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GENERAL ANAESTHESIA IN ACUTE INTERMITTENT PORPHYRIA

ABSTRACT

Acute intermittent porphyria (AIP) is caused by the deficiency of porphobilinogen deaminase, a haem synthesis enzyme, giving rise to crises characterized by abdominal pain, tachyarrythmias and psychiatric features[1-3]. Anaesthesia in AIP is challenging because it has to avoid precipitating an attack[1,3]. We report a case of a lady with AIP who underwent total abdominal hysterctomy whose anaesthesia was uneventful.

INTRODUCTION

Acute intermittent porphyria (AIP) is a type of acute porphyria caused by the deficiency of porphobilinogen deaminase, an enzyme involved in haem synthesis[1]. It may give rise to acute crises characterized by severe abdominal pain (but no signs of peritonism), muscle weakness, tachyarrythmias and psychiatric features[1-3]. Administration of anaesthesia may be challenging in that it requires a detailed preoperative assessment and a careful selection of safe drugs in order to avoid the precipitation of an attack during an already physiologically-stressful time[1,3]. We here present the case of a lady with known AIP who underwent major gynaecological surgery and whose anaesthesia was uneventful.

CASE REPORT

A 42 year old female, a known case of AIP, was scheduled for elective total abdominal hysterectomy with conservation of the ovaries. She was reviewed at the preoperative assessment clinic two weeks before the operation. She had been diagnosed with AIP at 14 years and had been in remission for the previous seven years. Other than this she had no other medical co-morbidities, was on no regular medications and had no known allergies. Physical examination was unremarkable. There were no indications of a difficult intubation. Preoperative blood tests (full blood count, renal profile and coagulation screen) were within normal limits. A chest radiograph was clear and an electrocardiogram was in sinus rhythm.

The patient was admitted a day before the surgery, was requested to refrain from any oral intake for eight hours prior the procedure and was placed first on the operating list. She was premedicated with 2mg of midazolam on arrival to the anaesthetic suite and an epidural catheter was inserted at L3/L4 for intra- and postoperative pain control. Anaesthesia was induced using 180mg of propofol and 100mcg of fentanyl and maintained using desflurane, oxygen and medical air. Muscle relaxation was achieved using 30mg of atracurium. The patient was intubated and mechanically ventilated with a target $ETCO_2$ of 30 to 35mmHg.

Intraoperatively, she was administered intravenous paracetamol (1g) and ondansetron (4mg) and two boluses of bupivacaine (12.5mg) with fentanyl (12.5mcg) epidurally. The fluid regime involved 2L of Hartmann's solutions and 400mL of 10% dextrose. Monitoring was non-invasive and included blood pressure readings, pulse oximetry, cardiac rhythm and capnography. She was mildly hypotensive for the first half an hour from induction, with the lowest recorded blood pressure value of 70/40, but this normalized with two phenylephrine boluses of 100mcg each.

Arterial blood gases and electrolyte measurement taken one hour into the surgery revealed a normal acid-base status but a potassium of 3.13mmol/L and a glucose of 16.8mmol/L. Potassium was supplemented to the Hartmann's solution (5mL of 20% KCl in 1L of Hartmann's) and the 10% dextrose was stopped.

The operation was completed successfully and emergence from anaesthesia was routine. In the recovery area, the patient was administered 12.5mg of prochlorperazine intramuscularly and another two boluses of epidural bupivacaine and fentanyl. A second blood test showed a potassium of 3.51mmol/L and a glucose of 8mmol/L. She was transferred to the ward once she was fully conscious and with the pain controlled.

The postoperative period was without any complications. The fluid prescription was of 1L of 5% dextrose and 2L of Hartmann's (with potassium added accordingly) per day.

