Surgical Aortic Valve Replacement for the Patient with Stiff Person Syndrome

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INTRODUCTION TO STIFF PERSON SYNDROME

Overview:

Stiff Person Syndrome (SPS) is a rare neuromuscular condition characterized by axial and proximal muscle stiffness and rigidity, with superimposed spasms, occurring in approximately 1-2 : 1 million patients. It is associated with certain HLA genes but has no known genetic inheritance pattern.[1] It can exist concurrently with other autoimmune conditions such as vitiligo, diabetes mellitus, thyroiditis, and pernicious anemia. Cancer may predispose the development of SPS as well.[3]

The etiology of SPS is autoimmune in nature: there are antibodies against glutamic acid decarboxylase (GAD-65, which produces the neurotransmitter gamma-aminobutyric acid, GABA) or the GABA receptor.[3] When activated, the GABA receptor normally causes cellular hyperpolarization and subsequently muscular relaxation, but with antagonistic antibodies, cells are more likely to depolarize and create stiffness and spasms. Treatment focuses on symptom management with muscle relaxation, biologic or immunosuppressive therapy, plasmapheresis in refractory cases.[1-3]

Most cases result in limited functional status and restricted mobility, but in more severe cases can produce aerodigestive tract dysfunction and paroxysmal autonomic dysfunction (transient hyperpyrexia, diaphoresis, tachypnea, tachycardia, pupillary dilatation, and arterial hypertension) leading to sudden death. Spasms may be triggered by external or internal stimuli, such as pain, voluntary movement, fear, or anxiety, and they are clinically manifested by an exaggerated “startle reflex”.[1]

HPI:

A 50 year old male with Stiff-Person Syndrome (SPS) was admitted with worsening muscle cramping and joint stiffness consistent with his usual symptoms, as well as fever and chills which were not part of his usual SPS symptom profile. Other past medical history was significant for non-obstructive coronary artery disease for which he received clopidogrel.

The patient underwent chronic plasma exchange (PLEX) and steroid therapy via bilateral tunneled subclavian pheresis catheters for his symptoms refractory to usual therapies. This therapy was complicated by gradually worsening erythema, purulent discharge, and pain at the catheter sites for several weeks prior to admission. Despite the concern for possible catheter infection, the catheters were used for ongoing PLEX therapy.

After two weeks of intermittent fever, the tunneled catheters were removed; catheter and blood cultures were positive for *S. caprae*. A temporary Trialysis catheter was placed for continued PLEX. Continued PLEX gradually improved his SPS symptoms. Serial blood cultures remained positive despite IV antibiotics. Worsening peripheral edema and dyspnea developed. TEE revealed a 1x1cm vegetation on the RCC of the aortic valve with severe valvular insufficiency but no annular or aortic root abscess.

PERIOPERATIVE MANAGEMENT

Preoperative Evaluation

PSH: C5-7 ACDF, no subsequent airway instrumentation

Home Medications:
- Diazepam 30 mg QID for muscle spasm
- Diazepam 5-10 mg PRN breakthrough spasms (greater need prior to admission)
- Clopidogrel 75 mg QD
- IVIG weekly
- Gabapentin 1200 mg TID
- Meloxicam 15 mg QD
- Magnesium oxide 800 mg for spasm

Physical Exam:
- 192 cm, 145 kg, BMI 38
- Mallampati class 3, thyromental distance >5 cm, mouth opening >5 cm
- Thick neck, normal cervical range of motion
- Large tongue, prominent mandible
- Thick moustache/beard
- Chest with edema/ecchymoses from bilateral clavicles to nipple line
- 13 Fr temporary dialysis catheter, right IJ
- 20 G PIV

Intraoperative / Postoperative Course

The patient was optimized with diuresis on the ward; his dry weight was achieved, and labs were at baseline and stable. His vitals remained stable and he became afebrile on antibiotic therapy.

He was premedicated with midazolam 10mg in divided doses starting in preoperative holding and throughout arterial line placement. Induction and endotracheal intubation were uneventful. Additional central venous access was unobtainable due to intraluminal thrombus in the left IJ, and clear signs of residual infection on the chest wall overlying subclavian sites.

Total time on cardiopulmonary bypass was 106 minutes, weaning was straightforward. Minimal vasopressor support was needed en route to the ICU. The patient was extubated within four hours postoperatively and was discharged to rehab on Postoperative Day 8.

