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Case report

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A case of fatal acute intermittent porphyria: laboratory diagnosis and pathogenesis considerations

Un caz fatal de porfirie acută intermitentă: diagnostic de laborator şi consideraţii patogenice

Rodica Bălaşa[1*], Smaranda Maier[1], Anca Moţăţăianu[1], Zoltan Bajko[1], Otilia Moldovan[2], Erzsébet Benedek[1]

1. University of Medicine and Pharmacy Tîrgu Mureş, România
2. Intensive Care Unit, Emergency County Hospital Tîrgu Mureş, România

Abstract

Acute intermittent porphyria (AIP) is a metabolic disease with an autosomal dominant inheritance, with porphobilinogen (PBG) deaminase as the deficient enzyme in heme biosynthetic pathway at cytosolic subcellular locations. This diagnosis must be evoked in all adults with unexplained symptoms, but some clinical features are suggestive: women with reproductive age; abdominal pain; muscle weakness; sever and prolonged hyponatremia; dark or reddish urine.

The authors present a fatal case of a 39-years old female who presented acute abdominal pain followed by severe peripheral nervous system lesions with tetraplegia. Urine analysis showed enormously increased levels of porphirins, PBG and Δ aminolevulinic acid. The diagnosis of AIP was established and even if the correct treatment (Hemine, glucose) was administrated, the patient died after 3 weeks from onset due to a septic shock.

The authors discuss the laboratory abnormalities that are found in AIP and also the pathogenesis of the acute attack of AIP as well as the mechanism of severe nervous system damage that is less understood.

In conclusion, laboratory testing must be performed early and if a diagnose of AIP is not made promptly serious consequences may follow for the patient.

Keywords*: acute intermittent porphyria, urinary porphyrins, heme biosynthesis, pathogenesis of attack in acute intermittent porphyria*

Rezumat

Porfiria acută intermitentă (PAI) este o boală metabolică, cu transmitere autosomal dominantă, cu alterarea căii de biosinteză a hemului prin deficitul enzimei porphobilinogen (PBG) dezaminaza. Acest diagnostic trebuie să fie evocate în toate cazurile de adultii care prezintă simptome inexplicabile, dar cu unele caracteristici clinice sugestive: femei cu vârstă reproductivă, dureri abdominale, slăbiciune musculară, hiponatremie prelungită şi severă, urină închisă la culoare sau roşie.

***Corresponding author**: Rodica Bălaşa, University of Medicine and Pharmacy Tîrgu Mureş, România, e-mail: rodicab2007@yahoo.com

Autorii prezinta un caz fatal de PAI la o femeie de 39 de ani, care a prezentat dureri abdominale acute, urmate de leziuni severe ale sistemului nervos periferic cu tetraplegie. Analiza urinei a arătat nivelurile de porfirine, PBG şi de acid aminolevulinic Δ crescute enorm. Diagnosticul de PAI a fost stabilit şi, chiar dacă tratamentul corect (heminei, glucoza) a fost administrat, pacienta a decedat după trei săptămâni de la debut prin şoc toxico-septic.

Autorii discuta despre diagnosticul de laborator din PAI şi, de asemenea, patogeneza atacului acut de PAI, precum şi mecanismul de producere a leziunilor severe ale sistemului nervos, care este mai puţin înţeles.

În concluzie, testele de laborator trebuie efectuate cât mai precoce deoarece neglijarea unui diagnostic de PAI poate avea consecinţe grave pentru pacienţi.

