

# Anesthesia for hemicolectomy in a known porphyric with cecal malignancy

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## ABSTRACT

Intraoperative management of a known acute intermittent porphyria patient is a challenge requiring awareness of factors, which trigger an acute crisis, clinical features of a porphyric attack, knowledge of safe pharmacologic intervention, and preparedness for reintubation and ventilatory support. The classical signs of a porphyric crisis such as pain abdomen, vomiting and neuropsychiatric symptoms are masked under general anesthesia and can be confused with postoperative pain and vomiting and postoperative cognitive dysfunction, especially for intra-abdominal surgeries. Eternal vigilance for onset of an acute crisis is imperative. After a crisis of acute intermittent porphyria, residual paresis may persist for years in the absence of further attacks.

**Key words:** *Acute intermittent porphyria, anesthesia, hemicolectomy*

## INTRODUCTION

The porphyrias are a group of autosomal dominant enzymatic defects of heme biosynthesis. The rate limiting step in heme synthesis is the condensation of succinyl CoA and glycine to form delta-amino-levulinic acid (ALA), catalyzed by the mitochondrial enzyme ALA synthetase.<sup>[1-4]</sup> Decreased negative feedback from heme contributes to the elevated baseline ALA synthetase activity characteristic of porphyrias. The manifestations of the disease are due to increased ALA synthetase activity, increased porphyrin accumulation in the tissues, or decreased heme production.<sup>[4-6]</sup>

The signs and symptoms of acute porphyric crisis are quite consistent: Severe abdominal pain, vomiting, anxiety, confusion, hallucinations, hysteria, psychosis, seizures, autonomic instability manifested by hypertension and tachycardia, dehydration, and electrolyte disturbances such as hyponatremia, hypomagnesemia, hypokalemia, and hypocalcemia, urine that darkens on standing and acute respiratory paralysis.<sup>[6-10]</sup> Most of the clinical features

subside within the time course of the acute crises, but residual paresis may persist for years in the absence of further attacks.<sup>[1]</sup>

## CASE REPORT

We report here the anesthetic management of hemicolectomy for cecal malignancy in a 46-year-old, 71 kg male patient, who had a history of 15 days hospitalization for acute intermittent porphyria (AIP), 11 years ago. The diagnosis of AIP had been earlier confirmed by elevated porphyrin levels in the urine and the presence of an R167Q mutation in the porphobilinogen (PBG) deaminase gene. Neurological examination revealed foot drop in the right lower limb, which was a sequel of the acute attack. Biochemical and hematological reports were now within normal limits.

The patient was reassured and premedicated with intravenous (IV) midazolam 1 mg. An IV infusion of 10% dextrose 1000 ml was given overnight. An exhaustive list of drugs documented or suspected of precipitating AIP and a list of safe drugs was prepared from currently available literature and placed in the operation theatre for ready reference. We utilized IV fentanyl 100 µg, IV morphine 4.5 mg and IV propofol 120 mg for induction of anesthesia. IV vecuronium 6 mg was the neuromuscular blocking agent injected and 60 s later when the peripheral nerve stimulator was switched on, the single second twitches had nearly disappeared. The trachea was intubated with a 7.5 mm ID, polyvinyl chloride cuffed orotracheal tube fixed at 22 cm after confirmation of

