

## CASE REPORT

doi: 10.5455/medarch.2020.74.153-155

MED ARCH. 2020 APR; 74(2): 153-155

RECEIVED: JAN 12, 2020019 | ACCEPTED: FEB 12, 2020

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# Uncontrolled Acute Intermittent Porphyrria as a Cause of Spontaneous Abortion

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## ABSTRACT

**Introduction:** The association of acute intermittent porphyria (AIP) with pregnancy and as a cause of spontaneous abortion is rare. **Aim:** To show a case of AIP known before pregnancy in a patient who had a spontaneous abortion. **Case report:** A gynecologist examined 26-year-old patient in the 8th week of gestation, due to initial spontaneous abortion, abdominal pain, constipation, muscle weakness, vomiting and dark colour of urine. Her therapy was dydrogesterone. In consultation with an anesthesiologist, a short intravenous anesthesia, vacuum aspiration, and curettage were performed. During hospitalization, the patient ceased to take harmful drugs and she was given haemarginate, glucose and symptomatic drugs, and she recovered completely. **Conclusion:** Treatment of threatened spontaneous abortion in AIP remains the subject of dilemma and controversy, and future research is needed.

**Keywords:** Porphyrrias, Abortion, Spontaneous, Contraceptives, Oral, Hormonal.

## 1. INTRODUCTION

Acute intermittent porphyria (AIP) is a rare autosomal dominant metabolic disease caused by a mutation in the gene for the porphobilinogen deaminase enzyme in the haem biosynthesis (1).

It is characterized by increased urinary excretion of the porphyrin precursors: delta-aminolevulinic acid and porphobilinogen (1). The attack of the disease is caused by many endogenous and exogenous factors such as "porphyrogene" drugs, pregnancy or menstruation, hyperemesis gravidarum, hormones, dietary changes, starvation, alcohol abuse, infectious diseases and surgery which all could trigger the appearance of symptoms (2).

Symptoms include attacks of abdominal pain, motor and/or sensory polyneuropathy, autonomic nervous system dysfunction, and electrolyte imbalances such as hyponatraemia, mental changes, and seizures (1). Pregnancy represents an essential risk factor for exacerbations in patients suffering from AIP (3).

The association of AIP with pregnancy and as a cause of spontaneous abortion is rare. We hereby present this case because of its rarity and limited gynecological and obstetrical experience of this disorder.

## 2. AIM

The purpose of this article is to show a case of AIP known before pregnancy in a patient who had a spontaneous abortion.

## 3. CASE REPORT

A gynecologist examined 26-year-old patient in the 8th week of gestation, due to initial spontaneous abortion, abdominal pain, constipation, muscle weakness, vomiting and dark colour of urine. Previously, she had had a seizure attack at home. Her therapy was dydrogesterone 10 mg, three times per day, during two weeks. In her personal history she stated to have had a porphyria. The last acute attack happened 7 years before the spontaneous abortion, and she did not have a checkup in that period.

In consultation with an anesthesiologist, in a short intravenous anesthesia, vacuum aspiration, and curettage were performed. The patient regained consciousness immediately after the intervention and reached full orientation and cooperativeness within few minutes. The post-intervention period remained uneventful and the neurological and psychological symptoms returned to the pre-exacerbation status.

In laboratory findings porphyrin derivatives (delta aminolevulinic acid 7.76 mg / dU- (reference range

1.5-7.5) and porphobilinogen 16.84 mg / dU- (reference range 0-3.4) were elevated. The therapy of glucose solution was administrated after which the patient's condition stabilized. Porphyria markers decreased within the next four weeks.

Seven years ago, the patient was admitted due to vomiting, severe intermittent pain in the abdomen, frequent urination, blood in the urine, and elevated body temperature. The last four months the patient was on oral contraceptives (0.035 mg ethinyl estradiol and 2.0 mg cyproteronacetat) due to irregular menstrual cycles. During hospitalization, at the time of the first day of menstruation, the patient developed grand mal seizures and expressed agitation. Seizures reached the epileptic status. Epileptic status cannot be ceased by maximal dose of diazepam, but only short intravenous anesthesia (midazolam maleate).