***Cuvinte cheie**: porfirie acută intermitentă, porfirine urinare, biosinteza hemului, patogeneza atacului acut de porfirie acuta intermitentă*

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Porphyrias are a group of inherited disorders of heme synthesis characterized by acute attacks of nonspecific neurovisceral symptoms. Delayed treatment and/or the use of precipitating drugs can lead to severe conditions**,** even death. Early diagnosis and treatment of acute porphyria frequently save lives. Symptomatically, acute porphyrias present with nervous system involvement, severe abdominal pain and mental disturbances, while cutaneous porphyrias present with skin manifestations after sun exposure. There are 9 major porphyrias described that can be classified into 3 groups: 1. the 4 acute hepatic porphyrias (acute intermittent porphyria –AIP-, Δ aminolevulinic acid –ALA- deficiency porphyria -ADP-, hereditary coproporphyria -HCP-, variegate porphyria -VP-, porphyria cutanea tarda –PCT-); 2. the 3 erythropoietic cutaneous porphyrias (erythropoietic protoporphyria -EPP-, congenital erythropoietic porphyria, X-linked erythropoietic protoporphyria); 3. the hepatoerythropoietic porphyria. The genes encoding these enzymes have been cloned, their chromosomal location is defined and DNA analysis have revealed heterogeneous molecular defects. The most common type, AIP is an autosomal dominant (> 200 mutations) acute hepatic porphyria with acute attacks only, without skin lesions of any kind. A deficient activity of a distinct enzyme in the heme biosynthetic pathway leads to acute porphyrias. The prevalence in European countries is about 1 in 75000 people (1- 3).

Because of the numerous symptoms and their lack of specificity, a misdiagnosis of AIP is relatively frequent. The most severe alterations are found in the nervous system. An attack of AIP can be life-threatening, so a rapid diagnosis, followed by an accurate medical management is mandatory together with the avoidance of any precipitating factors. Urinary porphobilinogen (PBG) is used as an initial rapid testing to diagnose AIP. Hemin therapy must be started early, in conjunction with glucose, in order to decrease heme synthesis (1-3).

Case presentation

The patient, Mrs. S.A. a 39-old woman, originating from the rural area, known with affective-depressive disorder, was under treatment with Sertraline because of a recurrent depression that she had been diagnosed with, 12 months before. Five days before onset she started a severe diet with a low caloric intake (less than 800 kcal). She had no skin manifestations regardless of sun exposure and her family history was not significant; there were three previous episodes of atypical abdominal cramps due to which she was hospitalized and investigated in a competent gastroenterological unit (discharged without a satisfactory conclusion as to the etiology of

these cramps, all investigations and abdominal imaging being normal). She was hospitalized on the 06.01.2013 in the Satu-Mare Surgery Unit with abdominal pain, incoercible vomiting and diffuse cephalalgia with 24 hours sudden onset, being suspected of having acute pancreatitis.

Common analgesic and antispasmodic drugs were administered, with partial remission. On the 15.01.2013 the patient developed an ascending motor deficit of the inferior members, subsequently including the superior members as well, urinary retention, due to which she was transferred to the Satu-Mare Neurology Unit where they determined flaccid tetraplegia, hyperchrome urine, thus the suspicion of polyneuropathy in the context of an AIP arose.

On the 18.01.2013 she was transferred to the Tirgu-Mures First Neurology Clinic. The same day she was taken over by the Intensive Care Unit with a severe general state of health, initially with efficient, spontaneous breathing, midposition pupils reactive to light, maintained eye mobility, bilateral peripheral facial diplegia, flaccid tetraplegia 1st degree proximal and 3rd degree distal of the superior members, 1st degree of the inferior members, abolished tendon reflexes, without pathological pyramidal signs, hypoesthesia and hypopalesthesia in all members with distal accentuation, bilateral amyotrophy of the legs and hands, bradylalia, consciousness, temporal-spatial orientation, somnolence. O_2 saturation 100%, hemodynamically stable, arterial blood pressure (ABP) 122/62mmHg, pulse 82/min., generalized edemas, distended, meteoristic abdomen, diuresis present, hyperchrome urine, APACHE score II=14. The laboratory examinations highlighted a serious hyponatremia (105mmol/l), hepatic dysfunction (GOT 81U/l, GPT 65U/l) and renal dysfunction (creatinine 2.62md/dl, urea 92.02mg/dl), negative procalcitonine test.

