We, herein, present an unusual case of porphyria diagnosed during the puerperium period in our health care service.

METHODS

Systematic Medline, PubMed, Cochrane, and upToDate search were done based on the terms pregnancy, puerperium, porphyria, acute crisis during the last five years. We then took the seven most relevant articles according to the qualification of the paper where it was published.

CLINICAL CASE

A 34 year old Caucasian woman presented intense abdominal pain during immediate puerperium.

Family background: of no interest

Personal background: allergic to penicillin, pantomime, and aspirin. The patient is reportedly an ex
smoker (ten cigarettes per day). Operated for meningo- 
gioplasty and uses a prosthetic eyeball, secondary to 
destruction during the M-11 terrorist attack in Madrid, 
Spain. She received psychiatric treatment for post-
traumatic stress syndrome.

In July 2008, the patient attended emergency room 
consultation for abdominal pain and also located in the 
episiotomy. Pain did not respond to pain killers 
previously prescribed on two occasions. Physical exa-
mination revealed a slight indurated episiotomy scar 
with no signs of infection or hematoma. All tests, 
including blood count, vital constants, and gynecological 
ultrasound, were normal. We decided on hospital 
admission in our service with the following diagnosis: 
incipient episiotomy infection and treated the patient 
with antibiotics and pain killers.

During the hospital stay, the patient did not respond 
to pain killers and was evaluated by psychiatric and 
anesthesiology services. She was finally diagnosed 
with adjustment disorder with anxiety and depression 
features.

Four days later, she was admitted to the intensive 
care unit after having three episodes of generalized 
seizures and was treated with phenytoin, midazolam, 
and manitol after dismissing brain damage and menin-
gitis. The patient was diagnosed with Recurrent Seizures 
and readmitted to the hospital ward.

During hospitalization, levels of TSH, ACTH, LF, 
FSH, thyroxine, and cortisol were determined to dismiss 
Sheehan syndrome; all levels were reported normal. 
CT scan was performed because of abdominal-
pelvic constipation objecting feces up to rectum-sigma 
union and distended intestinal bowel loops.

Finally, she began to present a progressive lethargic 
state with disorientation in time related to severe 
hyponatremia (109.8 mmol/l). She was then readmitted 
to the ICU, proposing Acute Neurovisceral Porphyria 
crisis demonstrated with the following values of 
porphyrins in urine.

ALAs: 40.8 mg/24 h (<7 mg/per day) 
PBG: 30.8 mg/24 h (<2 mg/per day) 
Total porphyrins (uro/copro) 4424 mg/24 h 
(15-300 mg/per day) 
Copro-porphyrins 3920mg/24 h (<250) 
Uro-porphyrins 504 (<50)

With these results, we started treatment with 
intravenous infusion of heme alginate, 150 mg/24 h 
during four days. With non-established porphyria and 
given the clinical stability, the patient was discharged 
from the hospital for future follow up.

COMMENTS

Porphyrias are a variety of disorders, inherited or 
not, involving the activity of enzymes involved in the 
synthesis of the heme group and other hemoproteins. 
As a consequence of its deficiency, intermediate toxic 
metabolites build up and are stored in different types of 
tissues in our body, developing the neurovisceral 
symptoms like abdominal pain, psychiatric signs, and 
neurological and photosensitive skin signs.

Diagnosis of each type of deficiency is given by 
identifying the metabolite produced in excess in the red 
blood cells, plasma, feces, or urine, as in our case. Most 
of them can be diagnosed by measuring the exact 
enzyme activity in the appropriate tissue1. Most mammal 
cells are able to synthesize heme, although it mostly 
occurs in the bone marrow, up to 85%.

Frequency is estimated in 1/10.000 but this can vary 
depending on geography2. Not all carriers of the disease 
develop clinical findings and there are significant 
interactions between the defect and environmental 
factors2.

There are as many porphyrias as enzymes involved 
in the metabolic route with exception of the first enzyme, 
α-Aminolevulinic acid (ALA), whose synthesis is 
increased in compensatory manner as it is normally 
hindered by its final product, heme1,3.

We found deficiencies of ALA dehydratase that 
correlates with acute intermittent porphyria, both with 
nervous symptoms.

Others like congenital erythropoietic porphyria 
(CEP), porphyria cutanea tarda (PCT), and erythro-
poietic protoporphyria deal with skin photo-
sensitivity1,3.