Potential Intraoperative Challenges

Premedication:
- Tolerance to benzodiazepines, titrate dose to effect, may be unnecessary with baseline medication use
- No high quality studies exist regarding specific anesthetic drug choices[1]

Positioning:
- MSK deformities from chronic spasm may make optimal positioning difficult
- Airway management, line placement, regional anesthetic techniques may be technically challenging
- Trouble positioning for surgery itself
- May be at risk for pressure injuries, utilize best practices for prevention of neuropathy[1,2]

Monitoring:
- Consider invasive arterial hemodynamic monitoring for potential paroxysmal autonomic dysfunction
- Train-of-four, or regional anesthetic (stimulating needle, paresthesia technique) may induce spasm
- Avoid hypothermia, shivering[1]
- Processed EEG may guide depth of anesthetic

Postoperative:
- Laryngospasm may occur with less stimulus
- Consider dedicated/isolation room in PACU to limit stimulation or triggers (pain, noise, light)
- Potential for delayed recovery with baseline medication profile
- Consider resuming home medications when safe

Anesthetic Drugs and SPS[1-3]

Sedative/hypnotics
- GABA-ergic drugs effective, likely require dose-adjustment for chronic benzodiazepine use
- Myoclonus with etomidate > propofol
- Usual medication-specific contraindications still applicable

Neuromuscular blocking drugs (NMBD)
- Anti-GAD antibody does not appear to act at the neuromuscular junction
- NMBD are reliably reversed with sugammadex, or cholinesterase inhibitors + anticholinergics
- Incidence of postop hypotonia unclear; some case reports describe this, but in the setting of medication overdose, inadequate NMBD reversal
- No data on succinylcholine effects on spasm, consider defasciculating dose

Volatile inhaled anesthetics
- Safe to use
- No apparent increased risk of MH
- MAC requirement likely increased given chronic benzodiazepine use
- Musculoskeletal limitations related to neurotransmitter deficit, not dystrophin or the sarcoplasmic reticulum

Anesthetic Considerations for Aortic Valve Insufficiency

Hemodynamic goals[4, 6]
- HR: normal / fast
- Rhythm: sinus
- Preload: low / normal
- Afterload: low / normal
- Contractility: maintain

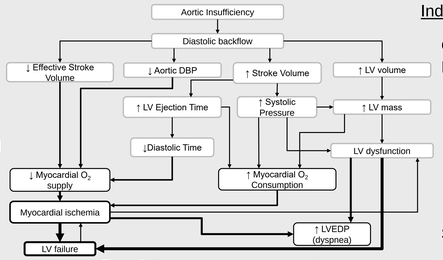

Figure 1: Pathophysiology of aortic valve insufficiency, adapted from Stoelting’s Anesthesia and Co-Existing Diseases

Indications for Replacement[4-6]
- Onset: acute vs chronic
- Etiology
  - Infective (vegetation, root abscess)
  - Aneurysmal, dissection
  - Congenital, bicuspid
  - Calcific disease
- Staging based on:
  - Anatomy
  - Hemodynamics

DISCUSSION

Stiff Person Syndrome (SPS) is an insidious, slowly-developing autoimmune disease affecting GABA-mediated neurotransmission, ultimately leading to neuromuscular junction (NMJ) hyperexcitability. It is not a disease of the NMJ itself and has no known association with malignant hyperthermia.[1] Although rare, when present it is often begins in middle-age, and it is associated with cancer or other autoimmune organ system diseases.[1-3]

The acute effects of SPS manifest in relation to a sudden stimulus and can be displayed as axial and appendicular skeletal muscle spasms, choking or upper airway obstruction, or imbalances in sympathetic and parasympathetic tone. Chronically, patients affected by SPS are limited in functional status and mobility. They may suffer from postural abnormalities as a result of persistent skeletal muscle hypertonus. This can be consequential to pulmonary function and mechanical ventilation if thoracic compliance is limited by kyphoscoliosis. Careful attention should be given to the patient’s range of motion, which if possible, should be actively examined preoperatively to determine what accommodations need to be made for the various aspects of the perioperative process.

Patients can be expected to have increased anesthetic requirements due to chronic use of benzodiazepines and membrane stabilizing medications; dose adjustments should be individualized and titrated to effect based on the clinical setting.

The approach to aortic valve replacement determined by etiology, surgical risk, symptoms, and severity, and is best decided by a multidisciplinary team.[6] No formal guidelines exist on additional or unique preoperative evaluation specific to patients with SPS.[1]

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