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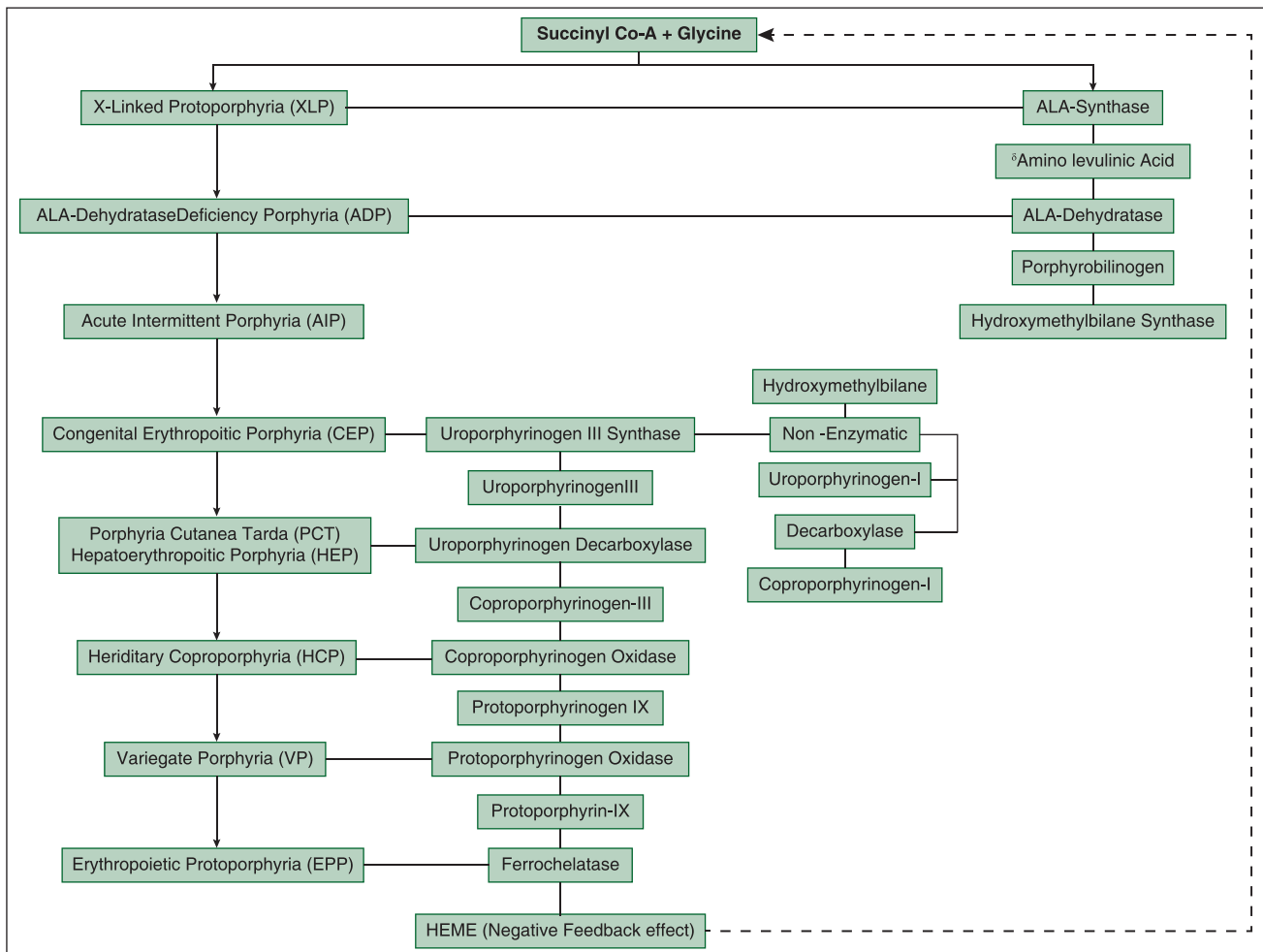
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placement by auscultation and capnography. A BIS-guided propofol infusion, desflurane in 66% air-oxygen mixture, peripheral nerve stimulator guided vecuronium infusion at 1 mg/h with two top-up boluses of 1 mg each were utilized for maintenance of anesthesia. The surgery lasted 2 h 30 min. The neuromuscular blockade was reversed with IV neostigmine 2.5 mg and IV glycopyrrolate 0.4 mg. The patient was extubated after he was seen to consistently generate a tidal volume of 450-500 ml for 15 min. He was given 3 mg morphine for pain at surgical site. After 20 min of extubation he became hysterical, complained of difficulty in breathing and developed stridor and had to be re-intubated with a 7.5 mm ID nasal endotracheal tube using awake fibreoptic intubation after 10% lignocaine spray on glottis and transtracheal block with 2 ml 4% lignocaine. We started a 10% dextrose infusion. The patient was extubated over bougie after 3h following full motor recovery. IV morphine 3 mg 6 hourly and IV paracetamol 1 g 12 hourly were utilized for postoperative pain relief. Normal colored urine was observed during hourly urine output monitoring throughout intraoperative and postoperative periods. The patient was discharged after 6 days.

**DISCUSSION**

Four types of hereditary porphyrias are classified as acute porphyrias (acute intermittent porphyria, variegate porphyria, hereditary coproporphyria, and 5-aminolaevulinic acid dehydratase deficiency) [Figure 1]. Enzymatic defects result in accumulation of porphyrin precursors (ALA and PBG) whose levels may be borderline normal in latent periods but increase to toxic levels during a porphyric crisis.<sup>[1,3]</sup>

Iatrogenic induction of ALA synthetase by triggering drugs (classically barbiturates) is the commonest precipitating factor of an acute porphyric crisis. Others include hypoglycemia, dehydration, infection, psychological stress, pregnancy, female sex hormones, folate deficiency, excessive alcohol intake, administration of specific drugs and repeated exposure to anesthetics.<sup>[3,5,6,10]</sup> Factors known to decrease synthetase activity include high carbohydrate loading, propranolol, and increased negative feedback from heme. This was the rationale behind using a 10% dextrose drip overnight. Many drugs cause porphyric crisis



