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Anesthetic Management of a Patient with Hereditary Coproporphyria

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Abstract

Hereditary coproporphyria (HCP) is an inborn error of metabolism that causes accumulation of porphyrins and porphyrin precursors, which can potentially lead to neurotoxicity and acute crisis with introduction of a triggering agent. Many anesthetic drugs have been labeled porphyrinogenic, therefore safe anesthetic management of patients with HCP demands understanding of the disease process. Although most of the current clinical reports are anecdotal and/or outdated, there is consensus that unsafe agents include: barbiturates, ketamine, and etomidate; and safe agents include: propofol, nitrous oxide, volatile agents, all neuromuscular blocking agents, all reversal agents, commonly used narcotics, antiemetics (excluding metoclopramide), and sedatives. Acute attacks of HCP exhibit a wide variety of metabolic defects that may result in life-threatening reactions, such as severe autonomic dysfunction and blood pressure (BP) lability. The anesthesia provider must be knowledgeable of concomitant triggers as well as appropriate treatment of porphyric crises. Further investigation of anesthetic management of the patient with HCP is indicated, given that most current clinical reports are anecdotal and/or outdated. The anesthesia provider should refer to the American Porphyria Foundation website for the most up-to-date information on porphyria and up-to-date drug database for healthcare professionals caring for porphyria patients

Anesthetic Management of a Patient with Hereditary Coproporphyria

Audrey F. Fisher, BSN, RN, CCRN, Texas Christian University

Introduction

- HCP is a rare (1:1,000,000) heme biosynthesis disorder inherited from either parent via autosomal dominance.
- HCP causes accumulation of porphyrins and porphyrin precursors which lead to neurotoxicity and subsequent acute attack in the presence of known triggering agents.
- Acute attacks can be life threatening and involve severe autonomic instability, respiratory failure, and paralysis.
- Triggering agents include many anesthetic agents that have been labeled porphyrinogenic; see Table 1.
- Safe anesthetic management of patients with HCP demands understanding of this disease process.

Purpose

- This case report describes the pathophysiology and anesthetic management of a patient with hereditary coproporphyria (HCP).

Case Description

- A 63-year-old, 101 kg, 180 cm, male presented for a right parietal temporal craniotomy for a glioblastoma tumor resection after suffering frequent left sided falls at home and subsequent loss of consciousness.

Pre-Anesthetic Evaluation

- *Medical History:* coronary artery disease, carotid stenosis, tobacco use, gastroparesis, pemphigus vulgaris, schizophrenia, and HCP.
- *Surgical History:* cataract surgery and heart catheterization.
- *Current Medication Regimen:* metoprolol, vitamin C, amlodipine, labetalol, nicotine patch, levetiracetam, famotidine, dexamethasone, risperidone, clonazepam, benztropine, and aspirin.
- *Diagnostic Testing:* MRI diagnosed 7.5 cm right temporal lobe mass with a left midline shift of 7 mm, abnormal labs WBC 17.6 and glucose 151.

Intraoperative Anesthetic Management

- Pre-induction vital signs: pulse 81 in NSR, BP 125/78 mm Hg, SpO2 100%, RR 20, and temperature 35.1 ° C.
- General anesthetic induction: fentanyl 100 mcg IV, lidocaine 100 mg IV, propofol 100 mg IV, and succinylcholine 140 mg IV.
- 8.0 ETT placed followed by Isoflurane titrated to 0.5 MAC.
- Remifentanil and phenylephrine infusions.
- Arterial line and internal jugular central line placed.
- Patient placed in prone position with head in Mayfield Keep skull pins which were verified and secured by the surgeon.

Intraoperative Course

- Preoperatively patient calm, pleasantly confused and denied discomfort.
- No signs of acute attack of porphyria.

Postoperative Course

- Patient transported to neuro ICU and remained intubated on mechanical ventilator and fentanyl, propofol, and nicardipine infusions.