On the 20.01.2013 orotracheal intubation and ventilatory support (BiPAP), FiO2 60% were initiated.

The EMG examination from the 21.01.2013 highlighted acute sensorimotor polyneuropathy with primary axonal damage. The cerebral magnetic resonance imagery MRI exam performed twice highlighted only moderate diffuse bilateral cerebral atrophy. The thoracic CT scan highlighted bilateral bronchopneumonic condensation and a few paratracheal ganglia with inflammatory aspect.

On the 23.01.2013, the values of urinary ALA (spectrophotometric cromatography method) were 27.38 mg/24h (normal values 1.5-7.5mg/24h) and urinary porphyrin (HPLC method) concentrations confirmed the diagnosis (tab.I). Also, the urinary PBG had enormous values, 103mg/24h (normal 0-4 mg/24h), thus the diagnosis of AIP was retained.

During hospitalization in the ICU Clinic, she benefited from hydroelectrolitic, acid-base and nutritive re-equilibration, anemia and thrombocytopenia (thrombocyte concentrate) and also hypoalbuminemia correction. Hypertonic glucose and Normosang 250mg/24h were administered in the 25-28.01.2013 period (following the confirmation of diagnosis). The value of serum ferritin was normal. Following Normosang, the evaluation of urinary porphyrins revealed that ALA values dropped to 3.67mg/24h (table no I).

Therapy received (allowed in AIP): antibiotherapy (Ceftriaxon subsequently Meronem), hepatoprotective, analgesic (subcutaneous morphine), anticoagulant (low-molecular-weight heparin), Glucose, IV Immunoglobulin (20g/day, 4 days).

On the 29.01.2013 tracheostomy was performed for prolonged ventilatory support and right pleurectomy for massive right pleurisy with transudate aspect.

Repeated hemocultures and the bacteriological examination from the bronchial aspiration were negative.

Until the 06.02 the general state was slightly improved, patient was conscious, with flaccid

tetraplegia, mechanically ventilated by tracheostomy cannula in SIMV mode, hemodynamically stable, with intermittent flare-up of ABP and sinus tachycardia, thrombocytopenia, renal failure, anemia, right pleurisy (drained). After this date, the patient's state worsens; she develops a toxico-septic shock and deceases with multiple organ and system failure on the 16.02, despite all therapeutic maneuvers.

Discussions

The neurologist is frequently the person who diagnoses AIP but also nurses the most feared manifestations, as acute attacks are due to nervous system damage: both central, peripheral and autonomic. As mentioned in literature, our patient was a female, in whom the attacks of AIP started in her middle thirties. The peak occurrence of acute attacks is within the third and fourth decade, women being more exposed probably because estrogen and progesterone levels affecting heme metabolism and activating ALA-synthase (3-7).

Most attacks begin with severe abdominal pain, vomiting, nausea and mild behavioral changes (anxiety, insomnia). Abdominal pain is present in 95-97% (12). The intensity of gastrointestinal symptoms led our patient to be initially hospitalized in a surgical department. Nonspecific psychiatric manifestations such as disorientation, neurotic behaviors and depression develop in approximately 20 to 30% of patients. In our patient, depression was diagnosed 2 years before the final attack and was treated with Sertraline, a drug that seems to be safe in porphyria cases (7).

Laboratory abnormalities

AIP has the following biochemical characteristics: high urinary levels of ALA and PBG (PBG>ALA) as detected in the present case. PBG is highly elevated during an AIP attack; quantitation has a great informative value even through spot sampling. In order to confirm the diagnosis, a 24-hour urine collection is needed for the carrying out of quantitative measurements; during an attack that could significantly delay the diagnosis. Using a diagnostic test, ideally PBG Kit, is preferable because results are promptly available (within hours), as compared to determining porphyrins as a result of a 24-hour urine collection. Diagnosis could be delayed several days in testing and a life-threatening state may occur. After treatment initiation, the hemin therapy needs to be followed by second-line testing in order to determine the type of porphyrin metabolism disorder: porphyrin levels in plasma, urine, feces and the level of erythrocyte porphobilinogen deaminase activity.

