Septic Shock

Morbidity and Mortality
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HPI

• 31 yr old male with PMH of paraplegia secondary to neurosarcoidosis with extensive decubitus ulcers of bilateral lower extremities admitted to ER on 8/6/09 from surgery clinic
• Patient well known to surgery service and ulcers were episodically debrided in clinic; pt often refusing debridement
• Patient was sent to ER from clinic for dehydration and worsening appearance of ulcers
Past Medical History

- Paraplegia secondary to Neurosarcoidosis diagnosed 2006
- Diabetes Insipidus
- Diabetes Mellitus
- Hypothyroidism
- Hypertension
- Dyslipidemia
- Asthma
- Seizure Disorder
Medications

- Metformin 500 mg q12
- Novolog Insulin 8 Units before meals
- Lantus 30 Units
- Levothyroxine 0.025mg daily
- Lexapro 10mg daily
- Metoprolol 50mg q12
- Desmopressin 100mcg intranasally daily
- Zocor 40mg daily
- Prednisone 40 mg daily
- ASA 81mg daily
- Keppra 500mg q12
Physical Exam

- Vitals: T 98  BP 80/40  HR 111  RR 16  O2 Sat 100% on RA
- Gen: A&Ox3; pale; dry mucous membranes
- Heart: sinus tachycardia; no murmurs
- Lungs: ctab
- Abdomen: soft, nt, nd, +bs
- Back: 10x10cm stage III sacral decubtus ulcer
- LLE: large Stage IV 30x20cm decubitus ulcer on posterolateral thigh with exposed femur and osteomyelitis; no motor or sensory function
- RLE: sacral decubitus ulcer extending to right buttock; no motor or sensory function
Labs

- CBC: WBC 27.6 (72% 19 Bands); h/h 5.5/20.5  Plt 792
- Chem: Na 123  K 5.9  Cl  83  HCO3 21  Bun 27  Cr 2.0  Glu 104  Ca 9.6
- LFTs:  TP 7.9  Alb 2.0  AST 36  ALT 10  ALK phos 590  TB 0.5
- Coags: PT 15  PTT 34  INR 1.8
- ABG 7.45/33/109/24/98/-0.6 on RA
- Lactate 4.6
- Cortisol 13.8 (3-22)
- Blood Culture: +Streptococcus Viridians
Hospital Course

• In ER left subclavian TLC and foley inserted and patient received 6L LR, 3PRBC and 2 FFP and patient transferred to ICU

• Broad Spectrum antibiotics initiated (Amikacin, Vancomycin, Meropenam)

• 8/7 Patient remained hypotensive to 80s/40s despite continued IV fluid resuscitation 2 additional units of PRBCs with CVP of 17; levophed initiated

• Stress Dose steroid and DDAVP started
Hospital Course

- 8/7 patient intubated secondary decreased mental status and hypoxia
- Patient underwent emergency debridement of left hip, sacral, right buttock ulcer
- Postoperatively patient with GCS of 3 and pupil fixed and dilated; CVA suspected
- CT Head 8/7 showed no evidence of CVA; TTE showed EF of 15-20% and troponins wnl
- 8/8: Patient was awake alert and oriented with no evidence of focal neurological deficit
- 8/8 Swan Ganz Pulmonary Artery Catheter Inserter for hemodynamic monitoring on dobutamine, levophed and vasopressin
Hospital Course

• 8/10: patient coded; ACLS protocol initiated for aystole and to which patient responded
• 8/16: weaned off pressor and started caspofungive fur fungemia
• 8/21: patient was extubated
• 8/28: patient underwent left hip disarticulation and placement of wound vac
• Hospital course protracted and complicated by pneumonia, respiratory failure, bacteremia and fungemia
Hospital Course

• 9/09: tracheostomy and open gastrostomy
• 9/28: diverting colostomy
• 10/30: IVC filter placed
• 11/04: Discharge to NH
• 11/09: Patient readmitted for urosepsis
• 11/18: Discharged to NH
Septic Shock

• Shock is the failure to meet metabolic demands of the body and the physiological consequences that ensue.

• Tissue hypoperfusion:
  – Direct consequence of the etiology of shock as seen in hemorrhagic, cardiogenic and neurogenic shock.
  – Indirect result of molecules and cellular products released that results in vasodilation as seen in SEPTIC SHOCK.
Pathophysiology of Septic Shock

• Dysfunction of the endothelium due to circulating inflammatory mediators and cells

• Enhance macrophage and neutrophil effector mechanisms in an attempt to eradicate pathogens

• Increased procoagulant activity and fibroblast activity to localize and contain pathogens causing coagulopathy

• Increase blood flow to enhance immunologic killing mechanisms in the area of infection
Pathophysiology of Septic Shock

• Due upregulation of NOS in endothelium which releases large amount of potent vasodilator NO

• NO causes vasodilation and resistance to vasoconstricting agents

• Immunological defense mechanism becomes systemic rather than localized
Classification of Sepsis

• **SIRS** Systemic Inflammatory Response Syndrome (2 or more of the following):
  • T > 38C or < 35C
  • HR > 90
  • RR >20 or PCO2 < 32mmHg
  • WBC > 12,000 or < 4,000

• **SEPSIS**: SIRS + Infection

• **SEVERE SEPSIS**: SIRS + Infection + Hypoperfusion/Organ Dysfunction (lactic acidosis, oliguria, mental status changes)

• **SEPTIC SHOCK**: SRS + Infection + Hypoperfusion/Organ Dysfunction + Hypotension (SBP < 90mmHg or > 90mmHg with pressors)
Management of Septic Shock

