Radiologic Evaluation of Complications following Hematopoietic Stem Cell Transplantation

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Overview

- Our patient R.D.: presentation on day +60 s/p auto-SCT
- Primer on hematopoietic stem cell transplantation (SCT)
- Common pulmonary complications of SCT
- Common abdominal complications of SCT
- Future of post-SCT complication imaging
Our patient R.D.: 37 y.o. man with AML s/p autologous SCT

- A 37 year old man with history of AML presents with fever on Day +60 s/p myeloablative autologous SCT
- **Vital signs:** T=102.9; HR=100; BP=120/70; RR=16, O2 sat:95 RA
- **Physical Exam:** HEENT: PERRLA, EOMI, OP clear, MMM
  Neck: no JVD, no LAD, neg Kernig’s&Brudz.
  CV: RRR, nl S1, S2, no MGR
  Lungs: CTAB, no WRR
  Skin: no rashes
- **Labs:** WBC = 9.3, Neut = 80.6%, Lymph = 11.6%
- **Medications:** Pentamidine prophylaxis, Protonix, Lantus
Primer on Stem Cell Transplantation

- (Hematopoietic) Stem Cell Transplantation (SCT)

  Bone marrow transplantation OR peripheral blood SCT. (BMT) (PBSCT)

- Treatment of hematologic malignancies (attempt to achieve cure by eliminating malignant cells) and solid malignancies (as an adjunct treatment to allow more aggressive treatment)

- Complications occur due to immune system dysfunction, can be lethal

Radiologic evaluation = cornerstone for timely diagnosis of complications
Outline of PBSCT:

Critical to know:
1. donor type
2. timing after SCT
3. extent of myeloablation & current immune status

Shlomchik et al, Nat Rev Imm 2007
Clinical factors to aid radiologic diagnosis:

- What type of SCT did the patient receive?
  - Autologous (donor = self)
  - Syngeneic (donor = identical twin)
  - Allogeneic (donor = HLA-matched sibling or unrelated)

- How long has it been since patient’s SCT?
  - 0-30 days: pre-engraftment phase
  - 30-100 days: early post-transplantation phase
  - 100 days+: late post-transplantation phase

- What conditioning regimen did the patient receive?
  - Full myeloablation: most autologous and allogeneic SCT
  - Non-myeloablative “mini-transplants”: allogeneic
SCT type and timing affect nature of post-SCT complications

<table>
<thead>
<tr>
<th>Type</th>
<th>Early complications (infectious, graft failure, VOD)</th>
<th>Acute GVHD (acute, chronic)</th>
<th>Chronic complications (infectious, autoimmune)</th>
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<tbody>
<tr>
<td>Autologous/Syng</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Allogeneic</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Myeloablative</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Non-myeloablative</td>
<td>-</td>
<td>+</td>
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</table>

Time (days) 0 30 100 >100
Let’s go back to our patient now…
Our patient R.D. with fever: Chest radiograph

1. ill-defined opacities
2. cardiomegaly
3. ground glass opacity/interstitial edema

Pertinent negatives:
- NO apparent pleural effusion*
- NO pneumothorax

* Costophrenic angles not visualized, can’t tell definitively

PA Plain chest radiograph (PACS, BIDMC)
Our patient R.D. with fever: CT of chest

- **Pericardial effusion**
- **“Halo sign”** associated with pulm hemorrhage
- **Ground glass opacities** associated with interstitial edema hemorrhage
- **ill-defined airspace opacities** associated with:
  - blood – pulmonary hemorrhage
  - pus – pneumonia
  - fluid – pulmonary edema
  - nodule - tumor
- **Pleural effusion**

CT chest with contrast (PACS, BIDMC)
Brief differential diagnosis

- **Immunocompetent:**
  
  (very broad)
  
  - **Tumor**
    - bronchoalveolar Ca
    - metastases - melanoma
  
  - **Infection (pneumonia)**
    - organizing pneumonia
    - eosinophilic pneumonia
    - atypical pneumonia
  
  - **Inflammation (vasculitis)**
    - Wegener’s

- **Immunocompromised:**

  - **Infection**
    - CMV
    - PCP
    - Aspergillus
    - TB
    - any infection

Rx: Voriconazole for presumed Aspergillus pneumonia
Other presentations of Aspergillus in SCT patients:

- 2 forms of Aspergillosis
  - Angioinvasive
  - Tracheobronchial

- Not to be confused with Aspergilloma!