Furthermore, as the attack starts to remit, the PBG will decrease in urine samples. Following an acute attack, urinary porphyrins usually maintain an elevated level for a more extended period of time than do ALA and PBG. Therefore, determining the amount of total urinary porphyrins should be part of screening for acute porphyrias. One has to keep in mind that these tests are not highly specific: urinary porphyrins have elevated levels in liver cancer, hepatitis, mercury or arsenic poisoning, whereas urinary coproporphyrins mark an increased level in several liver dysfunctions, ALA dehydrogenase deficiency and are equally present in lead poisoning and hereditary tyrosinemia type I (5).

Urinary porphyrins: In healthy subjects, PBG is present in urine in different levels. PBG, a pyrrole and ALA, an amino acid, are colorless in normal amounts. However, high levels of urinary PBG can produce uroporphyrins in a spontaneous manner, which give urine a reddish colour. Urinary PBG represents a very important stage in the diagnosis of a suspected acute attack of AIP. In hepatic porphyrias (AIP, HCP and VP) urinary ALA and PBG are increased. The highest concentrations are present in AIP. Determining

the amount of total urinary porphyrins should be part of screening for acute porphyrias. In our patient, total urinary porphyrins were excessively increased at 9841 µg/24h (normal values <150), one of the highest values we found on consulting the literature. Porphyrins are tetrapyrroles that after cell-synthesis are present in blood, urine and feces and undergo oxidation, becoming reddish. Furthermore, porphyrins are fluorescent and following exposure to long-wave ultraviolet light (UV-A), they acquire an intense red appearance. This appearance allows the precise measurement of porphyrins with the help of a spectrofluorometer. All porphyrins inside cells are intermediates in the heme biosynthetic pathway. They are colorless, non-fluorescent and appear in a diminished form, with the exception of protoporphyrin, the last intermediate, which is an oxidized porphyrin. Determination of the total porphyrins in urine is not difficult. It is an effective test for screening, nevertheless, increases in urine porphyrins are non-specific and may not be an indicator of AIP if ALA and PBG have normal values. In our case, both ALA and PBG were extremely elevated: 27.06mg/24h, 103mg/24h. Our patient's urine was red, a feature that characterizes AIP, due to the oxidation of porphyrin precursors in the presence of oxygen.

Different types of porphyrins are to be found in urine. In case of an important increase in total urine porphyrins, it is useful to analyse the individual porphyrins. The "high performance liquid chromatography" (HPLC) is the most used method for separating the individual porphyrins. HPLC measures the amount of porphyrins with four or more carboxyl groups present in urine (see Table I) and it was used in our case also. Analyzing the prevailing porphyrins is more effective than concentrating on the quantity of each porphyrin in interpreting HPLC results. Solubility in water of porphyrins is increased by carboxyl-groups. Porphyrins which have less than 4 carboxyl groups do not have a significant quantitative presence in urine. Porphyrins with 2-3 carboxyl groups, which are not as water-soluble, are mainly excreted into the bile and feces. Excretion of coproporphyrins occurs by both previously mentioned routes (8-10). (*Table I*)

In order to obtain correct values of urinary PBG, urine sample has to be collected for analysis: 1. during the acute phase (PBG could be normal when the patient is not presenting symptoms); 2. before the treatment, since therapy may reduce the number of PBG excreted (in our case, PBG dropped 5 times after treatment); 3. it is recommended to freeze the sample immediately after collection and protect it from light. PBG is prone to degradation at high temperatures, at pH <5.0. The Watson–Schwartz test and derivatives are used for urine PBG screening (9). It is carried out by mixing 1 mL of urine with 1 mL of Ehrlich's reagent (*p*-dimethylaminobenzaldehyde) and adding sodium acetate to urine in acid solution. A reddish-mauve colored compound is then

