

CRITICAL CARE COMPLICATIONS RELATED TO BONE MARROW TRANSPLANT IN PEDIATRICS

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Objectives:

- ▣ Identify the most common complications related to bone marrow transplant requiring intensive care in the pediatric population
- ▣ Review nursing assessment and management of critical care complications in the transplant patient.

Types of Transplants

- ▣ Autologous
 - Self-derived cells for marrow recovery
- ▣ Allogeneic
 - Alternate donor source for cell recovery and treatment of diseased marrow

Complications by Systems

- ▣ Pulmonary : most common reason for ICU stay
 - Acute
 - Chronic
 - Infectious
- ▣ Hepatic:
 - Veno-Occlusive Disease (VOD)
- ▣ Renal:
 - Hemorrhagic Cystitis
 - VOD
 - Nephrotoxicity

Complications:

- ▣ Gastrointestinal
 - Enteritis
 - Pancreatitis
- ▣ Cardiac
 - Pericardial Effusion
 - Congestive Heart Failure (CHF)
- ▣ Infection
 - Bacterial
 - Viral
 - Fungal

Complications

- ▣ Graft VS Host Disease
 - Acute
 - Chronic

Risk Factors

- ▣ Regimen related toxicity of conditioning (ablative vs. non-ablative)
- ▣ Immunosuppression
- ▣ Donor source
- ▣ Previous agent exposure prior to transplant in resistant malignant disease
- ▣ Previous infections or exposures

Most Common ICU Admissions

- ▣ Pulmonary (acute and chronic)
- ▣ VOD/Renal failure
- ▣ Infection
- ▣ Graft vs Host Disease (acute and chronic)

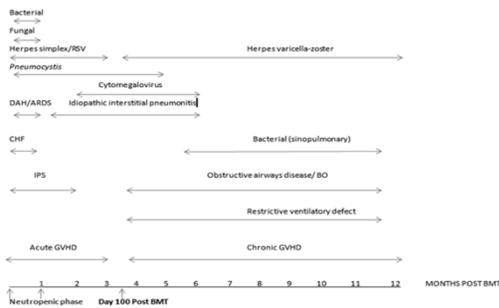
Pulmonary

- ▣ Acute:
 - Diffuse Alveolar Hemorrhage (DAH)
 - Engraftment Syndrome
 - Idiopathic Pneumonia Syndrome
 - Infection
 - GVHD

Prevalence

- ❑ Most common indication for admission to the Intensive Care Unit
- ❑ 60% of transplant recipients develop pulmonary complications
- ❑ 30% of deaths are related to pulmonary complications
- ❑ Predictable pattern in the post transplant timeline which is helpful in differential diagnosis and management

Pulmonary Complications after stem cell transplantation



Diffuse Alveolar Hemorrhage (DAH)

- ❑ Usually develops in the first 30 days post transplant
- ❑ Slightly more common in Autologous transplant
- ❑ Constitutes 40% of all causes of acute respiratory failure admitted to the ICU
- ❑ Primary risk factors: intensive chemotherapy, TBI, WBC count recovery and renal insufficiency

Assessment Findings

- ☐ Increased Dyspnea
- ☐ Fever
- ☐ Cough
- ☐ Hypoxemia
- ☐ Increased rate and effort of breathing
 - Flaring
 - Accessory muscles
 - Retracting

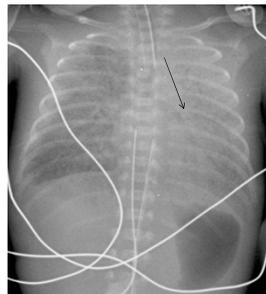
Diagnosis

- ☐ Confirmed by BAL: progressively bloody fluid return from 3 separate sub-segmental bronchi
- ☐ Evidence of bilateral widespread alveolar injury
- ☐ Absence of infection

Diffuse Alveolar Hemorrhage

Xray:

Bilateral interstitial and alveolar infiltrates



DAH

CT Scan:
ground glass
infiltrates



Treatment

- ☐ Supportive Care
 - Mechanical Ventilation
 - High dose steroids
 - Blood/ platelets and possibly factor replacement



Engraftment Syndrome

- ☐ Develops within 96 hours of engraftment (ANC greater or equal to 500)
- ☐ Seen in both allogeneic and autologous patients
- ☐ Coincides with neutrophil recovery and the release of cytokines by neutrophils
- ☐ Characterized by fever, erythematous rash, diarrhea, renal impairment, and diffuse pulmonary infiltrates
- ☐ May lead to severe hemodynamic collapse and MSOF

Assessment Findings

- ☐ New onset of fever ($> 38.5^{\circ}\text{C}$)
- ☐ Erythematous rash
- ☐ Diarrhea
- ☐ Pink frothy exudate with cough
- ☐ Increase in respiratory rate

