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Porphyria and pregnancy. Case report

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SUMMARY

The porphyrias are a group of diseases caused by a deficiency of enzymes responsible for the synthesis of heme, that ca lead to severe disease that requires early diagnosis to avoid complications. The frequency of the disease is low and it association with pregnancy unusual, but it is a good time for patients carrying develop the disease or suffer an exacerbatio of the same, hence the vital importance of prophylaxis of the factors risk.

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Keywords: *Pregnancy; Porphyria; Porphyrin precursors; Acute crisis.*

Porfiria y gestación. A propósito de un caso

RESUMEN

Las porfirias son un grupo de enfermedades producidas por un déficit de las enzimas encargadas de la síntesis del hemo que pueden dar lugar a un cuadro clínico grave que requiere un diagnóstico precoz para evitar complicaciones. La frecuenci de la enfermedad es baja y su asociación con el embarazo inusual, pero es un buen momento para que las pacientes portadora desarrollen la enfermedad o sufran una exacerbación de la misma, de ahí la importancia vital de la profilaxis de los factore de riesgo.

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Palabras clave: *Gestación; Porfiria; Porfirinas; Crisis aguda.*

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 pape where it was published.

CLINICAL CASE

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

Family background: of no interest

Personal background: allergic to penicillin, panto micine, and aspirin. The patient is reportedly an e

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smoker (ten cigarettes per day). Operated for meningoplasty 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 examination 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 meningitis. 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.

ALA: 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 tissue[1]. 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 geography[2]. Not all carriers of the disease develop clinical findings and there are significant interactions between the defect and environmental factors[2].

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 inhibited by its final product, heme[1,3].

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

Others like congenital erythropoietic porphyria (CEP), porphyria cutanea tarda (PCT), and erythropoietic protoporphyria deal with skin photosensitivity[1,3].

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[1].

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[4,5].

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[1]. Genetic counseling is important, specifically when both parents carry the affected gene[5]. Oral contraceptives should be avoided in patients and first grade relatives, as they can promote acute crisis[6].

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[5].

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[2,5].

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[4,5].

Glucose solution is also included in therapy and it i able to stop an acute crisis as it inhibits ALA activity It should be set up in all conflictive situations like labor surgery, etc[5].

DISCUSSION

As we have described, there are serious difficultie in diagnosing this illness during pregnancy an puerperium. Our patient was misdiagnosed severa times[4].

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

Revision of the literature concludes that the illnes can worsen because of symptomatic exacerbations estimated in 50% of cases[7].

Mothers' mortality rates range from 27% to 42.5%. Symptomatic exacerbations are generally due t exposing the patients to certain drugs that can modif the course of the pregnancy, resulting in abortion preterm births, and other pregnancy complications. U to 60% of pregnancy complications happen at th beginning, in early gestational ages[2].

Nearly 15% of the complications occur during th second trimester and are generally severe. Althoug during the last weeks of pregnancy, women presen high ALA and PBG levels in urine, in porphyrini pregnant women the levels tend to be higher[3].

An estimated 25% of the complications happe during puerperium. Maximum risks periods seem to b early gestational ages and puerperium. Children fron porphyrinic mothers are normal when born, independen of their genotype, although there has evidence of higher frequency of low birth weight and stillbirths[4].

CONCLUSIONS

It is important to highlight the possibility o diagnosing this illness during pregnancy and puerperiun in fertile women who are carriers of the defect, as thi

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.

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