Case Report

Anesthetic implication of tricuspid valve replacement in a patient with acute intermittent porphyria

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ABSTRACT

Facing a patient with acute intermittent porphyria (AIP), there is narrow safety margin which circumscribe all the therapeutic actions including choice of drugs. This would become even more complicated when it comes to a stressful and drug-dependent process like a cardiopulmonary bypass. According to author's researches, no specific AIP case of tricuspid valve (TV) replacement is reported recently. Furthermore, fast-track anesthesia was safely used in this 37-year-old male known the case of AIP, who was a candidate for TV replacement and removing the port catheter. The patient was extubated subsequently, only 3 h after entering the Intensive Care Unit.

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INTRODUCTION

Acute intermittent porphyria (AIP) is a rare metabolic disorder resulting from a partial deficiency of porphobilinogen deaminase, an enzyme in the heme biosynthetic pathway. Its inheritance is autosomal dominant.[1] A deficiency of porphobilinogen deaminase is not sufficient by its self to produce AIP, and other activating factors must also be present. These include some drugs, hormones, infection, injury, stress, dehydration, fasting, puberty, and alcohol. Of note, sometimes activating factors cannot be identified.

The disease is characterized by attacks that affect the visceral, peripheral, and central and autonomic nervous systems. Symptoms include abdominal pain, nausea and vomiting, hypertension, dark urine, tachycardia, electrolyte abnormalities, syndrome of inappropriate antidiuretic hormone, quadriplegia, respiratory paralysis, and seizures.[2]

It might be expected that the cytochrome-mediated metabolism and high lipid solubility of many anesthetics would make many of them porphyrinogenic, and anesthesia has certainly been implicated in the triggering of a number of severe porphyric reactions. Nevertheless, most porphyrics can relatively be anesthetized safely if the appropriate precautions are taken. The mainstay of safe anesthetic management of the porphyric patient depends on the detection of susceptible individuals, and the identification of potentially porphyrinogenic agents.

We have reported the case of a patient with AIP, affected by severe tricuspid regurgitation (TR)

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due to acute endocarditis, treated with tricuspid valve (TV) replacement and discussed the perioperative management of this disease. He was managed directly be the authors and written permission for publishing this paper has given by the patient, himself, after reviewing the case study.

CASE REPORT

A 37-year-old male was admitted with dyspnea, fever, weight loss, cough, sweating, paroxysmal nocturnal dyspnea, exertional dyspnea, orthopnea, and abdominal pain. He was diagnosed as having AIP 5 years ago. Moreover, he was an intravenous (IV) drug abuser that required a permanent indwelling venous catheter for his repeated attacks; so, he had a port since 9 months ago and received pethidine via that port during the attacks.

On admission, a chest computed tomography revealed multiple cavities in both lungs. A large mobile veg on anterior leaflet of tricuspid valve commissure (TVC) with severe TR was also demonstrated in his transthoracic echocardiography. After starting antibiotic therapy and removing the port, the patient underwent TV replacement.

In the day of surgery, prior to induction, all standard monitorings were applied; radial artery line and subclavian central venous (CV) line was also indwelled after induction.

Premedication was consisted of incremental doses of fentanyl and midazolam. We used propofol and atracurium for induction. Maintenance of anesthesia was done by propofol, atracurium, midazolam and fentanyl. Following sternotomy and heparinization, cardiopulmonary bypass (CPB) was initiated. The patient cooled to 32–34°C. Myocardial protection was provided by hypothermic antegrade blood cardioplegic. The TV was replaced. After 70 min of CPB, separation from CPB was achieved, and heparin was reversed by protamine. Rewarming and weaning from CPB was uneventful. Four units of packed cell were given during CPB; Hct was maintained about 30%.

Postoperatively, in Intensive Care Unit (ICU), the patient was extubated in 6 h. We started parenteral carbohydrate as dextrose 50% to prevent AIP attack, and the patient was encouraged to become per oral (PO) as soon as possible. Finally, he was discharged from ICU on day 2 after surgery. AB therapy was continued for several weeks.

By providing adequate IV crystalloid fluids, we had prevented any dehydration. The patient was cautiously observed for any symptoms of AIP attack. Throughout his stay in ICU, he had no symptoms such as abdominal pain, dark urine, and neurologic deficit.

DISCUSSION

Patients affected by AIP would face significant anesthetic challenges such as the attacks which can often be life-threatening.[3] The signs and symptoms of acute porphyric crisis are well-known and quite consistent; among the most frequent are severe abdominal pain, vomiting, anxiety, confusion, autonomic instability manifested by hypertension, urinary retention, paralytic ileus, restlessness, tremors, excessive sweating, fluctuating blood pressure and tachycardia, dehydration, and electrolyte disturbances such as hyponatremia, hypokalemia, and hypocalcemia.[4-6] Even, bradycardia and sudden cardiac arrest have been reported.[2] Persistent hypotension may require inotropic support.

From neurological aspect it should be a point that cranial nerves may be involved; however, motor weakness may be asymmetric and focal. Furthermore, progressive muscle weakness can lead to life-threatening respiratory and bulbar paralysis.[7]

With a peak age of presentation in the early 30's, the clinical manifestation of acute porphyria is highly scarce before puberty, and it is 4–5 times more common in females than in males.[8,9]

Cardiac surgery in patients with AIP requires careful perioperative management to prevent any exacerbation of the disease. Patients with this disease are at particular risk from general anesthesia because some IV induction agents may cause episodes of abdominal pain, neuropathy, or even fatal respiratory paralysis.

