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Anesthetic management of a patient with variegate porphyria

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Introduction

The porphyrias are a group of metabolic diseases that result from an autosomally inherited lack of functional enzymes involved in the synthesis of hemoglobin. Some porphyrias can cause life-threatening neurologic abnormalities. Certain drugs can induce δ-aminolevulinic acid (ALA) synthetase, thus exacerbating the disease process [1]. We report an anesthetic management strategy using propofol in a patient with variegate porphyria.

Case report

A 44-year-old woman (body weight 40 kg, height 143 cm) was scheduled for mastectomy. At age 29, she had experienced a severe acute attack of porphyria triggered by mefenamic acid and steroid involving muscle weakness in the extremities, muddled consciousness, extreme sweating, and respiratory deficiency. Urobilinogenuria had been detected and ALA had become markedly elevated. Her urinary ALA and coproporphyrin had been 35.7 mg·l^{-1} (normal <4 mg·l^{-1}) and 2973 μg·l^{-1} (normal <110 μg·l^{-1}), respectively. She had been treated with intravenous dextrose and insulin, but had taken more than 1 year to recover. Pre-operatively, her general health was good and electrocardiogram, chest X-ray, routine blood tests, and urine tests were normal. No neurological deficit was found.

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Premedication was with pethidine hydrochloride 35 mg intramuscularly 30 min before surgery. An epidural catheter was placed at the level of Th6/7. Induction was with atropine 0.3 mg, vecuronium 6 mg, fentanyl 0.1 mg and propofol 80 mg. The trachea was intubated, and anesthesia maintained with 66% nitrous oxide in oxygen, and a continuous intravenous infusion of fentanyl and propofol. Propofol was given intravenously at 40 ml·h^{-1} for the first 10 min, at 32 ml·h^{-1} for the next 10 min, and then adjusted as necessary. Fentanyl 0.1 mg was given intravenously at skin incision and continued at 40–60 μg·h^{-1}. Into the epidural space, 2 ml·h^{-1} of 0.25% bupivacaine and 25 μg·h^{-1} of fentanyl were infused continuously. The patient's intraoperative course was uneventful, there being no change in urine color, and she was extubated.

For the immediate postoperative period, the same dose of bupivacaine and fentanyl were continued epidurally, and there was no complaint of pain. On the second postoperative day, these were discontinued. On the third day, the patient complained of sweating, coldness of the extremities, and general stabbing pain. We started 3 ml·h^{-1} of 0.25% bupivacaine epidurally, and these symptoms disappeared. The epidural infusion was terminated on the fifth day. The patient was discharged without symptoms on the 15th day. Urinary porphyrins and their precursors were measured before the operation and for 2 weeks afterwards. Urinary levels of ALA and porphobilinogen (PBG) were normal (<4 mg·l^{-1} and <2 mg·l^{-1}, respectively). Uroporphyrin (normal <20 μg·l^{-1}) and coproporphyrin (normal <110 μg·l^{-1}) levels were slightly elevated on the day of the operation, but had recovered by the first postoperative day.

Discussion

In view of the increased urinary ALA and coproporphyrin during her acute attack, our patient was

thought to have hereditary coproporphyria or variegate porphyria [2]. After leaving the hospital, her fecal coproporphyrin and protoporphyrin levels were found to be elevated ($3300\,\mu g \cdot day^{-1}$ (normal $<640\,\mu g \cdot day^{-1}$), and $6200\,\mu g \cdot day^{-1}$ (normal $<1830\,\mu g \cdot day^{-1}$), respectively). Thus the diagnosis of variegate porphyria was reached [2]. Variegate porphyria is caused by a heterozygous deficiency in protoporphyrinogen oxidase activity, and is inherited in an autosomal dominant manner. In Japan, 40 cases have been reported [3].

In porphyria, a drug-induced acute attack may be life-threatening, and some of the commonly used anesthetic drugs are highly dangerous. An acute attack of porphyria may be prevented by identifying individuals at risk and avoiding the use of known porphyrinogenic drugs in porphyric patients [4]. As an induction agent, we chose to use propofol, this having been reported to be safe in porphyric patients [4]. As it has been suggested that pancuronium may be harmful [4], we used vecuronium as a muscle relaxant. Since the safety of inhalation anesthetics has not been established in porphyric patients [4], we maintained anesthesia with a continuous intravenous infusion of propofol and fentanyl.

In addition, we chose to employ a continuous epidural block with fentanyl and bupivacaine throughout the operation and postoperative period. Actually, epidural anesthesia in porphyric patients is controversial, because it is hard to distinguish the neuropathy of porphyria from complications of epidural anesthesia [5]. However, as the patient's earlier attack had been triggered by mefenamic acid, the analgesics that could be used postoperatively were extremely limited. To judge from her postoperative course, the epidural block was effective not only in relieving pain, but in preventing an attack. In fact, there have already been some reports that porphyria patients can be anesthetized uneventfully with an epidural block [6].

In our patient, with variegate porphyria, we adopted a strategy that involved: (a) avoiding porphyrinogenic drugs, (b) inducing and maintaining general anesthesia with propofol and fentanyl, and (c) employing a continuous epidural block with fentanyl and bupivacaine in the postoperative period. A severe attack did not occur during or after the operation.

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