LONESTAR BLOOD CANCER CONFERENCE
FEBRUARY 2013

LIVING WITH GRAFT VERSUS HOST DISEASE

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DEFINITION

- What: Common complication following an allogeneic stem cell transplant
- Why: The immune cells of the graft (donor) recognize the host (recipient) as "foreign"
- When: can happen anytime after engraftment (once donor stem cells recover in the host body)
  - Acute- typically in the first three months of transplant
  - Chronic- anytime after the first three months
- Where:
  - Acute: typically involves skin, gut, liver
  - Chronic: can involve any organ system of the body

CHRONIC GvHD

- Old classification:
  - Limited
  - Extensive
- New/current classification (NIH consensus criteria):
  - Based on clinical appearance
  - Chronic gvhd divided into classic and overlap
  - Describes severity
  - prognostic

CLASSIFICATION

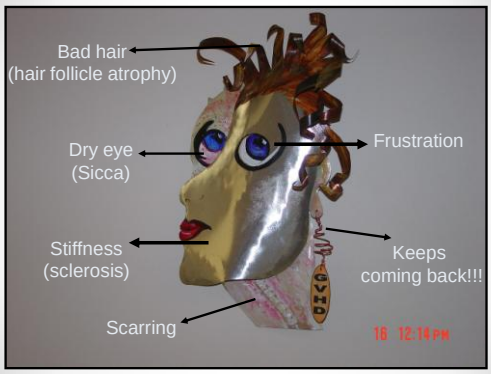
Mild – no significant impairment of function
- Only 1-2 organs (except lungs)
- Maximum organ score 1

Moderate – significant impairment but no major disability
- Three or more organs with max score 1
- One organ with max score 2
- Lung score of 1

Severe – major disability
- Score of 3 in any organ or site
- Lung score of 2

CHRONIC GvHD

- Most common long-term complication after allogeneic SCT
- Seen in 30% (younger patients)-70% (older patients) of allogeneic SCT survivors
- Median time to development 4-6 months
- >50% have multi-organ involvement
- Treatment usually for 2-3 years
- 15-20% require treatment for >5 years



PREVENTION OF GvHD

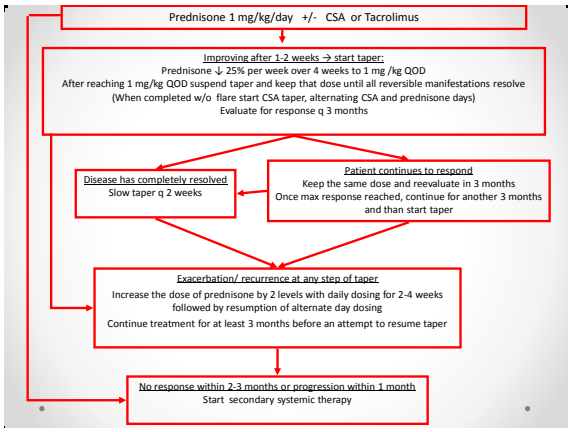
- PREVENTION BETTER THAN CURE???
  - AT THE COST OF DISEASE RELAPSE.....
- NEWER STRATEGIES TO REDUCE GVHD
  - NEW COMBINATIONS
  - GRAFT MANIPULATIONS
  - NEW DRUGS
    - VORINOSTAT
    - VIDAZA
    - MESENCHYMAL STROMAL CELLS

Indications for systemic treatment

Global severity	High risk for mortality *	Systemic treatment
Mild	No	No
Mild	Yes	Yes ‡
Moderate	No/Yes	Yes
Severe	No/Yes	Yes

* Platelets <100,000/microliter or receiving steroids at time of diagnosis of CGVHD
‡ The benefits of graft-vs.-tumor effect and the risk of CGVHD need to be weighted

Filipovic, BBMT 2005; 12: 945-955



Second line regimen = Clinical trial

- Progression on steroids
- Within 2-3 months if no improvement on steroids
- Inability to taper steroids without recurrence= steroid resistance
- Inability to tolerate steroids or calcineurin inhibitors (TTP)

Second line therapy laundry list

- Steroid pulse
- Tacrolimus
- MMF
- Sirolimus
- ECP
- Pentostatin
- Rituximab
- Hydrea
- Thalidomide/Revlimid
- Clofazamine
- Azathioprine
- ATG
- TLI
- Dacluzimab
- Infliximab
- Etanercept
- Imatinib
- Montelukast

