

Acute Intermittent Porphyria

Risk

- Prevalence: <200,000 cases of porphyria in USA, AIP: 5 to 10 in 100,000 worldwide.
- Highest in Northern Europeans.
- More commonly manifests in females, typically third to fourth decades of life.

Perioperative Risks

- Drugs and/or chemicals that induce heme containing hepatic CYP450 enzyme (e.g., barbiturates, estrogens, smoking, alcohol).
- Induction of ALA synthase enzyme by fever or fasting.
- Psychological stress.

Worry About

- Precipitation of acute crisis in periop period.

- Diagnosis of latent AIP requires high index of suspicion in pts with unexplained acute abdominal pain and neuropsychiatric manifestations.
- Potentially life threatening especially with delayed diagnosis.
- Once diagnosed, all first-degree relatives should be screened.

Overview

- One in eight inherited metabolic disorders of heme synthesis pathway is caused by mutations in the genes coding for each prospective enzyme in the pathway.
- Autosomal dominant with incomplete penetrance.
- Motor neuropathy, autonomic dysfunction, and psychiatric abnormalities.
- Pts may be encountered for acute and chronic pain management.

Etiology

- Gene mutation causing deficiency in PBG deaminase enzyme
- Accumulation of neurotoxic porphyrin precursors: ALA and PBG

Usual Treatment

- Avoid triggers of acute attack.
- Symptomatic treatment: paracetamol and opioids for pain, chlorpromazine and prochlorperazine for nausea and vomiting, propranolol for tachycardia and hypertension, and gabapentin for convulsions
- Oral/IV dextrose (carbohydrates)
- IV Hematin or Heme arginate (not FDA-approved)

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Autonomic neuropathy	Palpitation	Tachycardia Hypertension	ECG
RESP	Resp muscle weakness	Dyspnea	Difficult weaning after surgery	Peak expiratory flow rate Arterial blood gas (ABG)
GI	Enteric neuropathy	Severe poorly localized abdominal pain Nausea, vomiting, constipation Less commonly, diarrhea	Abdominal tenderness/rebound tenderness (uncommon)	X-ray may show mild ileus
GU	Neuropathic bladder dysfunction Accumulation of porphyrin precursors	Dysuria, hesitancy, urinary retention Dark or reddish brown urine	Bladder distension	Increased urine PBG and ALA -ve urine dipstick
ENDO	SIADH Electrolyte disturbances (hyponatremia, hypomagnesemia)		Seizures	Serum electrolytes Serum and urine osmolality Urinary Na
CNS	Neurotoxicity Psychiatric abnormalities	Anxiety Restlessness Insomnia	Seizures Depression Coma Delayed recovery after anesthesia	MRI brain: Reversible white matter densities resembling posterior reversible encephalopathy syndrome
PNS	Neuropathy (motor > sensory)		Motor: Weakness, begins proximally, UL > LL, quadriplegia, bulbar paralysis Sensory: Pain in ext/back, numbness, paresthesia	EMG Nerve conduction studies
ANS	Autonomic neuropathy		Postural hypotension Fever Sweating	

Key References: Herrick AL, McColl KE: Acute intermittent porphyria, *Best Pract Res Clin Gastroenterol* 19(2):235–249, 2005; Findley H, Philips A, Cole D, et al.: Porphyrias: implications for anaesthesia, critical care, and pain medicine, *Contin Educ Anaesth Crit Care Pain* 12(3):128–133, 2012.

Perioperative Implications

Preoperative Preparation

- Careful neurologic assessment: motor, sensory and autonomic dysfunction
- Care for withdrawal symptoms in pts on opioids for chronic pain
- Avoid triggers of acute attack:
 - Avoid prolonged fasting, administer oral/IV dextrose (300 g/day);
 - Sedation to avoid stress;
 - Identify unsafe drugs/chemicals.

Monitoring

- Standard monitoring
- Hgb/Hct
- Blood glucose
- Urine color, check urine for PBG/ALA
- Temperature

Airway

- Risk of aspiration

Preinduction/Induction

- Sedation: Midazolam, phenothiazines.

- Unsafe induction agents: Barbiturates, etomidate.
- Safe induction agents: Propofol, succinyl choline, all nondepolarizing muscle relaxants and opioids are generally safe.
- Care for BP and HRfluctuations.
- Regional anesthesia is not absolute contraindication; should be preceded by neurological assessment and documentation. Better avoided in acute crisis.
- Lidocaine, bupivacaine, and procaine are considered safe.

Maintenance

- Inhalational anesthetics are considered safe, incl NO
- Avoid anemia and hypoglycemia
- Normothermia

Extubation

- Evaluate consciousness to exclude neurotoxicity.
- Evaluate muscle power for possibility of ventilatory support.

Adjuvants

- Check websites for safe drug lists: <http://www.porphyrifoundation.com>, <http://porphyria.eu/>.

Postoperative Period

- Monitor for up to 5 days.
- Avoid metoclopramide as antiemetic, use chlorpromazine or ondansetron.
- Avoid diclofenac.
- Repeated detailed neurological assessment.
- Oral/IV dextrose to prevent hypoglycemia.

Anticipated Problems/Concerns

- Development of acute crisis:
 - Management: Withdraw triggers, pain control, oral/IV dextrose, IV hematin (3 mg/kg for 4 days in a large vein over 30 min or in central line), or IV heme arginate, to replenish heme pool and inhibit ALA synthase.
 - Peak expiratory flow rate for early detection of respiratory failure.
 - Monitor electrolytes and seizure activity.