CT chest w/o contrast
Companion patient #1 (PACS, BIDMC)

CT chest w/ (top) and w/o (bottom) contrast
Coy et al, Radiographics 2005
Companion patient #2: diffuse aspergillosis on CT

- 29 yo woman with **fever** and **neutropenia** on Day +14 s/p **induction** therapy for **AML**

“Tree-in-Bud” pattern associated with
- Aspergillosis
- TB
- M. Avium
- CMV
- RSV

CT chest with contrast (CAS, MGH)

Rossi et al. RadioGraphics 2005
Other pulmonary complications of SCT

- Pulmonary complications occur in 40-60% SCT recipients
- CMV pneumonia
- Diffuse Alveolar Hemorrhage
- Pulmonary edema; PCP, VZV and Zygomycetes pneumonia, etc.
Following the clinical course of our patient R.D., he presents to ED 4 months s/p auto-SCT with back pain...
4 months later, our patient R.D. fails auto-SCT

- 4 months s/p auto-SCT, patient presents with back pain
- recurrence of disease: WBC = 54K, 94% blasts, BM biopsy shows 90% intertrabecular space by blasts
- **Reinduction** therapy, complicated by repeat bouts of invasive aspergillosis

→ **Unmatched, unrelated mini-allogeneic SCT** (our patient does not have a matched related or unrelated donor)
Our patient R.D. presents on day +24 s/p allo-SCT with first complication

- Day +24 s/p unmatched unrelated mini-allo SCT

- Patient develops fever, 3 days of worsening watery non-bloody diarrhea, diffuse abdominal pain, NB/NB vomiting, decreased po intake secondary to nausea

- WBC = 7.4, Neut = 82%, Lymph = 2%

- Supine plain abdominal film demonstrating no evidence of pneumoperitoneum or obstruction
Our patient R.D.: diffuse bowel changes on CT

Featureless
(loss of mucosal folds)

Diffuse thickening of small and large bowel wall (4-5 mm)

Contrast study of GI
Companion patient #3

CT abdomen and pelvis with contrast (PACS, BIDMC)

Courtesy of Dr. Kruskal (BIDMC)
Our patient R.D.: diffuse bowel changes on CT

Halo of hypoattenuation within walls a.k.a. Target sign associated with Shock bowel Inflammation Vasculitis

Pertinent negatives:
No obstruction
No perienteric/ pericolic fluid
No pneumatosis

CT abdomen with contrast (PACS, BIDMC)
Brief differential diagnosis

- **Immunocompetent:**
  - (very broad)
  - Tumor (lymphoma)
  - Infection (enteritis)
  - Inflammation (Crohn’s)
  - Ischemia/vasculitis

- **Immunocompromised s/p allogeneic SCT:**
  - GVHD
  - GVHD
  - GVHD
  - Typhlitis
  - Aspergillus, Candida
  - Pseudomem. colitis

Rx: Steroids for Acute GVHD
Primer on Graft versus Host Disease

- **GVHD**: occurs in patients s/p allogeneic-SCT or immunodeficient patients receiving blood transfusions

- **Mechanism**: donor-derived T cells attack recipient’s tissues, severity related to degree of HLA mismatch

- **Sites**: 95% skin, 75% liver, 50% gut

- **Two stages**: acute (0-100 days) and chronic (100 days+)
  - Acute: small and large bowel mucosa diffusely abnormal
  - Chronic: esophageal strictures and webs

- **Prognosis** dependent on early treatment – early diagnosis is essential!
Menu of tests: additional imaging of GVHD

- **U/S Doppler:**

- **Wireless capsule endoscopy:**

- **PET:**

Neumann et al, Gastrointestinal Endoscopy 2007
Ausberger et al, Transplantation 2007
Other SCT-related abdominal complications

- **Infections** (eg *C. difficile* → pseudomembranous colitis; Candida, Aspergillus → microabscesses in liver, spleen, kidney)
- **Typhlitis** (neutropenic colitis)

- Hepatic veno-occlusive disease (VOD)
- Benign Pneumatosis intestinalis

Coy et al, Radiographics 2005
### Summary of BMT-related complications

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Conditions</th>
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<tr>
<td><strong>Pulmonary edema</strong></td>
<td>DAH</td>
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<tr>
<td><strong>Pre-engraftment</strong></td>
<td>DAH, CMV pneumonia, Idiopathic pulmonary syndrome, Viral (non-CMV) &amp; bacterial pneumonia, Cryptogenic organizing pneumonia, Constrictive bronchial obliterans, Pulmonary proteinosis</td>
</tr>
<tr>
<td><strong>Early post-transplantation</strong></td>
<td>CMV pneumonia, Idiopathic pulmonary syndrome, Viral (non-CMV) &amp; bacterial pneumonia, Cryptogenic organizing pneumonia, Constrictive bronchial obliterans, Pulmonary proteinosis</td>
</tr>
<tr>
<td><strong>Late post-transplantation</strong></td>
<td>CMV pneumonia, Idiopathic pulmonary syndrome, Viral (non-CMV) &amp; bacterial pneumonia, Cryptogenic organizing pneumonia, Constrictive bronchial obliterans, Pulmonary proteinosis</td>
</tr>
<tr>
<td><strong>C. Difficile colitis</strong></td>
<td>Acute GVHD, Hemorrhagic cystitis (late)</td>
</tr>
<tr>
<td><strong>Hepatic VOD</strong></td>
<td>Acute GVHD, Hemorrhagic cystitis (late)</td>
</tr>
<tr>
<td><strong>Hemorrhagic cystitis (early)</strong></td>
<td>Acute GVHD, Hemorrhagic cystitis (late)</td>
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Adapted from Coy et al. *RadioGraphics* 2005
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References


