LIVER TRANSPLANTS IN THE US

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OUTLINE

POST LIVER TRANSPLANT GVHD

Part 1: Case Presentations
Part 2: Diagnosis
Part 3: Pathophysiology

(Therapeutics)
A TALE OF TWO LIVERS

Case #1 Mr. P
- 67 yo M with ESLD from HCV s/p OLT from a 45 CMV+ M donor evaluated on POD#24 for low grade fever and rash x 5 days, new diarrhea and worsening cytopenias.
  - Post Tx Immunosuppression: ATG induction → Tacrolimus
  - ID ppx: Bactrim, Valgancyclovir, Ribavirin, Sofosbuvir

Case #2 Mr. S
- 66 yo M with ESLD from HCV s/p OLT from a 21 yo M donor admitted POD#67 with a rash. He subsequently develops diarrhea and pancytopenia.
  - Post Tx Immunosuppression: ATG induction → Tacrolimus (MMF d/c after 1 mo)
  - ID Ppx: Acyclovir, Fluconazole, Bactrim
A TALE OF TWO LIVERS ...
IT WAS THE BEST OF T CELLS, IT WAS THE WORSE OF T CELLS

Case #1: KP

Case #2: R.S.
A diagnostic maneuver was performed …
Bone Marrow Aspirate:
Case # 1. K. P.

Bone Marrow Core Biopsy (inaspirable):
Case # 2. R.S.

(Figures courtesy of Sarah Buckley and Xueyan Chen)
Bone Marrow Aspirate:

Hemophagocytosis

BONE MARROW BIOPSY, ASPIRATE SMEARS, PARTICLE PREPARATION AND PERIPHERAL BLOOD
1. Hypocellular marrow with markedly decreased hematopoiesis and increased hemophagocytic histiocytes

(Figures courtesy of Sarah Buckley and Xueyan Chen)
DIAGNOSIS

- Rests on demonstrating host-donor mixed leukocyte chimerism or complete donor chimerism
  - First fractionate the T cells with cell sorting
  - CD3 donor fraction > 20% → Acute GVHD

- Methods
  - FISH
  - HLA typing
  - Short Tandem Repeat Patterns

Figure 1 - Sample Test Result

Hashida, Biometrics, 2011 & Labcorp
ACUTE GRAFT VERSUS HOST DISEASE AFTER LIVER TRANSPLANTATION: PATTERNS OF LYMPHOCYTE CHIMERISM
CASE # 1

Peripheral Blood Chimerism (POD#27):

CD3+ T-cells
98% donor origin

CD 33+ Myeloid
0% donor origin

CD56+ NK Cells
21% donor origin

Bone Marrow Chimerism (POD#29):

CD3+ T-cells
93% donor origin

CD 33+ Myeloid
0% donor origin

CASE # 2

Peripheral Blood Chimerism (POD#71 and POD#97):

CD3+ T-cells
91% donor origin → 99%

CD 33+ Myeloid
0% donor origin → 0%

CD56+ NK Cells
21% donor → 28%

Bone Marrow Chimerism (POD#77):

Unsorted Cells
17% donor cell
83% host cells
GVHD

POST LIVER TRANSPLANT GVHD: EPIDEMIOLOGY

RARE: Incidence of about 0.1 – 1%
  • Fewer than 100 cases have been reported in the literature

FATAL: Mortality rate >80%
  • Related to bone marrow failure
    • Infection and infection-related multiple organ failure
    • End-organ failure from GVHD
    • Bleeding, especially gastrointestinal

TIMING: Week 2 to 6 post transplant
ETIOLOGY

- Activation of passenger lymphocytes
- The liver contains about $1.8 \times 10^{10}$ passenger T lymphocytes
- Can persist in the recipient over several years
- Role in tolerance induction

RISK FACTORS

- High lymphocyte load
  - Liver
  - Small bowel
- Age > 65
- Age disparity > 40 years
- Donor HLA homozygozity

**TRANSPLANT**

**Stem Cell Transplant**

*Matching*: HLA based

*Conditioning*:
- extensive (host)

*GVHD* common

**Liver Transplant**

*Matching*: ABO based
- HLA matching ↑ risk of GVHD

*Conditioning*:
- none (host)
- graft (variable)

*GVHD* rare

*Clinical*: No hepatic involvement
TREATMENT APPROACHES

- Increase the dose of immunosuppression
- Strengthen the recipient’s immunity
Standard and emerging therapies for the prevention of acute GVHD

Case # 1:

Case # 2:

KEY LESSONS:

• Early diagnosis matters
• Early treatment matters
• Worry about the degree of chimerism, not chimerism itself
• Treatment is controversial, but supportive care is not.
“Time, as it grows old, teaches all things.”

— Aeschylus, *Prometheus Bound*

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