Pathophysiology and Manifestations

- Heme is a vital porphyrin to hemoglobin because it is required to transport O_2, remove CO_2, and biotransform essential enzymes such as CYP450; see Figure 2.
- The porphyrias, a group of metabolic disorders, each lack any 1 of the 8 enzymes in the heme synthetic pathway resulting in the accumulation of porphyrin and porphyrin precursors ALA and PBG, subsequently producing a form of porphyria; see Figure 1.
- HCP lacks CPO, the 6th enzyme in the heme biosynthesis pathway, which originates from a genetic mutation of the CPOX gene on chromosome 3; see Figure 3.
- *Manifestations:* acute abdominal pain, cutaneous lesions, neuropsychiatric abnormalities such as confusion, seizures, mood disturbance, hysteria, syncope, autonomic instability, peripheral neuropathy, sensory loss and ascending muscle weakness mimicking Guillain-Barre; see Figure 4.

Figure 1. Heme Synthesis Pathway

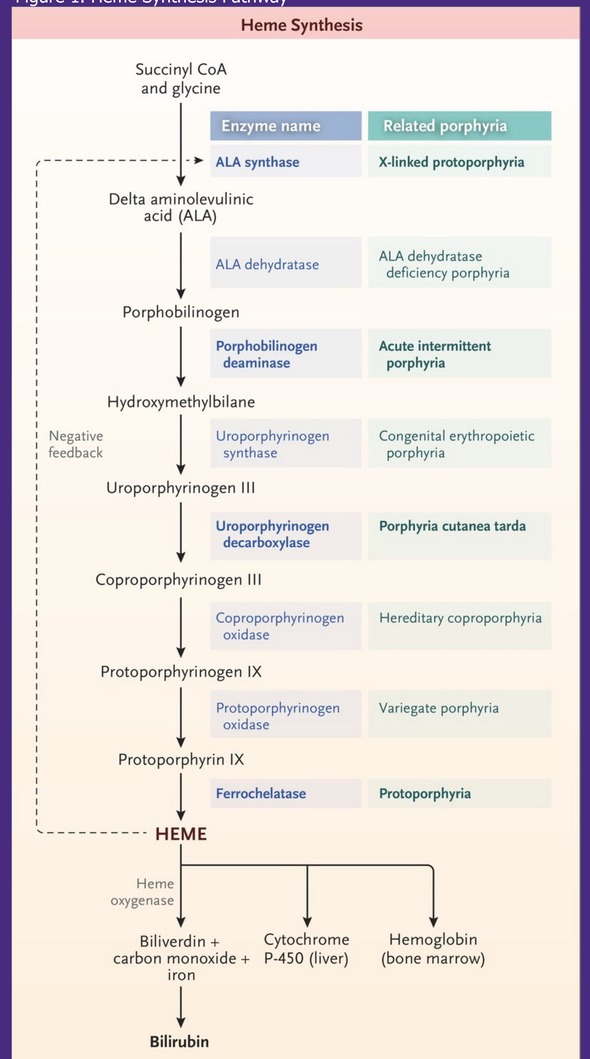

Figure 2. Hemoglobin Molecule

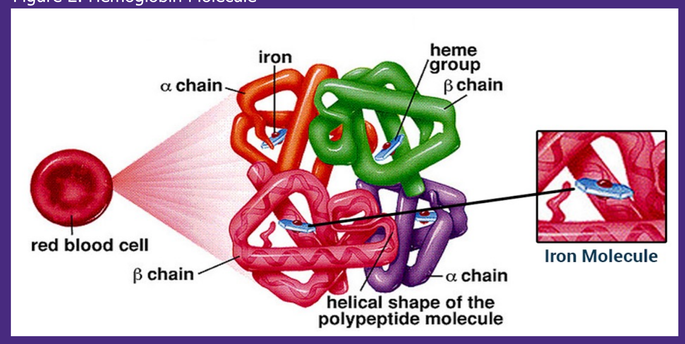

Figure 3. Location of CPOX Gene Mutation

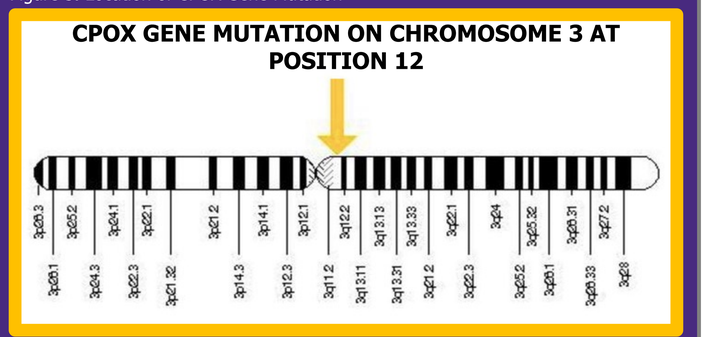

Figure 4. Apparent vs Nonapparent Symptoms

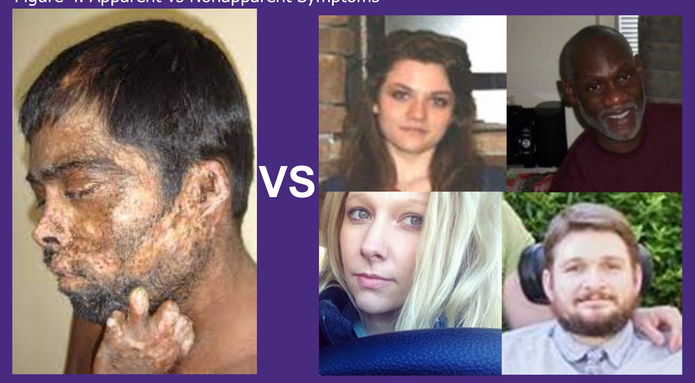

Table 1. Triggering Agents

Potential of Drugs to Provoke HCP Attacks

Safe Agents	Unsafe agents
•Propofol	•Barbiturates
•Nitrous Oxide	•Ketamine
•Volatile Agents	•Etomidate
•Depolarizing and Nondepolarizing NMB	•Decadron*
•Reversal Agents	•Calcium Channel Blockers*
•Antiemetics (excluding Reglan)*	•Ketorolac*

*majority consensus

Discussion

- The patient was at increased risk of an attack of acute porphyria due to PMH of HCP combined with the necessity to undergo general anesthesia.
- The decision to substitute the planned sevoflurane with isoflurane was an attempt to prevent an exacerbation of porphyria.
