An Overview of Blood and Marrow Transplantation

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Objectives

• What are the types of blood and marrow transplantation?

• Who may benefit from transplantation?

• Main diseases for which blood and marrow transplantation is undertaken

• What is graft versus host disease?
Goals of BMT

• Cancer therapy
  – Cure or prolongation of remission

• Marrow replacement
  – Aplastic anemia, thalassemia, sickle cell disease

• Developmental
  – Connective tissue diseases: scleroderma
  – Multiple sclerosis
  – Brain tumours
  – (Breast Cancer)
There are an estimated 50,000–60,000 hematopoietic stem cell transplants (HCTs) done annually worldwide. This slide reflects several notable events over the past decade. These include the initial enthusiasm and later disappointment about the use of autotransplants for breast cancer, the availability of targeted nontransplant therapy for chronic myelogenous leukemia (a leading indication for allogeneic HCT) and the increasing use of autologous and allogeneic HCT in older patients.
Halifax Transplant Activity
1992-2008
Types of Transplant

- Autologous
- Syngeneic
- Allogeneic
  - Related
  - Volunteer
  - Unrelated
Halifax Transplants by Type
Auto vs Allo vs MUD vs RICT

- RICT
- Auto
- MUD
- Allo

Year
- 1992
- 1994
- 1996
- 1998
- 2000
- 2002
- 2004
- 2006
- 2008

Counts
- 11
- 62
- 65
- 60
- 8
- 10
- 7
- 6
- 3
Types of Transplant

- Autologous
- Syngeneic
- Allogeneic

- Related
- Volunteer Unrelated
Autologous Transplant

• Age
  – ≤ 65 years old
    • ≤ 70 years old for myeloma

• Performance State
  – Organ function (heart, lungs, liver, kidneys)

• Chemosensitivity
Diseases for Autologous Transplantation

- Myeloma
  - Era of novel therapies
- Relapsed Lymphoma
  - Non-Hodgkin’s lymphoma
  - Hodgkin lymphoma
- Acute Leukemia
- Solid Tumours
  - Germ cell tumour
  - (breast cancer)
Indications for Hematopoietic Stem Cell Transplantation in North America 2005

- Multiple Myeloma
- NHL
- AML
- Hodgkin Disease
- ALL
- MDS/MPD
- CML
- Aplastic Anemia
- Other Leuk
- Other Cancer
- Non-Malign Disease
Autologous Transplant: Stages

1. Pre-transplant chemotherapy
2. Harvest
3. Conditioning
4. Infusion
5. Recovery
1. Pre-Transplant Chemotherapy

- Chemosensitivity
- In vivo purging
2. Harvest: Source of Cells

- Autologous Transplant
  - Bone Marrow
  - Peripheral Blood

“stem cells”
Bone Marrow Harvest

• Advantages
  – No chemotherapy
  – No growth factors
  – One day

• Disadvantages
  – General anesthetic
  – Large volume
Peripheral Blood Harvest

• Advantages
  – No general anesthetic
  – Small volume
  – Engraftment

• Disadvantages
  – Chemotherapy
  – Growth factors
  – Apheresis
3. Conditioning

- Standard Chemo
- Conditioning Chemotherapy
- Radiation (TBI)
4+5. Infusion to Engraftment

- Infection
- Bleeding
- Mucositis
- Organ Dysfunction
Late Effects

- Organ Damage: pulmonary, cardiac, renal
- Second Cancers
- Endocrinopathies
- Cataracts
- Infertility

• Relapse
Shelley beats odds – twice

Marrow transplant patient gives birth

By DEBRA SCHOOLEY
The Sun News

SHELLEY DOMINICK has beaten the odds twice.

The first time was almost four years ago, when she received a marrow transplant and went into remission.

The second was Monday, when she gave birth to a healthy boy – only the third known case in Canada of a child being born to a marrow transplant patient.

Mrs. Dominick had been told there was a 1 in 300 chance she would survive.

“Here’s something we really wanted,” says mom.

Michael Ronald Dominick was born at 11:11 a.m. in McMaster University Medical Centre with a head of dark hair and weighing eight pounds seven ounces.

“It’s pretty amazing,” said Dr. Michael Ross, one of two physicians assisting Mrs. Dominick.

“I was confident and had a positive attitude,” Mrs. Dominick said. “It was something we really wanted.”

