CUTANEOUS T CELL LYMPHOMA

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CTCL DEFINITION

- Group of non Hodgkins lymphomas T cell type
- Skin infiltrated with clonal malignant T cells
- T cell markers CD3, CD4, or CD8, CD45 RO+
- Reduced CD7 and CD26
- CD26 not available in our flow cytometry
- CD 164 is a marker for Sezary cells is not available in our facility
- CD164 identifies CD4 T cells that highly express genes in Sezary syndrome.
- Genes involved with CD 164 include T plastin, GATA-3, FCRL3, Tox, and miR-214
- Most important in advanced disease FCRL3 and miR-214

Arch Dermatol Res 2017 Jan vol 309 Benoit et al CD164 with Sezary syndrome. Signature genes FCRL3, Tox and mir-214
CUTANEOUS T CELL LYMPHOMA: TYPES

- Great variation in subtypes
- Most common type (Alibert type) Mycosis Fungoides with 3 phases 72 percent
- Sezary syndrome 3 percent
- Primary CD30 positive lymphoproliferative Disorder and Lymphomatoid Papulosa 20 percent
- Significant Mycosis fungoides subtypes:
  - Granulomatous Slack Skin
  - Pilotrophic and Syringotrophic Mycosis Fungoides
  - Subcutaneous T cell lymphoma two types alpha/beta and gamma/delta
  - Pigmented Purpuric Eruption
  - Poikilodermatous subtype 5 percent
CUTANEOUS T CELL LYMPHOMA : NUMBERS

• In 2002 incidence                          6.4 per one million persons
• In 2005 incidence                        12.7 per one million persons
• In 2005 in Europe                          80 percent present with stage 1A-2A
• In 2005 in USA                                66 percent present with Stage 1A-2A
• Progressive disease                        30 percent
• Indolent number                            70 percent
• In USA presenting with tumors 34 percent
• Mean age onset                             35 years
• Presenting before age 20 16 percent
CLINICAL STAGES IN MYCOSIS FUNGOIDES

- **1A** - less than 10 percent body surface covered with mostly macules and patches and very thin plaques. This form occurs in 30 percent of the patients with a 5 year survival rate of 100%.
- **1B** - more than 10 percent body surface covered with patches and thick plaques. This form occurs in forty-four percent of the patients with a 5 year survival rate of 88%.
- **2A** - like 1B with a palpable node and with a 5 year survival rate of 70%.
- **2B** - Patches, thick plaques tumors and node involvement.
- **3** - Erythroderma, Red skin with exfoliation. Plaques may be present. Patients presenting with stage 2B and Stage 3 have a 48% five year survival rate. This form may be classified as Sezary or CTCLE depending on blood involvement. The 5 year survival rate for Sezary syndrome is 24%.
- **4** - Malignant nodes and systemic disease with 5 year survival rate.
- When there is Transformation in MF the survival rate is 2 years.
- Pilotrophic MF the 5 year survival rate is 80%.
- **CD30** lymphoproliferative disorder has a five survival rate of 95%.
Mycosis fungoides stage 1A which is common in the axillary area and is often managed as eczema with topical steroids before diagnosis is established.
ORIGINALLY DIAGNOSED AS CONTACT DERMATITIS AND FOLLOWED FOR 20 YEARS WITHOUT ANY CHANGE IN LESION TYPE AND LESION REMAINS ACTIVE
PRESENTED WITH THIN HYPERPIGMENTED PATCHES WHICH INITIALLY RESPONDED TO SKIN DIRECTED THERAPY. HE WAS FOLLOWED FOR 8 YEARS BEFORE HE PROGRESSED AND TRANSFORMED HIS
MYCOSIS FUNGOIDES  STAGE 2A DISEASE WITH EXTENSIVE PATCHES AND PLAQUES WHICH ARE CONFLUENT WITH PALPABLE REACTIVE NODES. HE WAS TREATED WITH TOTAL BODY ELECTRON BEAM THERAPY WITH A GOOD RESPONSE
MYCOSIS FUNGOIDES STAGE 2B WITH TUMOR RIGHT SHOULDER AND RIGHT AXILLARY NODES TREATED WITH ELECTRONS TO SHOULDER AREA FOLLOWED BY PUVA THERAPY
DISEASE WITH MALIGNANT NODES AND SYSTEMIC INVOLVEMENT. THIS PATIENT ELECTED TO DECLINE ELECTRON BEAM THERAPY AND
MYCOSIS FUNGOIDES PATIENT WITH RED SKIN AND ERYTHRODERMA MILD WITHOUT BLOOD INVOLVEMENT. THIS IS CUTANEOUS T CELL LYMPHOMA WITH ERYTHRODERMA
POIKILODERMA AN EARLY FINDING SEEN IN THE INDOLENT FORM OF MYCOSIS FUNGOIDES AND CD30 LYMPHOLIFERATIVE
LYMPHOMATOID PAPULOSA IN A PATIENT WHO HAS A CD30 POSITIVE LYMPHOPROLIFERATIVE DISORDER WITH A HISTORY OF CD30 LYMPHOMA
LYMPHOMATOID PAPULOSA WITH MULTIPLE LESIONS WHICH WILL RESPOND TO METHOTREXATE THERAPY LOW DOSE
MANAGEMENT STAGE 1A MYCOSIS FUNGOIDES