- The patient did not have any porphyrinogenic-related reactions to the anesthetic agents administered intraoperatively.

Key Points

- Identifying drugs as either safe or unsafe is critical.
- Anxiolysis with benzodiazepines is recommended.
- Safe anticonvulsant therapy includes levetiracetam, clonazepam, gabapentin, and/or vigabatrin for seizure prevention.
- Correction or prevention of hyponatremia and electrolyte imbalances is recommended.
- IV hydration with glucose containing fluids (not to exceed 300 g/day) to downregulate aminolaevulinic acid synthetase (ALAS) and to minimize caloric restriction and dehydration.
- General and regional anesthesia are both possible and equally efficacious if initiating factors are avoided.
- Arterial line for hemodynamic monitoring is recommended due to likelihood of autonomic dysfunction.
- If a severe attack is suspected, IV heme (Panhematin) should be administered expeditiously.

Case Critique

- Although the patient was not anxious or agitated preoperatively, administration of an anxiolytic to reduce stress, a known trigger of porphyria, is indicated.
- The patient received dexamethasone despite many studies claiming it to be unsafe.
- It is widely established that sevoflurane is safe.

Conclusions and Recommendations

- A thorough perioperative workup must be performed in order to prevent an acute attack of porphyria which can be life-threatening.
- Determination of safe vs unsafe anesthetic medications is key.
- No evidence suggests a general anesthetic is safer than a regional anesthetic.
- Further investigation of anesthetic management of the patient with HCP is required because most of the current clinical reports are anecdotal and/or outdated.
- Refer to the American Porphyria Foundation website for the most up-to-date information on porphyria and up-to-date drug database for healthcare professionals.

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