She had the child even though she was unsure if she would be able to breastfeed her.
Causes of Death after Transplants

**AUTO**
- Relapse (75%)
- Organ toxicity (8%)
- IPn (2%)
- Infection (6%)
- Other (9%)

**UNRELATED**
- Relapse (32%)
- Organ toxicity (11%)
- IPn (7%)
- Other (17%)

**HLA-ID SIB**
- Relapse (38%)
- Organ toxicity (13%)
- Infection (17%)
- GVHD (14%)
- Other (13%)
Figure 2. Overall Survival According to Treatment Group.
The numbers shown below the time points are probabilities of overall survival (the percentages of patients surviving) and 95 percent confidence intervals.
Breast Cancer

- High Dose Chemotherapy
- Standard Therapy

Probability of Progression-free Survival vs Months after Randomization
Allogeneic Transplantation
Types of Transplant

- Autologous
- Syngeneic
- Allogeneic

Allogeneic:
- Related
- Volunteer
  - Unrelated
Allogeneic Transplantation

• Age
  – \( \leq 55 \) years old
  – \( \leq 50 \) years old (unrelated)
  – \( \leq 65 \) years old (reduced intensity)

• Performance State

• (Chemosensitivity)
Allogeneic Indications

• Leukemia
  – Acute leukemia, MDS > CML, CLL
• Lymphoma
  – Indolent lymphomas
• Myeloma
  – Uncommon in 2009
• Bone marrow failure
• Diseased bone marrow
Indications for Allogeneic Hematopoietic Stem Cell Transplantation, 2005 – Worldwide

- **Unrelated donor (Total N=7,670)**
- **Related donor (Total N=10,770)**

Transplants

- AML
- ALL
- MDS/MPD
- CML
- NHL
- Multiple Myeloma
- Other Leuk
- Hodgkin Disease
- Other Cancer
- Aplastic Anemia
- Non-Malignant Disease

**CIBMTR**

*Slide 8*
Sibling Allogeneic Transplants
Halifax: 2008

- Lymphoma: 7
- AML/ALL: 11
- CLL: 2
- Anemia: 2
- MDS: 1
Allogeneic: The Match
Each child inherits one set of HLA antigens from each parent
Allogeneic: The Match
Allogeneic Transplantations by Graft Source and Conditioning Regimen Intensity, Registered with the CIBMTR, 2005-2006
Graft versus Host Disease

Reverse of graft rejection
Immunologic attack of donor cells against the recipient
Acute Graft versus Host Disease

- Skin: Rash
- Liver: Inflammation
- Gut: Diarrhea

—Characteristics
Chronic Graft versus Host Disease (cGvHD)

- Skin
  - Scleroderma
- GI tract
  - Small, dry mouth
  - Strictures
  - Chronic diarrhea
- Liver
- Eyes
  - Sicca syndrome
  - Corneal ulceration
- Nervous System
  - Peripheral neuropathy
- Lungs
  - Bronchiolitis obliterans
  - (BOOP)
- Muscles and Joints
  - Lupus-like syndrome
  - Myositis
• The Immune Effect in Allogeneic Transplant
  – A double-edged sword
    • Graft vs Host Disease
    • Graft vs Tumour Effect
      – Donor Leukocyte Infusions
      – Reduced Intensity Transplants
        » “mini transplants”
Causes of Death after Transplants

**SIBLING**
- Relapse (38%)
- GVHD (14%)
- Infection (17%)
- Organ toxicity (13%)
- IPn (5%)
- Other (13%)

**UNRELATED**
- Relapse (32%)
- Organ toxicity (11%)
- Infection (19%)
- IPn (7%)
- Other (17%)
- Organ toxicity (11%)

Causes of Death after Transplants
Important Syndromes for the Internist

• Febrile Neutropenia

• CMV Infections
  – Allogeneic transplants
    • CMV pneumonia; CMV colitis; CMV hepatitis

• Pulmonary infections
  – PCP

• GvHD Syndromes
  – May mimic many connective tissue and autoimmune diseases
Important Syndromes for the Internist

• Cardiac
  – Myocardial damage related to chemotherapy, radiation
  – Acute pericarditis (GvHD)
• Pulmonary
  – Acute, subacute or chronic parenchymal lung injury from chemotherapy, radiation
  – **Bronchiolitis obliterans**
  – BOOP
  – Restriction due to scleroderma
• Renal
  – Chronic renal injury
    • Calcineurin inhibitors
• Endocrine
  – Hypothyroidism
  – Steroid-induced bone disease
Conclusions

• Autologous Transplant
  – Identifying which patients will benefit
    • cure (lymphoma)
    • disease control (myeloma)
  – Transplant schema
  – Indications
  – Risks and complications
Summary

• Identifying patients who may benefit
  – Myeloma (auto)
  – Lymphoma (auto and allo)
  – Leukemia (allo)

• Mechanics of transplantation

• Complications
  – GvHD
Conclusions

• Allogeneic Transplant
  – Identifying which patients will benefit
    • current challenge of CML
  – Transplant schema
  – Indications
  – Complications
  – Immune effect
Thank you