Assessment Findings

- ☐ Auscultation of rales bilaterally
- ☐ Difficulty breathing in a reclined position
 - Patient will posture in a position of comfort
- ☐ Decreased oxygen saturation
- ☐ Increase in weight
- ☐ Decrease in urine output

Diagnosis

- ☐ Two or more of the following symptoms within 96 hours of engraftment
 - Fever (without infectious etiology >38.5)
 - Non-cardiogenic pulmonary edema
 - hypoxia
 - Erythematous rash
 - Diarrhea
 - Renal impairment
 - Ascites with weight gain $\geq 2.5\%$ over baseline

Treatment

- ▣ Supportive Care
 - Mechanical ventilation
 - Systemic corticosteroids (shown to decrease duration and complications)
 - Diligent skin assessment and care due to diarrhea, rash and immobility with mechanical ventilation

Idiopathic Pneumonia Syndrome

- ▣ A syndrome of diffuse lung injury that develops following HSCT in which an infectious etiology is not identified
- ▣ Usually diagnosed in the first 2 months post transplant (D+1-D+60) with the mean onset from 21-65 days.
- ▣ High mortality rate estimated to be 74%

Risk Factors

- ▣ Older age
- ▣ Malignancy other than leukemia
- ▣ + CMV status of the donor
- ▣ High dose chemotherapy (myeloablative conditioning regimen)
- ▣ TBI
- ▣ Grade III-IV GVHD
- ▣ MSOF

Assessment Findings

- ▣ Increased respiratory rate and effort
- ▣ Hypoxemia (decreased O2 sat)
- ▣ Non productive cough
- ▣ Dyspnea
- ▣ Crackles, Rales, Rhonchi



Diagnosis

- ▣ Widespread alveolar injury including symptoms and signs of pneumonia, multilobar infiltrates and evidence of abnormal lung physiology
- ▣ Absence of active lower respiratory tract infection (BAL negative for known pathogens)
- ▣ Pathogenesis is not clear

Treatment

- ▣ Corticosteroids
- ▣ Supportive care- mechanical ventilation

Infection:

- ▣ Account for 23% of the admissions to the Intensive Care Unit
- ▣ Significant complication in transplant population due to the use of broad spectrum antibiotics, indwelling catheters, and mechanical ventilation
- ▣ Primary predisposing factors include impaired humoral and cellular immunity, neutropenia, immunosuppression and loss of mucosal and cutaneous barriers

Infection: Most Common

- ▣ Bacterial
 - Gram Negative: Pseudomonas and Klebsiella
 - Gram Positive: MRSA, Streptococcus viridans,
- ▣ Viral
 - CMV: highest risk is CMV -- pt. receiving CMV + donor cells.
 - RSV (Respiratory Syncytial virus)
 - HHV6
 - Herpes Zoster Virus
 - Adenovirus

Infection

- ▣ Fungal
 - *Candida*
 - *Aspergillus*



Assessment Findings

- ▣ Newly developed fever
- ▣ Increased respiratory rate and effort
- ▣ Positive fluid balance
- ▣ Change in mental status
- ▣ Prolonged capillary refill
- ▣ Air hunger as evidence by “unable to catch their breath” or posturing
- ▣ Diminished breath sounds
- ▣ Chest Pain

Diagnosis

- ▣ CXR: Radiographic findings with alveolar consolidation and diffuse involvement (bacterial)
- ▣ CT Scan: best for fungal evaluation. Note ground glass opacity (halo sign)
- ▣ BAL with infectious etiology identified
- ▣ If intubated, may also obtain ET aspirate for culture

Treatment: Manage the Sepsis and Provide Respiratory Support

- ▣ Organism specific antibiotic/antifungal coverage
- ▣ Stress dose steroids
- ▣ Fluid resuscitation (with caution)
- ▣ Pressors such as Dopamine, or Epi
- ▣ Tylenol for fever (IV, NG, PO)
- ▣ Supplemental oxygen
- ▣ Management of secretions
- ▣ Mechanical Ventilation



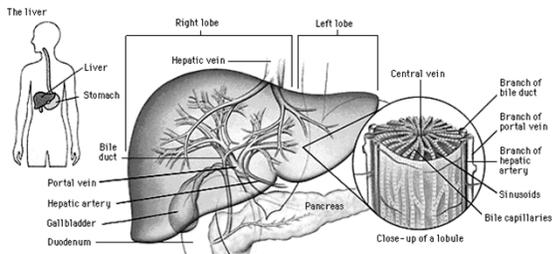
Hepatic

- ☐ VOD: Veno-Occlusive Disease
 - Fatal in 20-50% of patients
 - Occurs in the first 30 days post transplant with a mean of 21 days
 - Classic triad of symptoms: sudden weight gain with or without ascites, RUQ pain, and elevated bili (2.0 mg/dl) resulting in jaundice
 - Considered an emergency and must be managed immediately

