CASE REPORT


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# Acute intermittent porphyria – A case report

## Akutna intermitentna porfirija

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**Abstract**

**Introduction.** Acute intermittent porphyria is a rare inherited metabolic disorder caused by a decreased level of porphobilinogen deaminase. Subsequent accumulation of by-products in neural elements causes a classic triad of abdominal pain, neurological dysfunction, and psychiatric disturbances. **Case report.** A 22-year-old female patient with convulsions, episodes of blindness and progressive development of quadriparesis, bulbar paralysis, and respiratory failure was admitted to our intensive care unit twelve days after undergoing colon resection at the local hospital. The diagnosis was confirmed by a high level of porphobilinogen in urine. Previous use of oral contraceptives, antidepressants, and thiopental as induction agents for general anesthesia could represent precipitating factors. The patient was treated conservatively with high carbohydrate intake and human hemin. Six months after admission, the patient was transferred to the Department of Physical Medicine and Rehabilitation. **Conclusion.** Early diagnosis of acute intermittent porphyria is the cornerstone for successful treatment. The next step includes adequate therapy followed by the prevention of attacks.

**Key words:**
**diagnosis, differential; neurologic manifestation; porphyrias; porphyria, acute intermittent; porphobilinogen; risk factors; treatment outcome.**

**Apstrakt**

**Uvod.** Akutna intermitentna porfirija je redak nasledni metabolički poremećaj uzrokovan nedostatkom porfobilinogen deaminaze. Posledično nakupljanje međuproizvoda u nervnim strukturama dovodi do trijasa kliničkih simptoma: bol u trbuhu, neurološki ispadi i psihijatrijski poremećaji. **Prikaz bolesnika.** Dvanaest dana nakon resekcije debelog creva u lokalnoj bolnici, 22-godišnja bolesnica primljena je u jednicu intenzivnog lečenja zbog konvulzija, epizoda slepila i progresivne razvojne kvadripareze, bulbarne paralize i respiratorne insuficijencije. Dijagnoza je postavljena na osnovu visokog nivoa porfobilinogena u mokraći. Prethodna upotreba oralnih kontraceptiva, antidepresiva i tiopentala kao indukcionog agensa u opštoj anesteziji mogli su biti precipitirajući faktori. Bolesnica je lečena konzervativno visokim unosom ugljenih hidrata i humanim heminom. Šest meseci posle prijema prebačena je na Odeljenje fizikalne medicine i rehabilitacije. **Zaključak.** Postavljanje rane dijagnoze je osnovni korak uspešnog lečenja napada akutne intermitentne porfirije. Sledeći korak podrazumeva adekvatnu terapiju, praćenje i prevenciju nastanka ponovnih napada.

**Ključne reči:**
**dijagnoza, diferencijalna; neurološke manifestacije; porfirija; porfirija, akutna, intermitentna; porfobilnogen; faktori rizika; lečenje, ishod.**

### Introduction

Porphyrias are rare inherited or acquired disorders caused by partial deficiency of enzymes in the biosynthesis of heme. There are cutaneous and neurological forms of the disease. However, generally looking, the disease is a result of enzyme dysfunction of the same biosynthetic pathway, but differences in organ affection are from mistakes in different isoenzymes of one enzyme, different processing of mRNA, and different microenvironment in cell matrix [1]. Acute intermittent porphyria (AIP) is a rare autosomal dominant disorder. Prevalence in Europe is 1–2 *per* 100,000 (highest is in Scandinavia with 1 *per* 1,500) [2–4].

### Case report

A 22-year-old female patient was admitted from the local hospital under suspicion of developing sepsis. After

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interviewing her parents, we found out that, at the beginning of the year, she had laparoscopic surgery of ovarian cysts and subsequently received advice to take oral contraceptives (one of the main provoking factors). After just a few weeks, she stopped the suggested therapy because of nausea, vomiting, apathy, and sleepiness. Three months later, she was hospitalized in a local hospital with significant epigastric pain and vomiting, back pain, and constipation that lasted for four days. During her hospital stay, she had also suffered from insomnia and hallucinations. The ward doctor consulted a psychiatrist who established the diagnosis of the somatoform disorder and prescribed her sulpiride (Eglonyl®, Alkaloid AD, N. Macedonia), one of the porphyrinogenic drugs. After series of medical tests and examinations, the patient was discharged with the diagnosis of biliary gastritis. The next day, at the request of her parents, she was admitted to a higher-level hospital in a town nearby due to further worsening of the abdominal pain and the appearance of a new symptom – inability to climb the stairs (due to proximal neuropathy). Computed tomography (CT) scan of the abdomen revealed widening of the transverse colon, which was interpreted as toxic megacolon, and the patient underwent a transversal colon resection. Twelve days later, she was transferred to our hospital.