Table I. Urinary Porphyrin names, the corresponding number of carboxyl groups, values in our patient before and after Hematine

Porphyrin names (normal value µg/24h)	Number of carboxyl groups	Init.value (µg/24h)	After Hematine (µg/24h)
Uroporphyrin (octacarboxyl porphyrin) (<25)	8	9341.3	564.5
Heptacarboxyl porphyrin (<5)	7	325.5	125.5
Hexacarboxyl porphyrin (<2)	6	154.8	58.8
Pentacarboxyl porphyrin (<5)	5	123	91
Coproporphyrin I (tetracarboxyl porphyrin) (<25)	4	342.5	285.5
Coproporphyrin III (<75)	4	864.9	576.8
Total porphyrins (<150)		11152	1702

evaluated at λ_{max} 553–555 nm. Nevertheless, the test is unspecific due to interferences with urobilinogen, medication and its metabolites or other endogenous compounds. It lacks sensitivity, so for the detection, a high concentration of PBG (ten times above normal) is required. In order to increase specificity and sensitivity of the method, the PBG can be separated in a column on an ion-exchange resin, unnecessary compounds being washed off. PBG is eluted and reacted with Ehrlich reagent (10). PBG can be quantified in this manner, but this "gold standard" method requires a relatively long time. Lately, a screening method has appeared that uses a syringe prepacked with ion-exchange resin. The sample is adsorbed, washed, and eluted; final color formation being performed with Ehrlich's reagent. Visual assessment is achieved by means of a color chart and a dye color calibrator (2).

Due to the dramatic evolution of the case, we have not had the time to perform other plasmatic, serum or feces tests. Some tests are not specific for AIP but they will be presented for informative purposes. In order to characterize the type of porphyrias and evaluate families with cases of porphyria, a complete evaluation would have included:

1. Genetic analysis*:* The PBG-D or hydroxymethylbilane synthase (HMBS) gene on Ch11q23.3 is responsible for AIP. 317 mutations have been found in the HMBS gene. One must keep in mind that PBG-D protein exists in 2 isoforms. They derive from 2 different mRNAs by alternative splicing (the erythroid mRNA contains an extra exon 1, which is spliced out in the other cells of the body). Therefore, a mutation in this area does not cause AIP, but it generates in a false positive erythrocyte assay. In other sections of the gene, molecular defects may appear, resulting in abnormal erythroid and hepatic isoforms of PBG-D. They also allow the biomolecular diagnosis of AIP through testing the HMBS activity in the erythrocytes (8). Even though significant genetic progress has been achieved in porphyrias, most of the diagnosis still relies on biochemical determination of the excess porphyrin and its precursors both in plasma and urine.

2. Blood tests—plasma or serum: Regularly, only small amounts of porphyrins can be found in plasma; increased concentrations are found especialy in subjects with cutaneous porphyrias. The test is highly efficient when porphyria is considered to be the cause of photosensitivity. Determination of plasmatic PBG is used when the suspicion of acute porphyria exists, and it is impossible to collect a urine sample (patients with kidney failure). In case of acute porphyrias, serum PBG is increased. However, with normal kidney function, the serum concentrations are lower than in urine.

Erythrocyte porphyrins: The protoporphyrin that regularly exists in erythrocytes is found as zinc protoporphyrin. In other situations, such as lead poisoning, iron deficiency, disorders that affect erythrocytes zinc protoporphyrin is also augmented. Consequently, an increase in erythrocyte porphyrins is not specific for porphyrias. EPP is the only condition in which free protoporphyrin that is bound with/TO zinc is increased. Concerning cases of AIP in which urinary PBG excretion is often normal, a useful diagnosis method is the measurement of PGB-deaminase activity in the erythrocite (9).