AIP triggering includes medications such as barbiturates, etomidate, and steroids, as well iron deficiency, smoking, low carbohydrate diets, dehydration, infection, fever, and psychological stress.[10,11] Although, regional and neuraxial anesthesia may cause difficulty differentiating between anesthesia and progressive porphyric neuropathy, they are not absolutely contraindicated.

Perhaps fast-track anesthesia might lead to exacerbation of AIP attacks by increasing the probability of stress

and anxiety, but this technique can be beneficial due to a diminution in ICU stay and decreasing the duration of hospitalization. This remark was not insisted until now; in this case, we adjusted our plan according to fast track technique and the patient was extubated, while he was totally alert and awake, 3 h after his entrance to ICU. Eager monitoring of patients hemodynamic is an unavoidable path to understand the sympathetic status.

The treatment of AIP includes withdrawal of the offending agent, hydration, IV glucose, propranolol, and IV heme.[12] Providing a CV pressure around 18 mmHg would be a good monitor for being assure about patient's hydration.

CPB is a specific problem, as there are different additional stresses existing, such as the stresses imposed by hypothermia, the hemolysis induced by the bypass pump, blood loss, and the large amount of pharmacological agents that need to be administered; these might all increase the risk of development of a porphyric crisis. However, there are several reports of the safe performance of cardiac surgery in porphyric patients provided that appropriate drug regimens are selected.[13-16] Particular attentions should be given to the presence of peripheral neuropathy and autonomic instability, as they will influence the anesthetic technique and also indicate active disease, with increased risk of acute crisis.

Classifying drugs as porphyria safe or unsafe is too simplistic; the duration of exposure and the absolute dose dictate whether an acute crisis would be triggered or not and how would the severity be like. Multiple confounding factors in the perioperative period mean that the trigger for a crisis may be unclear.

Propofol has been considered as a safe drug for both induction and maintenance of anesthesia in the patients with AIP.[17-19] Modern inhalation agents are generally considered safe in porphyric patients. Sevoflurane has been reported as a safe agent for both induction and maintenance of anesthesia. Safe use of isoflurane has also been reported;[20-22] therefore, it should probably be classified as safe, although further information needs to be obtained. Enflurane has been shown to induce porphyrin synthesis in animal models[20] but has been used safely in patients. Reports of a possible association of halothane with crises contradict both experimental and clinical experience.[23,24]

Preoperative starvation should be minimized; if a prolonged fast is unavoidable, a dextrose–saline infusion should be given during the preoperative period. In view of the frequency with which hyponatremia is encountered in acute attacks, the IV fluids containing dextrose alone should be avoided. Most (but not all) benzodiazepines commonly used for premedication like midazolam, are considered safe. The phenothiazines may have particular advantages.[25] Good anxiolysis has been recommended as advantageous. Where antacid administration is considered appropriate, sodium citrate may be given, and ranitidine may be considered. Cimetidine has been recommended for the treatment of acute porphyric crises since it may decrease heme consumption and inhibit aminolevulinic acid (ALA) synthesis activity.[10] The barbiturates are the archetypal inducers of ALA synthesis, and all barbiturates, including thiopental, must be considered unsafe. Although there are numerous reports of the safe use of thiopental in porphyric patients in the quiescent phase,[26] 7 out of 10 patients in acute porphyric crisis had their symptoms worsened following induction of anesthesia with thiopental.[27] Thus, although thiopental will not always precipitate a crisis, all barbiturates must be considered contraindicated in porphyric patients. Etomidate is potentially porphyrinogenic in animal models[17] at least one human porphyric crises has been reported after its use.[28] etomidate should probably be considered unsafe. Although there are some reports showing ketamine's potentiality in triggering AIP crisis,[24] it might be safe because it has been used safely in quiescent AIP.[24,29,30] Succinylcholine has been used for many years and has been proven to be safe, as has tubocurarine.[31] Though both pancuronium and alcuronium have been classified as unsafe by some authors, they have been widely used by many anesthetists without harm. Atracurium[21,22,32] and vecuronium[33] have been used safely in small numbers of patients despite some experimental evidence for porphyrinogenicity. We safely used atracurium in the current patient. Morphine and its analogues (including codeine) are of proven safety, and fentanyl has been shown to be safe both in chick embryo culture models and in clinical use. Alfentanil has also been used frequently with no reported complications. More recently, fentanyl[16] and sufentanil[15] have been used as a major component, in combination with isoflurane and atracurium, in open heart surgery without a significant problem.[21] Cardiac surgical reports also refer to the safe use of heparin. Pethidine (meperidine) has a proven track record of safety despite a single case report implicating

it in a porphyric attack.[34] There is evidence both for[35] and against[36] the porphyrinogenicity of pentazocine in experimental systems.[37] Of the nonopiate analgesics, aspirin, acetaminophen, indomethacin and naproxen have proven safe.

However, CPB is a specific problem,[13-16] we used it uneventfully. Blood loss, with its consequent increase in heme demand by the bone marrow, does not appear to stress the heme synthetic pathway sufficiently to provoke a porphyric crisis.[38]

CONCLUSION

It can be told that although there are different educational sources which safety of the drugs in AIP can be checked, utilizing a specific drug regimen can be sophisticated; because the various interaction between drugs can lead to a catastrophic income. In this case, we successfully used fentanyl in combination with propofol, midazolam, and atracurium with no disadvantage.

On-pump surgery method was used uneventfully for this patient with avoiding deep hypothermia. Furthermore, the feasibility of fast-track anesthesia usage as a safe anesthesia technique and plan, in this case, is proved.

The patient was discharged from ICU without any complication and therefore, the safety of the proper approach for TV replacement was accepted.

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Conflicts of interest

There are no conflicts of interest.

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