- Narrow band UVB for multiple patches. If no response at 2000 millijoules for skin type 4, 5, and 6, PUVA is offered to the patient or UVA-1 is offered if nausea is a problem with oral 8-methoxy-psoralen. ORR for NBUVB is 80 percent.
- If light therapy is inconvenient, topical nitrogen mustard is available but it is expensive. Financial help is available. It is applied once daily. Response rate is 60 percent. Overall there is a 20 percent withdrawal rate due to irritation.
- Topical class 1 steroid cream is frequently used by all clinicians but the overall response rate is not good with advancing lesions which alerts the dermatologist to offer a skin biopsy. In the early disease with flat lesions only 90 percent response rate.
- Targretin gel applied 2-4 times each day for thin plaques the response rate 30-40 percent.
NEW THERAPY FOR STAGE 1A AND EARLY 1B MF

• BCNU in ointment form {0.0004 %} applied in topical form 1 – 2 times daily. Response rate 30 percent
• Imiquamid {Aldara} applied daily until an inflammatory reaction occurs.
• 308 Excimer Laser. This especially used in sites not responding to NBUVB.
• Tazarotene gel. This is less irritating than Targretin gel.
• Hypercin topically and activated by visible light. I have not used this therapy
• Photodynamic therapy. Here you topically apply a topical Porphrin and apply blue light a 400 nm light.
• Ointment based or nitrogen mustard in water applied topically an old therapy revived. the product is applied daily.
THERAPY FOR STAGE 1B MF

- All the therapy for 1A disease plus PUVA with Acitretin or oral Targretin
- Electron Beam when there is PUVA failure.
- Interferon alpha 2B given three time per week at 6 million units
THERAPY MYCOSIS FUNGOIDES STAGE 2A

- Electron beam or xray therapy for tumors followed with PUVA therapy plus a retinoid Targretin or Acitretin
- Intron A- alpha 2 B
- Low dose Methotrexate
- HDAC inhibitors
THERAPY FOR STAGE 3 MF WITH ERYTHRODERMA

- Extracorporeal photophoresis for all patients with erythroderma
- Interferon alpha 2B-
  - 3 to 6 million units 3 times per week
- Low dose methotrexate
- HDAC inhibitors Vorinostat or Romidepsin
- Electron beam
- Targretin with levothyroxine and
- Single agent chemotherapy
- Low dose alemtuzumab anti-CD 52 Best for E-mf
- Anti-CCR {mogamulizumab} in trials
THERAPY MF STAGE 4A AND B

- Single chemotherapy to include cyclophosphamide, chlorambucil, anthracyclines.
- Purine analogs, etoposide, gemcitabine, pentostatin and doxorubicin
- Vorinostat or romidepsin
- Denileukin diftitox targets the IL-2 subunit of CD25
- Pralatrexate, lenalidomide or proteasome inhibitors
- New agents for clinical trials to include brentuximab vedotin (anti-CD 30) and
- Mogamulizumab (anti-CCR4) and anti KIR3DL2
- Stem cell transplant
PROGRESS MADE IN MY 50 YEARS

- Mycosis fungoides begins as a lymphoma beginning in the skin.
- Progress in the classification and prognostic stratification.
- There is no tumor specific antigen.
- High-throughput sequencing studies in SS and MF show marked genomic changes.
- Heterogeneity and small molecule inhibitors may not be an effective agent.
- MF and Sézary syndrome are usually resistant to chemotherapy and long term responses are unusual but 30 percent will respond.
- Allogeneic stem transplantation has produced complete remissions but not all are successful.
- The most difficult problem is how to obtain enough patients with advanced disease properly classified for clinical trials.
- A new registry is on the horizon.