Our case offers some doubts about classification; 
first, because a second determination of urine porphyrins 
was made when the patient had already started treatment. 
In the second place, because our lab results could well 
determine mixed porphyria that appear to have acute 
crisis.

After the clinical findings and high incidence, the 
patient was initially diagnosed as acute intermittent 
porphyria, also called Swedish porphyria. It is a
metabolic error that affects more women than men and is inherited in autosomal dominant manner, causing a partial deficit in the porphobilinogen deaminase enzyme.

Presentation with abdominal pain is well known and up to 95% of these patients start with this symptom. Abdominal symptoms are followed by progressive neuro-psychiatric features (periphery motor neuropathy, breathing paralysis, seizures, or loss of consciousness).

Other clinical findings that can appear during the process are tachycardia, hypertension, and bladder retention; seizures are usually due to severe hyponatremia. It is essential to understand that seizures can occur and that antiepileptic medications can be harmful.

Acute intermittent porphyria should always be considered in the differential diagnosis of abdominal pain presented with neuro-psychiatric features, even if there is a previous family history or not. Once we have the diagnosis, the family should be tested to determine PBGD levels.

Prenatal diagnosis is of interest, especially in determining erythropoietic porphyria. Techniques that may be involved are measuring porphyrins in amniotic fluid and amniotic cell culture. Genetic counseling is important, specifically when both parents carry the affected gene.

Oral contraceptives should be avoided in patients and first grade relatives, as they can promote acute crisis.

Treatment is symptomatic and oriented to improving the skin condition and clinical manifestations. It is important to avoid precipitating factors involved in developing acute crisis. Some examples are estrogens, valproic acid, barbiturates, sulfonamides, and hydantoins. Other factors involved in acute crisis are alcohol, hypocaloric diets, and infections.

The objective of treatment with hematine is to fill up deposits with free-regulating heme. Secondary effects are due to its degradation products. There is also heme arginate, which is more stable with a recommended dose of 2-3 mg/kg/day during four consecutive days administered in slow infusion during 15-20 minutes in a saline solution. Effects on the fetus are unknown; therefore, this treatment should not be used during pregnancy.

Two vulnerable moments are at the beginning of pregnancy and puerperium. It is recommended to avoid pregnancy until at least 18 months have passed without symptoms.

Glucose solution is also included in therapy and it is able to stop an acute crisis as it inhibits ALA activity. It should be set up in all conflictive situations like labor, surgery, etc.

DISCUSSION

As we have described, there are serious difficulties in diagnosing this illness during pregnancy and puerperium. Our patient was misdiagnosed several times.

Information about porphyria and pregnancy is scant and insufficient. The information we have is from attending on individual cases as the frequency of the affection is low and association with pregnancy is rare. This complicates our knowledge on the behavior of the illness in pregnant patients. What should not be forgotten is that hormonal changes, prolonged fasting due to hyperemesis, and several drugs can initiate an acute porphyric attack.

Revision of the literature concludes that the illness can worsen because of symptomatic exacerbations, estimated in 50% of cases.

Mothers’ mortality rates range from 27% to 42.5%. Symptomatic exacerbations are generally due to exposing the patients to certain drugs that can modify the course of the pregnancy, resulting in abortion, preterm births, and other pregnancy complications. Up to 60% of pregnancy complications happen at the beginning, in early gestational ages.

Nearly 15% of the complications occur during the second trimester and are generally severe. Although during the last weeks of pregnancy, women present high ALA and PBG levels in urine, in porphyric pregnant women the levels tend to be higher.

An estimated 25% of the complications happen during puerperium. Maximum risks periods seem to be early gestational ages and puerperium. Children from porphyric mothers are normal when born, independent of their genotype, although there has evidence of a higher frequency of low birth weight and stillbirths.

CONCLUSIONS

It is important to highlight the possibility of diagnosing this illness during pregnancy and puerperium in fertile women who are carriers of the defect, as this
period is of special risk. Diagnosis should be performed by measuring excretion of porphyrins or, better still, by running genetic tests. Thus, we will be able to avoid precipitating factors.

Porphyria can be a negative influence in pregnancy and, in turn, pregnancy can precipitate acute crisis. Women who carry the deficiency should be well informed about risks and receive health information about the symptoms and precipitating factors so they can have healthier pregnancies and healthier children.

REFERENCES