3. Fecal Porphyrins: Total fecal porphyrins show significant growth in active HCP and VP, while in PCT have slightely lower levels. Porphyrins with 2-4 carboxyl groups are usually excreted by the liver into the bile, afterwards flow into the intestine and later in feces. As is the case of urine, measuring the total amount of porphyrins in feces is essential. If we find an increased value, then the laboratory should determine by HPLC the type rather than the amount of each porphyrin. It may be difficult to determine fecal porphyrins because results may be modified by variations in fecal flow, type of diet and internal

bleeding of the stomach or intestines. In cases of AIP, they are not mandatory.

Pathogenesis of AIP: Heme is the essential constituent of hemoglobin, respiratory and P450 liver cytochrome, myoglobin, catalase and peroxidase. Heme function plays a key role in cellular metabolism. Heme synthesis is realized through the porphyrin pathway, consisting of 8 enzymes (4 acts in the cytoplasm and 4 in the mitochondrion) that convert glycine and succinil-coenzyme A to heme. These enzymes are encoded by 9 genes; as the first enzyme in the pathway, ALA-synthase has 2 genes. The pathway is under a regulatory control, mainly in the liver, where heme biosynthesis is modulated through feedback control and rate-limited by the 5-aminolevulinate synthase 1 (ALAS1). AIP is a hepatic type of porphyria, the deficient enzyme being hydroxymethylbilane synthase (PBG deaminase); the affected persons have a 50% reduction of this enzyme's activity. This deficiency leads to 2 consequences: less heme production and accumulation of heme precursors called porphyrins. In porphyrias, the accumulation of porphyrins is toxic for some tissues (2).

Pathogenesis of Acute Attacks in AIP: For the attack to occur, the patient needs a precipitating factor such as: drugs (barbiturates, anticonvulsivants, progestins, etc), progesterone, smoking, fasting/dieting, infections, surgery, stress, etc. Any substances that induce heme synthesis also produce an increase in heme precursors (only protoporphyrin is used in heme synthesis, all others must be excreted in faces, plasma and urine). Our patient had been on diet for several days, which probably provoked the last and most severe attack of AIP. Starvation activates oxygenase, which depletes the hepatic heme pool leading to ALA synthesis (4).

The mechanism of the neurvous system (NS) damage is less understood:

1. A hypothesis is that neurological symptoms (both central and peripheral) are secondary to the toxicity of porphyrin precursors themselves rather than a deficiency of heme in nerve tissue. An argument to sustain this hypothesis is that in literature we can find several case reports of patients diagnosed with AIP who have undergone liver transplantation that both normalized their urine and completely eliminated the recurrent neurological attacks. These facts support the hepatic overproduction of heme precursors in causing the neurological symptoms. Among the precursors, ALA seams the key factor leading to neuronal toxicity, supported by the following observations: a) other pathologic conditions that lead to increased urinary ALA excretion (lead poisoning, tyrosinemia type I) have symptoms resembling those of AIP, like abdominal pain, peripheral neuropathy; b) induction of cytochrome P450 enzymes by some drugs that exacerbate porphyria, increase the hepatic heme turnover; c) ALA is neurotoxic (it blocks the peripheral myelin formation; in the presence of heavy metals, such as iron, generates free oxygen radicals that damage cell structure; induces necrotic cell death of mouse astrocytes; during a porphyria attack ALA appears in measurable quantities in CSF). Unfortunately, the question whether ALA is involved in the neurological symptoms of acute porphyria remains controversial because many symptomless patients with AIP have high excretion of ALA (1, 6).

2. The peripheral NS can be accessed by neurotoxic substances that accumulate in porphyria through the neuromuscular junction, where there is no blood-nerve barrier, then are transported to the cell body causing its death (6).

3. Heme deficiency produces decreased levels of key heme proteins (nitric oxide synthases, cytochrome), resulting in direct and indirect effects on the nervous system, disrupted axonal transport and axonal death. This hypothesis is not scientifically based due to the intraneural heme pool that should not diminish during an acute attack of hepatic porphyria; in NS there

is little cytochrome P450 activity and ALA synthase should not be induced therefore, neuronal aerobic metabolism would not be compromised. Other conditions (iron deficiency) that affect heme synthesis do not produce neuropathic syndromes (6,7,12,13).

