Graft-versus-Host Disease: Gastrointestinal Tract and Liver

Celebrating a Second Chance at Life Survivorship Symposium

April 29 – May 5, 2023

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Graft-versus-Host Disease: Gastrointestinal Tract and Liver

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Disclosures

• I am a gastroenterologist
• I assume most are post-transplant
• I love coffee
• I have none, I am your tax dollars

Problem

• Alone
• Overwhelmed
• Not understood
• You are the first patient I have seen with... Not meant to happen...
• And the time
• And the cost
Uncertainty

• Lets talk about it

Secret

• I will deny I said this
• In some ways these organs are pretty dumb
• Hickam’s dictum

• So it is even worse???
No! There are solutions

• Get involved, be proactive, it is not hopeless
• Educate
• BMT InfoNet
• Academic Centers
• NIH
• Clinical Trails
• Embrace and beware of Dr. Google

What is the geography?

[Diagram of the gastrointestinal tract with labels for various organs]

https://www.britannica.com/science/gastrointestinal-tract/media/1/15454/1087
What is the elephant in the room? GVHD

- New immune self does not recognize old self
- Good: Graft vs Tumor
- Bad: Graft vs Host

How often?

- GI GVHD: 13 to 50 to 74%
- Liver GVHD: 6 to 30 to 44%
Let’s start

• Before
• During (~100 days)
• After

Before

• Pre-existing conditions
  • Often overlooked because of the urgency
• Liver: Metabolic syndrome, iron overload, chemo damage, viruses (HBV)
• GI: Less significant
• Risk stratify and prophylaxis
  • Calcineurin inhibitor: Cyclosporin or tacrolimus
What to do?

• Come in optimized!
• If you know, tell
• Don’t smoke or drink
• Plant based diet
  • Microbiome
  • Sometimes no choice

During (~100 days)

• Classic acute GVHD
• Inflammatory
• Company it keeps
  • Liver, gut, skin
• Overlap
What will I see or feel?

• Gut
  • Nausea/Vomiting
  • Diarrhea
  • Bleeding
  • Mucous
  • Not hungry at all
  • Feel full

• Liver
  • Nausea/Vomiting
  • Not hungry at all
  • Feel full
  • Yellow eyes
  • Dark urine
  • Light stool
  • Swollen stomach

Have to ask: What else could it be?

• Gut
  • Viruses
  • Bacteria

• Liver
  • Drug induced liver injury (dili)
    • livertox
  • Viruses
  • Cholangitis Lenta
  • Sinusoidal Obstructive Syndrome
  • Thrombotic microangiopathies
Investigate and think!

- **Gut**
  - History
  - Exam
  - Blood tests for infection
  - Stool tests for infection
  - Endoscopy

- **Liver**
  - Blood tests
    - Cholestatic (ALP/GGT/Bili)
    - Hepatitic (ALT/AST)
  - Exclude other causes
  - Imaging
    - Ultrasound to start
  - Biopsy

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**Endoscopy (see and sample!): GVHD**

Now what?

• **Team** work makes the dream work
• Transplant, Infectious Disease, Gastroenterology, nutrition, nursing, PT/OT
• **Diagnose** before treating
• **Treat** early
• Define **severity**
  • Determines extent of treatment
Things to consider during treatment

• Monitoring
  • How does the patient look and feel
  • Stool volume
  • Blood work
  • Infections (prophylaxis)
  • Endoscopy
  • Other causes
  • Symptomatic treatment
  • Nutrition and activity

Treatment for GVHD

• To date, no consensus has been reached ... for management of steroid-resistant ... acute graft-versus-host disease. The choice of treatment has been guided largely ... trial and error according to physician experience, ease of use, need for monitoring, risk of toxicity, and potential exacerbation of preexisting comorbidity.

  • Martin PJ, Blood (2020)
But! Treatment is effective

- **Steroids** are the initial mainstay
- **Both** oral and “first pass” drugs
- Examples are methylprednisolone and budesonide
  - Weeks then tapered over months
- Should see **response within 7 days**
- Worsening by 5 days is also considered significant
- If no response or worsening then **steroid resistant or refractory**

Beyond Steroids

- **Ruxolitinib**
- If no response then consider mycophenolate, etanercept, Pentostatin, Alpha-1 antitrypsin, sirolimus, and extracorporeal photopheresis
  - And others!
- **Clinical trials**
General thoughts

• Can be transient and never again
• For some lifelong
• It can recur
• Lifestyle modifications are so challenging
  • Things change over time
  • Aim for a heart healthy diet but limited by tolerance and illness
    • Would not aim for Burgers/Fries/Steaks/Beer/Spicy
• Keep active as much as possible

After

• Classic Chronic GVHD
• Late acute GVHD
• Fibrotic
• More organs
• Overlap
What will I see or feel?

• Gut
  - Malabsorption (Pancreas)
  - Weight loss
  - Failure to Thrive
  - Difficulty swallowing
  - Strictures – can dilate

• Liver
  - Nausea/Vomiting
  - Not hungry at all
  - Feel full
  - Yellow eyes
  - Dark urine
  - Light stool
  - Swollen stomach

Have to ask: What else could it be?

• Gut
  - Viruses
  - Bacteria

• Liver
  - Drug induced liver injury (dili)
    - livertox
  - Viruses

Textbook...

  - Syndrome
  - Thrombotic microangiopathies
Investigate and think!

• **Gut**
  - Look at weight
  - Look at muscle mass
  - Think about frailty
  - Stool tests for pancreatic function
  - Blood tests for nutrition

• **Liver**
  - Blood tests
    - Cholestatic (ALP/GGT/Bili)
    - Hepatitic (ALT/AST)
    - Exclude other causes
  - Imaging
    - Ultrasound to start
  - Biopsy

Questions for your provider…(in a nice way…)

• **What else** could this be?
• **Are there treatment** alternatives?
• **Why am I** not responding?
• **Am I on the** safest, lowest dose medicine needed?
• **What are the** complications?
• **Are we** monitoring for them?

• [https://www.bmtinfonet.org/gvhd-directory](https://www.bmtinfonet.org/gvhd-directory)
Example of persistence paying off

- 302 patients, 151 hepatic cGVHD based on NIH Consensus Criteria

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<thead>
<tr>
<th></th>
<th>Biopsy</th>
<th>Biopsy no</th>
<th>Total</th>
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<tbody>
<tr>
<td>6 had only hepatic GVHD, 10 hepatic GVHD with either iron overload, nodular regenerative hyperplasia, or steatosis.</td>
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Yang, A et al Transplantation and Cellular Therapy 2022.

More thoughts...

- A systematic, meticulous approach will make the **correct** diagnosis

- Although we try to avoid it, sometimes an invasive procedure is the right choice

- And! Diagnosis is crucial because treatment **makes a difference**
Imagine a future...

- No need for transplant
- Biomarkers
- Personalized treatment
- Induction of tolerance
- Microbiome
- HCV analogy

Build a team

- Family
- Friends
- Health care professionals
  - Open
  - Will learn with you
  - Available / accessible
  - Build trust
  - There in case of crisis
  - Center of excellence - caring
  - Even better if experience
  - Two tiered system of care – not always possible

Don’t forget to live!!!
Thank you!
BMT InfoNet, Patients, Dr. Pavletic and Dr. McDonald

QUESTIONS?

Theo Heller, MD
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LET US KNOW HOW WE CAN HELP YOU

Visit our website: bmtinfonet.org

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