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Ketamine Induction for Cesarean Section in a Patient with Acute Intermittent Porphyria and Achondroplastic Dwarfism

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Acute intermittent porphyria (AIP) is a rare inherited disorder that limits the pharmacologic agents available to the anesthetist. Pregnancy can be dangerous because it may precipitate an attack, and cesarean section *per se,* if needed, further limits the anesthetic options. Superimposing achondroplastic dwarfism constitutes a rare clinical entity that merits special anesthetic considerations.

REPORT OF A CASE

A 21-year-old 50-kg female, gravida 1 para 0, full-term achondroplastic dwarf with acute intermittent porphyria was admitted for elective cesarean section. Family history of AIP included the patient's mother, maternal uncle and aunt, and three sisters. The patient's uroporphyrinogen synthetase red blood cell level was 17.3 $nm \cdot ml^{-1} \cdot RBC \cdot hr^{-1}$ (Normal = 37.9 + 7.7 $nm \cdot ml^{-1} \cdot RBC \cdot hr^{-1}$). She denied having had symptoms of an acute attack of porphyria.

No preoperative medications were administered. Five per cent dextrose in lactated Ringer's solution was infused iv. General anesthesia was induced with ketamine 2 mg/kg iv, followed by succinylcholine 100 mg iv, endotracheal intubation, and controlled ventilation with 60% nitrous oxide and oxygen. A succinylcholine drip provided muscle relaxation. After delivery of the baby, meperidine 25 mg iv was given twice. Vital signs remained stable, with arterial blood pressure varying between 120/50 and 135/80 mmHg. After surgery, when succinylcholine and nitrous oxide were discontinued, spontaneous ventilation resumed and the trachea was extubated. The postoperative course was uneventful. Two months later no neurologic or psychiatric difficulties were evident.

The infant's APGAR scores after 1 and 5 min were 7 and 9, respectively. Uroporphyrinogen synthetase red blood cell level was normal, with retesting scheduled for 2 years later.

DISCUSSION

AIP is a rare disorder of red blood cell production (approximately 1 in 80,000) that is inherited in an autosomal dominant pattern with a variable phenotypic expression. Hepatic and erythroblastic porphyrin production are under separate genetic control, and porphyrias are classified according to the site of the defect. AIP is associated with a partial deficiency of hepatic uroporphyrinogen I synthetase, one of several enzymes involved in the biosynthesis of protoporphyrinogens and hemin in the liver, and is termed a hepatic porphyria. The resulting hemin deficit impairs the feedback inhibition of hemin on both mitochondrial aminolevulinic acid (ALA) synthetase, the initial enzyme in hemin synthesis, and globin polypeptide chain synthesis. Because ALA synthetase is derepressable particularly by lipid soluble compounds that induce cytochrome P450,[1] exposing patients with AIP to these agents results in markedly elevated ALA and porphobilinogen levels. These intermediate compounds are associated with the neuropsychiatric dysfunction of hepatic porphyrias.[2] The use of a dextrose solution is recommended, because fasting augments and glucose inhibits ALA synthetase induction.

Clinically, an attack of AIP may present with nonspecific abdominal pain, constipation, vomiting, hypertension, tachycardia, peripheral neuropathy, respiratory muscle paralysis, syndrome of inappropriate antidiuretic hormone secretion, seizures, depression, psychosis, or coma. There may be residual paresis after an attack.

The appropriate anesthetic management of AIP is controversial because of limited clinical experience. Because anesthetic induction with barbiturates, known inducers of cytochrome P450, may precipitate an attack and because cesarean section precludes narcotics before delivery, other methods were considered. Similarly, benzodiazepines should be considered potential precipitating agents.[2] Stove and Munson described a case report of diazepam-induced AIP attacks in 1979.[3] An inhalational induction is dangerous in a patient who has a "full stomach." There is theoretic objection to inhaled anesthetics, because they are, to varying degrees, metabolized by and induce the cytochrome P450 system. Parikh and Moore demonstrated augmented ALA synthetase activity in rats exposed to 2.25% enflurane for 2 hours per day for 4 days. However, similar administration of N_2O (80%) or halothane (1.5%) did not induce a significant change.[4] Documented clinical experience with halothane and enflurane is insufficient, although N_2O reportedly is safe.[1,5]

Lumbar regional anesthesia in achondroplastic dwarfs

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is dangerous because the adult achondroplast's spinal cord frequently fills the spinal canal.[6] However, Walts *et al.*,[7] while noting technical difficulty in performing subarachnoid or epidural anesthesia in eight achondroplastic dwarfs, did not have neurologic sequalae. However, they considered general anesthesia preferable because of the neurologic problems associated with achondroplasia.[7] Although the safe use of ketamine (2 mg/kg) for anesthetic induction in cesarean section has been established,[8] clinical experience with ketamine in AIP is limited. Rizk *et al.*[9] describe a patient with AIP who underwent induction of anesthesia with ketamine (4 mg/kg) twice within 1 week without neuropsychiatric sequelae. Experimental data are conflicting. Although ALA synthetase activity significantly increased in 17-day-old chick embryos injected with ketamine (5–15 μg),[10] studies in rats failed to demonstrate a change in activity of this enzyme after ketamine 20 mg/kg was administered ip.[11]

The use of barbiturates, narcotics, and possibly regional techniques were contraindicated in this patient. The sparse documentation of clinical experience with various anesthetics in AIP, ketamine, and N_2O with a succinylcholine drip was a reasonable and ultimately safe alternative.

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Total Spinal Blockade during Local Anesthesia of the Nasal Passages

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Total spinal anesthesia is a rare complication of properly performed spinal anesthesia. More commonly it is a complication of lumbar epidural or caudal anesthesia. On rare occasions, a total spinal block has occurred as a complication of stellate ganglion block, brachial plexus block, intercostal nerve block, lumbar paravertebral sympathetic nerve block,[1] or retrobulbar block. Recently, we have encountered a case of total spinal block resulting from injection of local anesthesia into the nasal passages.

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Key words: Anesthetics, local: cocaine, lidocaine. Anesthetic technique: infiltration, topical. Complications: total spinal.

Report of a Case

A 42-year-old woman was admitted with a diagnosis of chronic ethmoiditis. She had a persistent headache of 3 weeks' duration that was located laterally in the right orbit with radiation to the right ear. An intranasal anterior ethmoidectomy was scheduled to be performed under local anesthesia administered by the otolaryngologist.

Medical history revealed no previous systemic neurologic abnormalities. Anesthetic history included an abdominal hysterectomy and a mandibular resection performed under general anesthesia without complications. Current medications were limited to estrogen, which the patient had taken since her hysterectomy. She was noted to have an allergy to ampicillin.

On physical examination, pertinent positive physical findings were limited to examination of the nasal passages and paranasal sinuses. Tenderness to palpation was noted over the right frontal sinus. The right middle turbinate was noted to be compressing the lateral wall of the nose; thus obstructing the middle meatus. Local anesthesia of the middle meatus with topical application of 2% tetracaine and phenylephrine relieved her symptoms.

She was a normally developed woman (175 cm, 63 kg) without evidence of other physical abnormalities. No neurologic abnormalities were noted. Admission laboratory data, including hemogram, coagulation studies, urinalysis, roentgenogram of the chest and paranasal sinuses, and electrocardiogram, were normal.