PORPHYRIAS ARISE FROM ENZYME DEFICIENCIES IN HAEM BIOSYNTHESIS RESULTING IN A PARTIAL BLOCK OF THE CASCADE AND THE ACCUMULATION OF THE PORPHYRINS

Oral intake was started six hours after the surgery and the intravenous infusion was discontinued once this was re-established. The epidural was removed after 24 hours because of the patient's concern over a moderate sensory deficit in the right upper thigh. Analgesia was then achieved with regular intravenous paracetamol and as required, intramuscular pethidine.

She was discharged after four nights in hospital.

DISCUSSION

PORPHYRIAS

Porphyrias are diseases of haem synthesis specifically involving the constitutent porphyrins. Porphyrins are cyclic molecules capable of forming complexes with several metals such as iron. The combination with the latter allows for the formation of haem and consequently of essential structures such as haemoglobin, myoglobin and the cytochromes[1]. Haem is procuded by a cascade of enzyme-mediated reactions principally under the control of aminolevulinic acid (ALA) synthetase which in turn depends on the level of haem in a negative feedback mechanism[1,2].

Porphyrias arise from enzyme deficiencies in haem biosynthesis resulting in a partial block of the cascade and the accumulation of the porphyrins[1,3]. They can be classified either by the site of porphyrin overproduction (hepatic or eythropoietic) or in terms of presentation (acute or non-acute). The latter is the most useful and it includes four types of porphyrias: acute intermittent, variegate, hereditary coproporphyria and plumboporphyria[1,2]. They are commoner in women and in the third and fourth decades of life[1].

AIP is the commonest of the acute forms and results from low levels of the porphobilinogen deaminase enzyme encoded on chromosome 11q24. It is inherited in an autosomal dominant fashion with incomplete penetrance[2,4]. Patients have a good prognosis once diagnosed, however, AIP gives rise to the severest presentation and is the most likely to be fatal in an acute attack[1,2]. Such an event is precipitated by an increase in the demand for the haem molecule and this typically occurs with the activation of the hepatic cytochrome P450 in starvation, dehydration, infection, hormone fluctuations and the administration of drugs which require this enzyme for their metabolism[1,3]. Patients thus have inadequate haem production, increased ALA synthetase activity and a widespread build-up of porphyrins[2].

An acute event varies from a mild attack to a life-threatening neurovisceral crisis. The commonest feature is severe abdominal pain with little or no clinical signs and is accompanied by nausea, vomiting and occasionally diarrhoea. There may be muscle weakness (proximal more than distal, and in upper limbs rather than lower) which may progress to quadriparesis and respiratory failure. Cardiovascular features include tachycardia, arrhythmias and hypertension and these are characteristic of autonomic disturbance. Psychiatric problems are also intimated and these range from mood disturbance and confusion to full-blown psychosis[1-3].

Diagnosis of AIP requires the detection of increased ALA, porphyrins and their precursors (particularly porphobilinogen) in urine[1].

AIP AND ANAESTHESIA

AIP represents an anaesthetic challenge because of the careful selection of drugs necessary[1,2]. Certain agents in routine use, such as thiopentone, sevoflurane, dexamethasone, non-steroidals and ephedrine are described as unsafe in AIP and should be avoided[3].

We induced anaesthesia with drugs that have long been listed as safe in porphyric patients (propofol and fentanyl), but maintained it with desflurane which, although its use in AIP has been documented for some time, has been included in the safe drugs list for porphyrias only recently[5,6]. This case thus further exemplifies the safety of desflurane in AIP.

We administered ondansetron and prochlorperazine as antiemetics and established analgesia with intravenous paracetamol and epidural bupivacaine and fetanyl. Vasopressor support was provided using phenylephrine, which is metabolised by the liver monamine oxidase[7]. Ephedrine was avoided since it induces ALA synthetase and cytochrome P450 and thus its use risks precipitating an AIP attack[8].

This case also highlights the importance of close monitoring of the patient's intraoperative metabolic status. Earlier and more frequent blood analysis could have allowed for tighter glycaemic and electrolyte control. This is essential to minimize the physiological stressors associated with surgery, and should also include the shortening of the preoperative starving period and the use of dextrose in intravenous infusion regimes[3].

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