Nursing Management of Graft versus host disease

John Murray
Nurse Clinician BMT
aGvHD pathophysiology
GVHD sensors, (APC)-mediators and (T cell) interactions. The critical interaction for induction of GVHD is the activation of its primary mediators, donor T cells by the primary sensors, the professional APCs

New perspectives on the biology of acute GVHD S 2010 Paczesny, D Hanauer, Y Sun and P Reddy BMT45 1-11
Network of immune cell interactions in GVHD. Complex interactions exist between the various factors that contribute to the pathophysiology of GVHD. The lines between the nodes represent interactions and the node size is proportional to the number of factors interacting with the node.

*New perspectives on the biology of acute GVHD (2010)* S Paczesny, D Hanauer, Y Sun and P Reddy BMT 45 1-11
Nail Dystrophy
Keratoconjunctiva sicca
Erythema ulceration hyperkeratinisation
Injury induced
Scleradermatous like skin

• University of Utrecht
Infection
In the old days

• 40 years ago noted that donor cells NOT from a monozygotic twin caused another disease
• Called GvHD
• 3 standard tenets for GvHD to exist Billingham 1966
  • Donor graft must have immune competent cells
  • Recipient must have tissue antigens that are not present in the donor
  • Recipient must be incapable of rejecting cells
• Pathological classification came from a description of 20 patients in the 1970’s
What is it

• Donor T cells are activated by:
  • HLA major antigens in MUD or mismatched MUD
  • Minor HLA antigens in identical siblings
  • Tissue damaged by therapy
  • Apoptosis caused by damage starts a cytokine storm as antigen presenting cells are activated
Where is affected

- Eyes
- Mouth
- Skin
- GI tract and Liver
- Lung
- GU
- Musculoskeletal
- Haematopoietic
- Neurological
- Psychosocial, body image, sexuality
Do you want it

• Yes
• Relapse rates are lower in patients who develop GvHD v those who don’t
• Same cells that cause GvHD give some tumour effect and therefore protection
• High morbidity and mortality from the GvHD itself though
• Delicate balance
How badly

- GvHD grade 0-1 gives a TRM of approx 28%
- GvHD grade 2 3 4 TRM of 43% 68% and 92%
- Prophylaxis is crucial as treatment of GvHD is poor

Greinix, 2008
Occurrence of aGvHD

- 60% siblings
- 80% MUD
- Amount of disparity increases risk
- Age
- Gender sex mismatch
- Parity
- PBSCT and its dose
- Intensity of conditioning
- HLA immunisation
- TBI
- DLI
Diagnosis

- Historically limited or extensive after D+100 even if indistinguishable from aGvHD
- NIH 2005 criteria
- Distinction from aGvHD, should be clinical manifestations and not time from BMT
- Appearance of diagnostic cGvHD and absence of signs of aGvHD without any time limit
- Mixed acute chronic simultaneous presence of symptoms of both without any time limit
- The number of organs and sites and then graded as mild moderate or severe
aGvHD

• No reliable laboratory test
• Clinical assessment
• Biopsy
What we see clinically

- Rash
- Anorexia with N+V+D
- Cholestatic hepatitis looking jaundiced
- Occurring within 100 days or post DLI
- Often on withdrawal of immunosuppression
Grading of aGvHD

- Glucksberg 1974
- Adds up extent and type of skin involvement
- Jaundice
- Diarrhoea volume
- Graded from 1-4
- No longer strictly acute and chronic 100 day markers
- National Institute of Health Consensus Development Project on Chronic GvHD 2005
- Clinical scoring system
## Clinical Scoring System

<table>
<thead>
<tr>
<th>Score</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>No manifestations or symptoms</td>
<td>No significant impairment of function ADL</td>
<td>Significant impairment of ADL no major disability</td>
<td>Significant impairment of ADL with major disability</td>
<td></td>
</tr>
</tbody>
</table>

Filipovich et al. Biology Blood Marrow Transplant 11: 945-955, 2005
What does it mean for our patients?

• Looks and feels dreadful
• They want it to be controlled
Prophylaxis

- Prevention always better
- Gold standard of care since Seattle devised in 1980’s Ciclosporin and Methotrexate
- Newer drugs also now used such as;
  - Campath
  - ATG
  - MMF
cGvHD

• Pathological changes to;
  • Skin
  • Lung
  • Mucous membranes
  • GI
  • Musculoskeletal system
• The presence of at least 1 diagnostic clinical sign of chronic GvHD or the presence of at least 1 distinctive manifestation
  • Oesophageal web
  • Keratoconjunctivitis sicca
Confirmation cGvHD

- Biopsy or relevant test
- Manifestations such as lichen planus like skin or scleradermatous changes are obvious and don’t need biopsy
- Oral changes similar
- Vaginal scarring stenosis
- Joint contractures
- Usually occurs within 3 years and often follows aGvHD
Grading

_Mild_
- Involvement 1 or 2 organs except lung
- No clinically significant functional impairment max of 1 in all areas

_Moderate_
- At least 1 organ of score 2
- 3 or more organs with no clinically significant functional impairment max score 1
- A lung score of 1

_Severe_
- Major disability score of 3
- Lung score of 2
Clinically

- Nail dystrophy or loss of nails
- Bronchiolitis obliterans
- Xerostomia
- Ulcers on all membranes
- Dry eyes sicca syndrome
- Hypo hyper pigmentation
- Sweat impairment
- Pruritis
Education and Information

- Clinical team, everyone
- Patients
- Relatives and carers
- Forewarned is forearmed
- No matter how hard you try will never be able to describe fully and exactly what someone will go through
- TRY
Cutaneous GvHD
Poikiloderma

Atrophic and pigmentary changes
Lichen Planus

Erythematous violaceous flat-topped papules or plaques with or without surface reticulations or a silvery or shiny appearance on direct light
Hypo/hyperpigmentation, sclerosis

Morphea like skin, superficial sclerotic features localized patchy areas of moveable smooth or shiny skin with a leathery-like consistency, often with dyspigmentation
Injury induced

Severe sclerotic features characterized by thickened, tight, and fragile skin are often associated with poor wound healing, inadequate lymphatic drainage, and skin ulcers from minor trauma.
Nursing Skin Care

- Roel Weijer spoke at EBMT workshop 2009 on skin care
- Use oil based creams and lotions
- Hydrate first or moisturise no consensus
- High SPF and cover up when outside
- Massage or exercises suggested but not widely used
Have we moved on?

