

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 30Units
- 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 decubitus 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 Insertion 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 $PCO_2 < 32\text{mmHg}$
 - $WBC > 12,000$ 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* ($SBP < 90\text{mmHg}$ or $> 90\text{mmHg}$ with pressors)

Management of Septic Shock

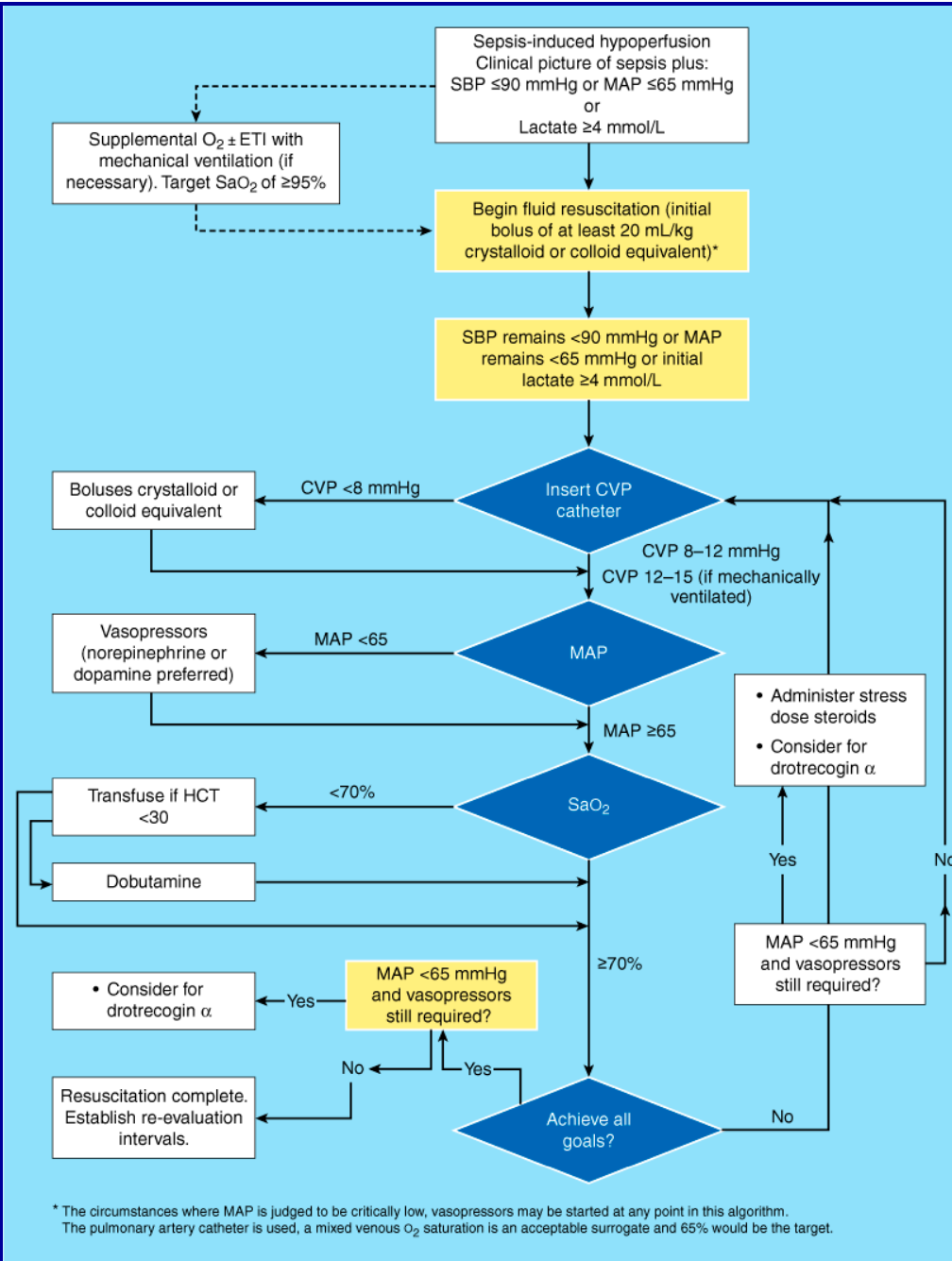
- Secure Airway and Ventilation +/- ETI
- Fluid Resuscitation
- Broad Spectrum Antibiotics
- Control of Source Infection
 - Drainage of infected fluid collections
 - Removal of Infected Foreign Bodies
 - Debridement of Devitalized Tissues
- Assessment of Perfusion
- Early Goal Directed Therapy within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

- $SVO_2 \geq 70$
- $MAP \geq 65$
- CVP 8-12 mmHg
- $UOP \geq 0.5 \text{ mg/kg/hr}$
- Vasopressors (Dopamine, Vasopressin, Levophed)
- $MAP \leq 65$ – Stress Dose Steroids or Xigris
- Dobutamine if $SVO \leq 70$ with $MAP \geq 65$



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:
 - Multicenter Double-Blinded RTC 2001-2006 (CAN, US, AUS)
 - 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

Vasopressin Versus Norepinephrine Infusion in Patients with Septic Shock

Russell et al. NEJM 2008

- 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 versus Levophed arm (26.5% vs 35.7% p=0.05)
- There was no significant difference in 28 or 90 day mortality in stratum of more severe shock (44% vs 42%)

- Conclusions:

- Although Vasopressin may be beneficial in achieving resuscitation endpoints in septic shock; it does not improve mortality

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