- Secure Airway and Ventilation +/- ETI
- Fluid Resuscitation
- Broad Spectrum Antibiotics
- Control of Source Infection
  - Drainage of infected fluid collections
  - Removal of Infected Foreign Bodies
  - Debridement of Devitalized Tissues
- Assessment of Perfusion
- Early Goal Directed Therapy within 6 hours
Assessment of Perfusion

- Arterial Line
- TLC for ScVO2 and CVP
- PAC if indicated for CO, PCWP and SVO2
  - not recommended as standard of care in treatment of septic shock
  - PCWP poor predictor of fluid responsiveness
  - Increase Complications and have not been shown to improve outcome
Assessment of Perfusion

- SVO2 ≥ 70
- MAP ≥ 65
- CVP 8-12 mmHg
- UOP ≥ 0.5 mg/kg/hr
- Vasopressors (Dopamine, Vasopressin, Levophed)
- MAP ≤ 65 – Stress Dose Steroids or Xigris
- Dobutamine if SVO ≤ 70 with MAP ≥ 65
Sepsis-induced hypoperfusion
Clinical picture of sepsis plus:
SBP ≤90 mmHg or MAP ≤65 mmHg or
Lactate ≥4 mmol/L

Supplemental O₂ = ETI with mechanical ventilation (if necessary). Target So₂ of ≥96%

Begin fluid resuscitation (initial bolus of at least 20 mL/kg crystalloid or colloid equivalent)*

SBP remains <90 mmHg or MAP remains <65 mmHg or initial lactate ≥4 mmol/L

Boluses crystalloid or colloid equivalent

CVP <8 mmHg

Insert CVP catheter

CVP 8–12 mmHg

MAP <65

MAP ≥65

• Administer stress dose steroids
• Consider for drotrecogin α

MAP <65 mmHg and vasopressors still required?

Yes

No

MAP ≥65 mmHg and vasopressors still required?

Yes

No

Resuscitation complete. Establish re-evaluation intervals.

Achieve all goals?

Yes

No

Dobutamine

Transfuse if HCT <30

<70%

Vasopressors (norepinephrine or dopamine preferred)

MAP ≥65

So₂

×70%

Source: Brunner FC, Anderson BR, Billiar TR, Dunn DL, Hunter JO, Matthews JB.
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* The circumstances where MAP is judged to be critically low, vasopressors may be started at any point in this algorithm.
The pulmonary artery catheter is used; a mixed venous o₂ saturation is an acceptable surrogate and 65% would be the target.
Management of Septic Shock

• Activated Protein C (Xigris)
  • Endogenous protein promotes fibrinolysis and inhibits thrombosis and inflammation
  • Reduced the 28-day mortality rate from 31 to 25%
  • Several follow-up studies have suggested that APC may not improve mortality when patients are followed up to 6 months
Management of Septic Shock

- Septic Shock often accompanied by adrenal insufficiency
- 50 mg hydrocortisone IV q 6 hours
- Improves MAP response to vasopressors
- Low doses of hydrocortisone and fludrocortisone reduced risk of death in patients with septic shock and relative adrenal insufficiency (2002).
- Follow-up RTC showed that stress steroids do not change mortality in septic shock (Sprung et al. 2008)
- Stress dose steroids cannot be recommended as routine adjuvant therapy for septic shock
Vasopressin Versus Norepinephrine Infusion in Patients with Septic Shock

Russell et al. NEJM 2008

• Background:
  – Vasopressin improves BP response to catecholamines and decreases catecholamine requirements in septic shock; effect on mortality is unknown
  – Adverse Side Effects of catecholamine vasopressor agents
    • Decreased CO
    • Decreased O2 delivery
    • Mesenteric Ischemia
    • Skin necrosis

• Hypothesis: Does low dose Vasopressin as compared to Levophed reduce mortality in patients with septic shock?
Vasopressin Versus Norepinephrine Infusion in Patients with Septic Shock

Russell et al. NEJM 2008

• **Study Design:**
  – Patients older than 16 with septic shock resistant to fluids or requiring vasopressor (at least 5ug Levophed for 6 hours)
  – Randomly assigned to receive Levophed (5-15 micrograms/min) or Vasopressin (0.01-0.03 Units/min) titrated to MAP 65-75
  – Open label vasopressors were infused if MAP target could not be reached
  – Patient were stratified according to degree of shock based on Levophed requirements
    • 5-14 micrograms/min – Less Severe Shock
    • >15 micrograms/min - More Severe Shock

• **Statistical Analysis:**
  • Chi-Square Test and Kaplan Meier Curves Used to evaluated endpoint
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• Results:
  • 778 pts randomized 396 received Vasopressin and 382 Levophed
  • No significant difference in 28 day mortality (35% vs 39% p=0.26)
  • No significant difference in 90 day mortality (44% vs 49% p=0.11)
  • No significant differences in serious adverse events (10.3% vs 10.5%)
  • In the stratum of less severe shock 28 day mortality decreased in
    Vasopressin verses Levophed arm (26.5% vs 35.7% p=0.05)
  • There was no significant different in 28 or 90 day mortality in stratum of
    more severe shock (44% vs 42%)

• Conclusions:
  • Although Vasopressin may be benificial in achieving resusciation
    endpoints in septic shock; it does not improve mortality
References

- Sabiston’s Textbook of Surgery
- Schwartz’s Principles of Surgery, Eight Edition
- Cinel I, Dellinger RP: Advances in pathogenesis and management of sepsis. *Curr Opin Infect Dis* 20:345, 2007 (Flowgram)