Etiology

- ☐ Endothelial cellular destruction and cellular debris (related to pre-transplant conditioning) obstruct the sinusoidal blood flow of the liver
- ☐ Doppler ultrasound of hepatic vessels shows reversal or decreased flow
- ☐ Develop hepato-renal syndrome
- ☐ May be mild and self limiting to a rapidly progressing fatal outcome resulting in MSOF

Liver Structures



Diagnostic Criteria

Baltimore : hyperbilirubinemia $\geq 2\text{mg/dL}$ before day 21 after transplant and, at least two of the following:

- Hepatomegaly (usually painful)
- Ascites
- Weight gain greater than 5% from baseline

Seattle: presence before day 30 after transplant of at least two of the following features:

- Jaundice
- Hepatomegaly and RUQ pain
- Ascites and/or unexplained weight gain

Prophylaxis and Management

- Low dose dopamine $\sim 2.9\text{ mcg/kg/min}$ as CI
- Heparin 100u/kg/day as CI
- Investigational:
 - Ursodiol
 - Defibrotide
- Limit number of drugs metabolized by the liver
- Aggressive fluid balance/restriction
- Mechanical ventilation related to fluid overload or aspiration
- CRRT related to renal insufficiency

Maintain Urine Output!!

- Suggest use of Spironolactone vs. Lasix
- Question the use of bumex???
- Follow albumin infusion with diuretics for maximum benefit
- Follow output every 2 hours
- Obtain CVP every 8 hours
- Follow fluid status with Arterial line if in place

Labs

1. ↑ BUN/CR
2. ↑ LDH/Bili (direct/indirect)
3. WBC recovery and ANC
4. Trending CRP with any new fever
5. Pending cultures
6. ↓ Total Protein and Albumin
7. Basic metabolic panel (daily electrolytes)

Nursing Assessment

- ☐ Rapid onset of RUQ pain
- ☐ Increased liver size and tenderness
- ☐ Generalized edema
- ☐ Change in breath sounds with increased fluid overload
 - Rales
 - Rhonchi
 - Diminished breath sounds

Nursing

- ☐ BID weights
- ☐ **Report any sudden increase of weight gain with decreased urine output ***
- ☐ Strict parameters with intake and output



Nursing

- ▣ Abdominal girth (twice daily)
- ▣ Suggest all fluids be placed in minimal volume
- ▣ Restrict volume wherever possible
- ▣ Consolidate lab draws



One Word?

- ▣ Leaky!!
 - Very prone to leaking fluid into the abdomen, lungs, tissues. All of the complications discussed are interrelated and require aggressive fluid management regardless of the etiology

Wrapping it Up

- ▣ Nurses are the consistent eyes and ears of the team and hold valuable information in early treatment of complications in the patient post transplant
- ▣ Knowing the most common complications, what to look for and the predictable time line of when they will happen is imperative in the care of the BMT patient.

References

Dhillon, G.S. & Rizk, N.W. (2009) critical care of the hematopoietic cell transplant recipient. In Appelbaum, F.R., Forman, S.J., Negrin, R.S., Blume, K.G., Thomas' hematopoietic cell transplantation (pp 1539-1547) Oxford, UK: Wiley-Blackwell.

Kaner, R.J. (2013) Pulmonary complications after allogeneic hematopoietic cell transplantation. Retrieved from:
http://www.uptodate.com/contents/pulmonary-complications-after-allogeneic-hematopoietic-cell-transplantation?detectedLanguage=en&source=search_result&search=Pulmonary+complications+after+allogeneic+hematopoietic+cell+transplantation&selectedTitle=1~150&provider=noProvider

Kumar, S., DeLeve, L.D., Kamath, P.S., & Tefferi, A. (2003) Hepatic veno-occlusive disease (sinusoidal obstruction syndrome) after hematopoietic stem cell transplantation. *Mayo Clinic Proceedings* 78: 589-598

References

Richardson, P.G., Ho, V.T., Giralt, S., Arai, S., Mineishi, S., ...Soiffer, R. (2012). Safety and efficacy of defibrotide for the treatment of severe hepatic veno-occlusive disease. *Therapeutic Advances of Hematology* 3 (4) 253-265.

Soubani, A.O. (2006). Critical care considerations of hematopoietic stem cell transplantation. *Crit Care Med* 34 (9) s251-267

Summers, E.; Frey, M.A.; Kurtzberg, J. Engraftment Syndrome. (2007) *Biology of Blood and Marrow Transplantation* 13 (2) p. 148
DOI: 10.1016/j.bbmt.2007.01.044. ISSN: 1083-8791.