The patient was in a state of high psychomotor agitation after the epileptic status. The brain CT pointed at the left parietal paramedian hypodense area 16 mm in diameter. The MRI of the brain described the bilateral symmetric lesions of cortico-subcortical distribution, parieto occipital and frontal, which according to MRI characteristics primarily refer to posterior reversible encephalopathy within the metabolic disorder. In laboratory findings, pronounced hyponatremia, hypokalemia, hypomagnesemia, and hypocalcaemia were verified. Biochemical was proven of AIP, high positive variability of total porphyrins (700 µg / dU- reference interval <220), uroporphyrin (185 mg / dU), copro-porphyrin (515 mg / dU), delta amino levulinic acid (19.50 mg / dU) and porphobilinogen (98 mg / dU)). During hospitalization, the patient ceased to take harmful drugs and she was given haem arginate, glucose and symptomatic drugs, and she recovered completely.

## 4. DISCUSSION

### Gynecological issues

The first attack in our patient was most probably provoked by taking hormonal contraception. The progesterone and estrogen levels modified heme biosynthesis in subjects with AIP during menstrual cycle. Increased levels of progesterone were considered more important than estrogen in precipitating AIP attacks (2, 4). The clinical evidence suggests that hormonal oral contraceptives can lead to a manifestation of AIP in 25% of the women with AIP, in most cases can lead to their first attack (2). If, for any reason, e.g. irregular menstrual bleeding or threatened spontaneous abortion, oral hormonal contraceptives or gestagens are used, monitoring of porphyrin precursor levels is recommended during the first month, in order to be able to interrupt the treatment should it increase concentrations (2, 4). The AIP gene carriers are advised to refrain from using oral contraceptives, in line with European recommendations (4). AIP is usually manifested in adult women, which means that it is seldom developed before puberty and after menopause the frequency of attacks declines (4).

### Obstetric issues

The second attack of porphyria in our patient was provoked most likely by taking of dydrogesterone, which had been given as a therapy against a threatening spontaneous abortion. Spontaneous abortions are most likely caused by uncontrolled AIP. AIP is mainly presented by acute attacks, especially during the first trimester of pregnancy, like in our patient (3, 5). Pregnancy in women with AIP is associated with higher rates of spontaneous abortion (3, 4). An especially challenging problem is in labor management, because methergine is contraindicated in patients with AIP (1, 3). There are only limited reports supporting the use of hemin during pregnancy, but the experience indicates that the use of hemin during pregnancy is safe (1, 3). An acute attack during pregnancy does not seem to have a detrimental effect on the baby (3, 5). Despite the fact that pregnancy in women suffering from AIP is related to higher rates of morbidity and complications, closely monitoring throughout the porphyric pregnancy could ensure a good outcome (1, 3). There is no consistent guidance available for the pregnancy. The current expert consensus is that asymptomatic women with an AIP should begin with pregnancy without any restriction. In symptomatic patients, the current consensus is to avoid getting pregnant until 1 year after their last acute porphyria attack (6, 7).

### Anaesthesiological considerations

Patients with AIP are at particular risk from general anaesthesia as most of the intravenous agents including barbiturates and volatile agents are contraindicated. Asymptomatic patients can benefit from local and regional anesthesia with bupivacaine for both labour analgesia and caesarean section (8, 9), but for symptomatic patients, or patients in crisis, we should rather choose general anaesthesia for caesarean section. Several clinical reports suggest that the hypnotic agent of choice for both induction and maintenance of such anaesthesia is propofol (8, 9). In our case short intravenous anaesthesia was induced with a bolus of propofol, alfentanil and diazepam.

AIP may also trigger posterior reversible encephalopathy syndrome (PRES), a rare condition that is characterized by acute neurological symptoms, like in our case. The clinical and radiological symptoms usually disappear through the elimination of PRES-triggering factors and appropriate treatment (10).

## 5. CONCLUSION

Treatment of threatened spontaneous abortion in case of AIP remains the subject of dilemma and controversy, and future research is needed.

- **Declaration of patient consent:** The authors certify that they have obtained all appropriate patient consent forms.
- **Authors contribution:** All authors were included in all steps of preparation this article. Final proof reading was made by the first author.
- **Conflict of interest:** None declared.
- **Financial support and sponsorship:** Nil.

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