Some attacks leave neurological axonal nerve damage represented by chronic symptoms (motor deficits, neuropathic pain in the extremities, chronic pain in the gut, etc).

In the peripheral nervous system we found a predominantly motor acute polyneuropathy of axonal type as suggested clinically and electro-physiologically. This is the most frequent neurological feature in AIP during an attack (1,2). Approximately 40% of patients with porphyria develop neuropathy: pure motor, pure sensitive, sensorimotor, small fiber, autonomic neuropathy. Most studies consider the axonal lesion as the primary event. Porphyria affects short motor axons (innervating proximal muscles and cranial nerves), in contrast to other metabolic axonopathies where there is a length-dependent pattern. At autopsy, neuronal loss and chromatolysis of cells of the anterior horn of the spinal cord, as a plausible result from retrograde degeneration secondary to axonal damage, are observed. Our patient had an ascending paralysis as has been described by many experts, but Waldenstrom mentioned in 1937 that this is the exception rather than the rule (6). A patient with a history of gastrointestinal illness that presents an acute-onset ascending motor neuropathy (as was the case of our patient), can easily be misdiagnosed with Guillain-Barre syndrome. The prognosis after an attack of acute hepatic porphyria is generally good. We must underline that considering Hematine, the motor deficit of our patient had a slight tendency to remit but the septic shock was fatal. In a series, the recovery was complete in 85% of cases, depending on the severity of axonal degeneration and appearing after many months; distal muscles begun to recover (12, 14).

A severe hyponatremia (103mEq/l) was found in our patient as in 40% of porphyria cases, it being the most frequent electrolyte abnormality seen in this pathology and is determined by the inappropriate antidiuretic hormone secretion as a presumably result of hypothalamic abnormality (15).

Regarding the **treatment** of AIP in our patient, a 10% glucose infusion was started in the 9th day folowing the attack onset. Glucose is a key element in the treatment of acute attacks because it inhibits ALA synthase. Hematine arginate (represses heme synthesis) was administered as soon as the diagnosis was confirmed, in recommended dosage (4mg/kg/day for 4 days) but late for the clinical course, respectively after 3 weeks from onset. The literature is very firm that in order for this drug to be effective, it needs to be administered very early in an attack; even in this case, effectiveness varies amongst individuals. It is not a curative treatment but can reduce the intensity and shorten an attack by inhibiting ALA synthase and hence the accumulation of toxic precursors. Hemin therapy determines a dramatic decrease of urinary results but it does not usually last long. In our patient, after the treatment with Hemin, we could observe an important drop (more than 9 fold) of porphyrin precursors (see tab I). Hyponatremia, as a sign of the syndrome of inappropriate antidiuretic hormone, was intensively and cautiously treated in order to avoid pontine myelinolysis, secondary to excessive sodium administration.

When a porphyric patient needs treatment, the physician must verify if it is safe and/or unsafe, as prevention is essential for disease prognosis.

Conclusions

The symptoms of AIP are common so this disease should be suspected quite often. If the diagnosis of AIP is not made promptly, serious

consequences for the patient may follow. Laboratory testing must be performed as soon as possible and if the result is positive, the treatment must be started immediately. The causes of severe neurological injury during an acute attack of AIP remain a controversial issue.

Abbreviations

ABP - arterial blood pressure
ADP - deficiency porphyria
AIP - acute intermittent porphyria
ALA - Δ aminolevulinic acid
ALAS1 - aminolevulinate synthesis genes1
CSF - cerebrospinal fluid
CT - computer tomography
EMG - electromyography
EPP - erythropoietic protoporphyria
HCP - hereditary coproporphyria
HMBS - hydroxymethylbilane synthase
HPLC - high performance liquid chromatography
ICU - intensive care unit
MRI - magnetic resonance imagery
NS - nervous system
PCT - porphyria cutanea tarda
PBG - urinary porphobilinogen
VP - variegate porphyria

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