ECP

- Photoactivation of blood MNC by 8-methoxypsoralen (8-MOP) and PUVA
- Apoptosis of alloreactive T cells, normalization of CD4/CD8 ratio; increases NK cells, shift towards immature DC, induction of T-regs
- Best responses in skin, mouth, liver, ocular
- No prospective RCT
- Response seen 2-3 months after initiation
- Response rate can be as high as 50-60%
  - Higher in *de novo* cGVHD
- Follow up too short to ascertain impact on survival

Greinix, Blood 1998; 92
Seaton, Blood 2003; 102
Salvaneschi, Transfusion 2001; 41
Apisarnthanarax, BBMT 2003; 31
Smith, BBMT 1998; 4
Couriel , Blood 2006; 107

ORGAN SPECIFIC LOCALIZED TREATMENTS

- SKIN
  - PUVA
  - TOPICAL STEROIDS
  - TOPCAL TACROLIMUS CREAM
  - MOISTURIZERS
- MOUTH
  - STEROID RINSE
  - STEROID GEL (CLOBETASOL)
  - PROTOPIC OINTMENT
  - PREVENTION OF INFECTIONS SUCH AS HERPES, THRUSH
  - ROUTINE DENTAL VISITIS
  - FLOURIDE TREATMENTS

ORGAN SPECIFIC LOCALIZED TREATMENTS

- EYES
  - TOPICAL STEROIDS
  - RESTASIS EYE DROPS
  - SERUM TEARS
  - LUBRICANTS
  - PUNTAL PLUGS
  - CONTACT LENS
  - PROSE TREATMENT (BOSTON LENS)-Prosthetic replacement of the ocular surface ecosystem

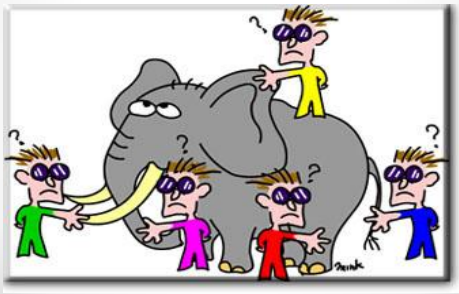
ORGAN SPECIFIC LOCALIZED TREATMENTS

- LIVER
  - ACTIGALL/URSODIOL
- LUNG
  - FAM THERAPY (FLUTICASONE, AZITHROMYCIN, MONTELUKAST)
- JOINTS
  - PHYSICAL THERAPY
  - REHAB, INCREASE RANGE OF MOTION OF JOINTS
  - DEEP MASSAGES
- VAGINAL
  - STEROID CREAMS
  - LUBRICANTS

SO, IS IT POSSIBLE TO LIVE WITH GvHD?

- Absolutely, YES!
- Early detection is important
- Aggressive treatment
- Important to identify progression and steroid refractoriness and change treatments
- Get ancillary services involved
- Multidisciplinary approach

Alone we can do so little
Together we can do so much
Helen Keller



NON-GvHD ISSUES IN PATIENTS WITH CHRONIC GvHD

- STEROID SIDE EFFECTS
  - VITAMIN D LEVELS
  - BONE DENSITY
- SECONDARY CANCERS
  - SCHEDULE PAP SMEARS, MAMMOGRAMS, COLOSCOPY
  - STOP SMOKING!!!!!!
- INFECTIONS
  - PROPHYLACTIC ANTIBIOTICS
  - REVACCINATIONS
- ORGAN TOXICITIES AND FAILURE
  - KIDNEY
  - NEUROPATHY

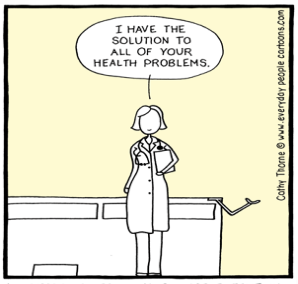
NON-GvHD ISSUES IN PATIENTS WITH CHRONIC GvHD

- MEDICAL PROBLEMS
  - DIABETES
  - HYPERTENSION
  - LIPID PROBLEMS
  - METABOLIC SYNDROME
- PSYCHOSOCIAL ISSUES
  - DEPRESSION
  - LIVING WITH UNCERTAINTY
- COGNITIVE
  - CHEMO BRAIN
- SEXUALITY AND FERTILITY

POST TRANSPLANT GUIDELINES

- http://www.cibmtr.org/ReferenceCenter/Patient/Guidelines/pages/index.aspx

Some of this is true, not all of it!



ALL YOU HAVE TO DO IS CHANGE EVERYTHING ABOUT THE WAY YOU LIVE.