**Figure 1:** Metabolic defects in porphyrias

[Table 1]. Most are hepatic enzyme inducers subjecting the patients to acute porphyric attacks by decreasing heme levels, thus decreasing negative feedback and thereby increasing ALA synthetase activity. We avoided giving any documented porphyrogenic drug and drugs dependent on liver for metabolism. Muscle relaxants reported as safe include vecuronium and atracurium but some steroids are considered unsafe in porphyria. Vecuronium and pancuronium share a steroid structure, but only the latter has been incriminated as unsafe based on animal model data.<sup>[1,2]</sup> Monitoring for the potential onset of porphyric crisis should be continued for up to 5 days, since onset may be delayed. The onset of crisis may be heralded by either neurologic signs or autonomic nervous system stimulation.<sup>[7]</sup> If anti-emetic therapy is indicated, metoclopramide should probably be avoided and hence, ondansetron was our choice.<sup>[6]</sup> Neurologic evaluation should focus on mental status and peripheral neuropathy.

Mechanisms of porphyric neuropathy include direct neurotoxicity of ALA (not PBG) by interaction with gamma-amino butyric acid receptor, altered tryptophan metabolism, or a neural respiratory haem dependent enzymatic deficiency in nerve cells<sup>[1,6]</sup> Axonal degeneration of peripheral and autonomic nerve fibers rather than demyelination seems to be responsible. If an acute crisis is suspected, attention to cranial dysfunction and bulbar symptoms may predict impending respiratory failure. Acute porphyric attack is known to cause acute respiratory failure.<sup>[4,5,7]</sup> Hence, we promptly reintubated the patient when he complained of inability to breathe and developed stridor. The classical signs of a porphyric crisis like pain abdomen, vomiting and neuropsychiatric symptoms are

masked under general anesthesia and can be confused with post-operative pain and vomiting and postoperative cognitive dysfunction. Haem arginate unfortunately cannot be used prophylactically, indeed too frequent use may, by inducing the enzyme haem oxygenase, induce its own catabolism with resultant loss of effect. A standard dose of 250 mg (5 ml) given daily for 4 days is recommended. Mix the haem arginate into 100 ml human albumin and infuse intravenously over 20 min.

Peripheral nerve stimulation at 40 mA done before extubating the patient for the second time showed twitches, which were of subnormal magnitude and the patient though awake complained only of slight discomfort. This was paradoxical and unexpected at 3h 30 min after giving the reversal agent. Polyneuropathy and painful flaccid paralysis of an acute crisis predominantly involve upper limbs, preferentially affecting the proximal musculature with occasional sensory involvement.<sup>[4]</sup> Residual paresis persists indefinitely.<sup>[1]</sup> This may partly explain the above paradox.

Acute porphyria bearers are recommended to wear identification at all times in case they suddenly deteriorate resulting in inability to explain about their condition and contraindicated drugs to health care professionals.

## CONCLUSION

Our experience suggests that fentanyl, propofol, vecuronium, lignocaine, desflurane, paracetamol, ranitidine and ondansetron are probably safe for IV use in acute intermittent porphyria. Meticulous neurological evaluation and documentation, 10% dextrose drip overnight and intraoperatively, avoidance of known porphyrogenic agents, keeping a list of safe and unsafe drugs at hand in the OT, keeping heme arginate injections at immediate disposal, alertness for bulbar symptoms like stridor and preparedness for reintubation and ventilatory support if required are important considerations in anesthetic management of a known porphyria patient. The patients should receive a special identification card and an up-to-date list of safe drugs.

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**Table 1: Safety of drugs in bearers of acute porphyria (adapted from [http://www.wmic.wales.nhs.uk/porphyria\\_info.php#resources\\_patients](http://www.wmic.wales.nhs.uk/porphyria_info.php#resources_patients) and American porphyria foundation)**

Safe analgesics/others	Safe anaesthetics	Contraindicated drugs
Alfentanyl	Atropine	Barbiturates
Aspirin	Bupivacaine	Ketamine
Buprenorphin	Diazepam	Primidone
Fentanyl	Desflurane	Phenytoin
Ibuprofen	Isoflurane	Valproic acid
Morphine	Lignocaine	Clonazepam
Paracetamol	Midazolam	Alcohol
Pethidine	Muscle relaxants	Estrogen
Tramadol	Neostigmine	Progesterone
Gabapentin	Nitrous oxide	Pyrazenamidine
Glucocorticoids	Prilocaine	Ergots
Insulin	Propofol	Rifampicin
Ranitidine	Remifentanyl	Sulphonamides
Penicillin	Suxamethonium	Griseofulvin
Betablockers	Chlorpromazine	Calcium channel blockers

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