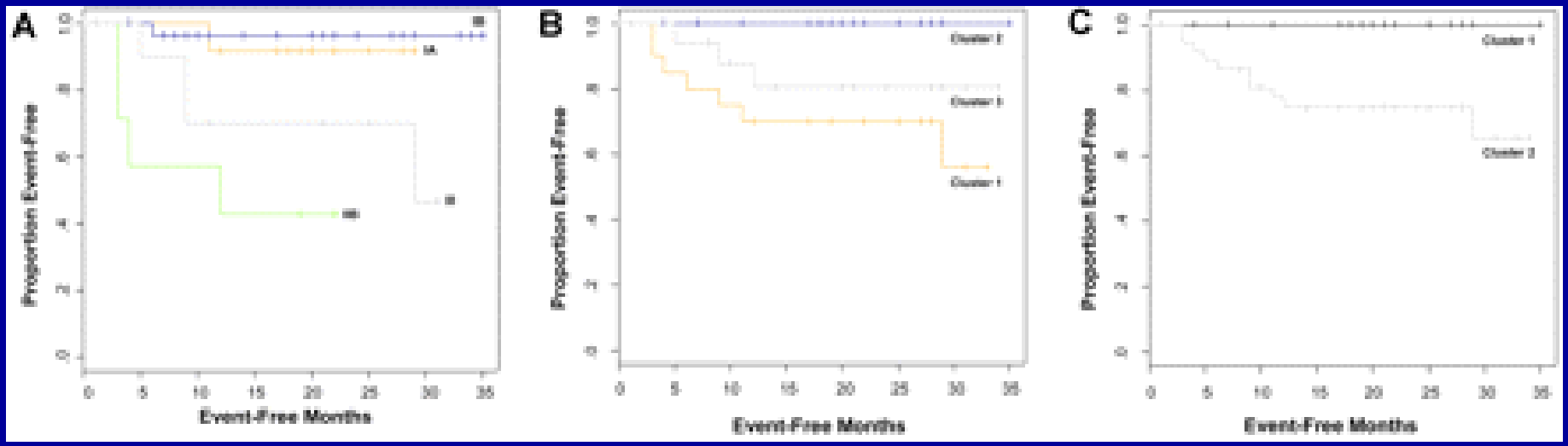
CTCL isn't always eczematous

- Typical: a red, scaly eruption in the bathing-trunk area
- Hypopigmented: often pruritic, +/- scale
- Psoriasiform: message is we need to biopsy
- Follicular: may have alopecia, may look like eczema
- Ichthyosiform
- Poikilodermatous: common finding in typical CTCL
- Morphea-like
- Purpuric

If you suspect CTCL (and you should)

- Full Skin Exam + nodes, liver, spleen
- Full ROS, especially:
  - night sweats
  - weight loss
  - reduced appetite
- Serial skin biopsy every 6 months
  - Help differentiate between, e.g. CTCL and vitiligo
  - Stains can differentiate variants (e.g. aggressive CD8 CTCL)
- +/- Gene-rearrangement
  - non-specific, + in LP, PLEVA, LSA, pseudolymphoma
- CT, flow cytometry if still suspicious

Cluster 2 patients do better



- Event-free interval, by cluster
- Study period too short for mortality differences