• What do people use as treatments?
• Topical steroids
• Tacrolimus cream
• UV light
• Anti histamines for pruritis
• How about severe skin?
• What would you do with this?
Scleradermatous like skin

• University of Utrect
Skin

- What function does skin perform?
- Protection
- Immunological
- Fluid, protein and electrolyte homeostasis
- Thermoregulation
- Neurosensory
- Social – interactive
- Metabolism
Skin Infections and GvHD

- Compromised blood flow may lead to cell necrosis
- Clinical management that will promote the recovery of this includes:
  - Wound dressing chosen to aid moist wound healing
  - The use of topical antimicrobial agents
  - Adequate fluid resuscitation and hydration
  - Elevation of area to minimise oedema
  - Advising patient to avoid smoking
  - Management of systemic diseases such as diabetes monitor & stabilise blood sugar levels especially if on steroids
Wound Care

- Care of the wound itself should be designed to;
  - Promote spontaneous healing
  - Prevent further tissue loss
  - Prevent infection
  - Provide optimal conditions for surgery if required
  - Be as painless as possible
  - Be acceptable to the patients needs
  - Nurse in sand beds or equivalent
Cleaning and debridement

- In burns patients beneficial to use warmed solutions
- Warm ambient temperature
- Avoid lengthy dressing changes
- Avoid exposure of wet wound surfaces
- Debridement can contribute to a decrease in the bacterial load on the wound surface
- Use of moist dressing such as hydrogels or hydrocolloids
- Surgical debridement with scissors or scalpel
- Enzymatic e.g. fibrinolysins, (mashed papaya is used in Africa)
- Mechanical, pulse lavage, gentle washing
- Biological with larvae of *Lucilia sericata*
Eyes
GvHD Eyes

- 2 of the following (Jagasia, 2008)
- New onset subjective symptoms of dry eye
- Tear film instability (TBUT ≤ 5 seconds)
- Lacrimal insufficiency (Schirmer ≤ 5 mm at 5 minutes)
- Ocular surface abnormality (vital staining grade I or higher)
- Conjunctival inflammation
Nursing interventions

- GvHD or something else find out
- Bathing
- Swabs
- Review with ophthalmologist
- Regular eye drops
- Lubricating, steroid, anti biotic
- Punctal plugs
- Cauterisation
- Sun glasses
4 Stages

• Lubrication-artificial tears
• Control of evaporation-glasses
• Control of drainage-temporary or permanent plugs
• Decreasing ocular surface inflammation-steroids under close supervision
Lichenoid buccal mucosa
GvHD Mouth

- *Lichen planus-like changes* - white lines and lacy appearing lesions of the buccal mucosa, tongue, palate, or lips
- *Hyperkeratotic plaques* - leukoplakia
- *Decreased oral range of motion in patients with sclerotic features of skin GvHD*
- Distinctive features include xerostomia dryness, mucoceles, mucosal atrophy, pseudomembranes, and ulcers. Infectious pathogens such as yeast or herpes virus
- Secondary malignancy must be excluded
- Manifestations common to both acute and chronic GVHD include gingivitis, mucositis, erythema, and pain.
Nursing Care

- Not mucositis but can still be painful especially with spicy foods
- Rule out other causes before starting anything
- Appropriate analgesia, caphosol, gelclair?
- Mouth washes to keep clean, difflam for pain, good old plain water pH 7!
- Artificial saliva, chewing gum
- Assess other concurrent medications for side effects of dry mouth
- Exercises to reduce risk of contractures
GvHD GI and Liver
The Christie NHS Foundation Trust

GvHD GI + Liver

- Oesophageal web, stricture, or concentric rings
- Pancreatic exocrine insufficiency
- Wasting syndrome
- Dysphagia- difficulty swallowing
- Odynophagia- pain on swallowing
- Heartburn
- Anorexia
- Nausea and vomiting
- Abdominal pain, cramping
- Diarrhoea
- Weight loss and malnutrition
- Cholestasis with increased bilirubin, ALP AST
Nursing Care

- Is it GvHD?
- Stool samples
- Nutrition, weight, fluid balance
- Mobility to toilet 24/7
- Hygiene
- Faecal collection devices such as the Flexi Seal, Liebersbach from Leeds spoke about in Vienna 2010
Lateral Thinking

- Other disease groups have similar problems but different causes
- Learn from other specialities
- Get out of your comfort zone
Effects of GvHD treatments

- Patients have multiple problems such as
- Debilitating effects on musculoskeletal system, joint contractures
- Loss of sight
- End stage lung disease
- Long lasting immunodeficiency leading to increased morbidity mortality through infections as T cell depleted
- Reactivation of latent virus’
- Diabetes
- Hypertension
- Osteoporosis
- Avascular necrosis
- Fluid retention, moon facies
- Insomnia
We Should

• Try to influence outcome
Questions