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Case Report

Acute intermittent porphyria and pregnancy: an obstetric challenge

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ABSTRACT

Acute intermittent porphyria is a rare autosomal dominant disease caused by a mutation in the gene coding for the porphobilinogen deaminase enzymes in heme biosynthesis. The disease manifests as acute attacks of neuropsychiatric dysfunction and neurovisceral manifestations presenting as acute abdomen. In pregnancy, 54% patient has exacerbation of attacks in the form of seizures and acute abdomen occurs due to hormonal changes. Prevalence of acute intermittent porphyria is 1-2/200000 in general. Here we report a case of 36 year old women, G4P1L2A2 presenting at 10+4 weeks of gestation requesting pregnancy termination. Patient was diagnosed as case of acute intermittent porphyria with porphyric polyneuropathy 6 months back. At that time her main symptoms were acute pain abdomen with numbness and weakness in all four limbs. Her urinary porphobilinogen and 5 ALA raised. Her CECT of brain and nerve conduction studies were normal. Since then she is on Tablet Gabapentin 300 mg H.S. She underwent successful pregnancy termination by suction and evacuation under spinal anesthesia and she refused for copper-T insertion. Only safe drugs were used for procedure and she was discharged with advice of barrier contraception.

Keywords: Porphyria, Medical termination, Pregnancy

INTRODUCTION

Acute intermittent porphyria is a rare autosomal dominant disorder associated with deficiency of enzymes involved in the heme biosynthesis pathway; Commonest is the mutation in the gene coding for the porphobilinogen deaminase enzyme. Prevalence of acute intermittent porphyria is 1-2/2 lakhs person in general. Acute intermittent porphyria (AIP) is most severe form of the disease with symptoms of neuropsychiatric and gastrointestinal manifestations such as acute pain abdomen, vomiting, peripheral neuropathy (motor, autonomic, sensory), hypertension, depression, psychosis, seizures. The association of acute intermittent porphyria with pregnancy is rare. Exacerbation of acute attacks usually in the form of seizures and acute abdomen occur due to hormonal changes. Complications of AIP in pregnancy are not fully known and abortion, preterm

delivery, preeclampsia and perinatal death are reported in literature.

CASE REPORT

A 36 year old female with G₅P₂L₂A₂ presented at 10+4 weeks of gestation as a diagnosed case of acute intermittent porphyria with porphyric neuropathy, requesting for termination of pregnancy. She was asymptomatic at the time of admission.

Patient had first episode of acute abdomen and neuropathy 8 years back. She had 2nd similar episode 6 months back, when she was hospitalized for work up. All her routine investigation was normal; CT scan, MRI, and nerve condition studies were normal. Urinary porphobilinogen (PBG) and 5-aminolevulinic acid (ALA) were raised, which were diagnostic of acute porphyria.

Patient was managed symptomatically with dietary precautions; avoid precipitating factors and medication gabapentin and thiamine.

On admission this time, her general physical and pelvic examination was normal. Per vaginal examination revealed the uterus to be anteverted, 10-12 weeks size. Patient was planned for surgical evacuation under spinal anesthesia. Preoperatively 5% dextrose was started to prevent hypoglycemia. Injection morphine and propofol were used intraoperatively. She received medications augmentin, pantoprazole, and paracetamol according to drug safety list. Patient was discharged on third postoperative day in satisfactory condition.

DISCUSSION

AIP mainly affects nervous and gastrointestinal systems; autonomic disturbances are also common. Patients with frequent attacks can develop chronic neuropathic pain due to axonal nerve deterioration. Depression and seizure often accompany the disease and treated symptomatically.

Porphyria may worsen in majority of women during pregnancy. 54% of women with the disease had an acute attack during pregnancy or puerperium.² The female sex hormones, especially docosahexaenoic acid (DHA), which are increased in pregnancy, are known inducers of haem synthesis. The triggering factors responsible for acute attack are hyperemesis gravidarum, infections, hormones, starvation, medication, malnutrition etc.

The maternal and fetal prognosis is considered poor due to high morbidity and mortality. Pregnant patients with acute intermittent porphyria have higher incidence of acute attacks (24-95%), spontaneous abortion (6-12%), hypertension (16%), maternal mortality rate (2-40%), low birth weight infants and increased perinatal mortality (2-42%).^{1,3}

Diagnosis is by porphyrins metabolites in urine. During acute phase, color of urine may turn red or port wine due to porphyrins present in urine. The following metabolites are measured: delta-aminolevulinic acid (normal <50 mg/24 hour), porphobilinogen (normal <50 mg/24 hour) and total porphyrins (normal 15-300 mg/per day)³.

Treatment

Mild attack is managed symptomatically. A high carbohydrate diet (more than 400 gm/day), 10% glucose infusion, increased calorie intake, fluid replacement in mild acute phase can decrease porphyrin precursor excretion. For severe attacks, specific treatment of choice is intravenous infusion of heme arginate/ hemeatin, 3mg/kg/24 hour for 4 days in acute phase.⁴ This action is likely due to the inhibition of delta-aminolevulinic acid synthetase, the enzyme which limits the rate of the porphyrin/heme biosynthetic pathway. For abdominal

pain phenothiazines can be used. Critical monitoring of vitals, intake, output, fluid and electrolyte balance is essential. Porphyrigenic drugs should be avoided and infections should be treated.

Contraceptives of choice are barrier methods / Cu-IUCD. Following is the list of drugs which should/ should not be used in porphyria.⁵

Table 1: List of Potentially safe and unsafe drugs used in porphyria.

Potentially safe drugs	Potentially unsafe
<ul style="list-style-type: none"> • Oxytocin, • Dinoprostone, • Carboprost • Cephalosporins • Amikacin, Augmentin, • Amoxicillin, Tazopip • Gabapentin • Glucocorticoids • Insulin, Eltroxin, • Trenexamic acid • Narcotic analgesic, • Diclofenec, Tramadol • Propranolol, • Paracetamol • Vitamins, Vaccines, • Metformin 	<ul style="list-style-type: none"> • Steroids • Frusemide • Methergin • Estrogens • OCP • Erythromycin • Hydralazine • Methyl dopa, • Nifedepine • Barbiturates • Mifepristone and • Misoprostol

CONCLUSION

Acute attacks of porphyria are increased during pregnancy and carry high maternal and fetal mortality. It is important to prevent acute attack by avoiding precipitating factors including drugs. Minor procedure like medical termination of pregnancy can be life threatening in porphyria; hence watchful management and avoidance of unwanted pregnancy is desirable.

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