Upon admission, the patient was awake, had brief periods of confusion, dyspneic with $SpO_2$ 85% on room air, blood pressure 160/100 mmHg, heart rate 140/min, body temperature 37.7°C, central venous pressure (CVP) 6 $cmH_2O$, abdominal pain, active peristalsis, intestinal contents visible on stoma, and light yellow urine in urine bag. Laboratory values were: erytrocyte sedimentation rate (ESR) 47 mm/h, C-reactive protein (CRP) 119 mg/L (normal range less than 5 mg/L), leukocytes $17.4\times10^9$/L (normal range 3–12 $\times 10^9$/L), pH = 7.38 (normal range 7.35–7.45), $PaCO_2 = 52$ mmHg (normal range 38–42 mmHg), $PaO_2 = 119$ mmHg (normal range 75–100 mmHg), $HCO_3^- = 30.8$ mmol/L (normal range 23–29 mmol/L).

After admission, the patient had episodes of epileptiform seizures that lasted for a few minutes, and they were accompanied by apnea and complete loss of responsiveness. CT of thorax, abdomen, and pelvis revealed bilateral pleural effusions and pneumothorax on the right side, which was drained with a chest tube. After consulting with a neurologist, a CT scan of her head, electroencephalography (EEG) and electromyoneurography (EMNG) were performed. On the next day, further deterioration with more episodes of convulsions, quadriplegia, bulbar paralysis, and respiratory failure occurred, and eventually, intubation and mechanical ventilation were applied. We took blood cultures, smears, and 24 h collection of urine for porphobilinogen.

Brain CT scan revealed signs of suprasellar subarachnoid recession in the sella turcica and parenchymal cortical reduction frontally, bilaterally. There were no areas of demyelination.

EEG finding was well expressed with minor diffuse dysfunction and elevated irritability of frontal regions bilaterally. EMNG findings showed a loss of conduction in the proximal group of muscles with the existence of spontaneous muscle activity and preserved sensory fibres. Finally, when the results of porphobilinogen in urine arrived (904 μg/24 h, and normal values are less than 150 μg/24 h) diagnosis of acute porphyria was made.

Hyponatremia, present from the beginning, was treated with 3% saline infusions and specific therapy with 10% and 50% dextrose i.v. along with enteral feeding and administration of human hemin (Normosang® 25 mg/mL, Orphan Europe SARL, Puteaux, France) in the dose of 4 mg/kg/day, four days in a row. Therapy with Normosang® was given on two occasions, after 30 days and after three months. The first dose led to a minimal improvement in clinical symptoms, while the second dose had a better effect.

The patient was tracheotomized, and a percutaneous endoscopic gastrostomy was done. After 160 days of intensive care, she was transferred to the Department of Physical Medicine and Rehabilitation. The patient was discharged from the Intensive Care Unit with spontaneous breathing, an act of swallowing, and movements in all extremities (Figures 1 and 2).

**Fig. 1 – Patient on discharge from the Intensive Care Unit.**

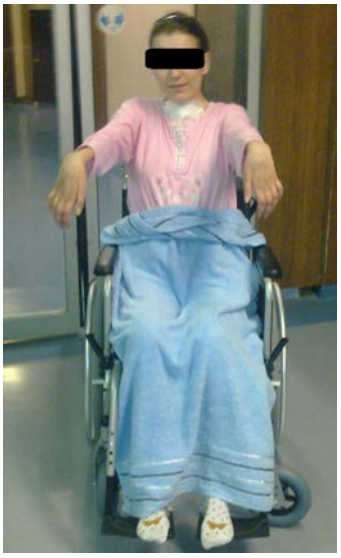

**Fig. 2 – Patient with renewed movements in the extremities.**

## Discussion

AIP symptomatic is mainly heterozygotes and rarely homozygotes. It is characterized by a long latent period, and symptoms become manifested after puberty in the third and fourth decade of life after exposure to some provoking factors [5]. There are no cutaneous manifestations. AIP is a metabolic disorder caused by a deficiency of porphobilinogen deaminase (PBGD). Patients with AIP have acute attacks of neurovisceral symptoms (affection of the autonomic nervous system) followed by a high level of porphyrin precursors in urine. The first presentation of the disorder is in 85%–95% abdominal pain and in 45% peripheral neuropathy with motor weakness. The exact mechanism of neuronal damage is unknown; one of the proposed theories is the crystallization of byproducts in neural structures [5, 6].

A variety of clinical presentation is considerable: abdominal pain, nausea, vomiting, paralytic ileus, urinary retention or incontinence, tachycardia, arterial hypertension, sweating, tremor, postural hypotension, peripheral neuropathy (proximal because of axonal degeneration and demyelination), sensory neuropathy (paresthesias and dysesthesias), cranial neuropathy (VII and X), periodical cortical blindness (caused by vasospasm), epileptiform seizures and rarely bulbar paralysis, and death [7, 8].

Deficiency of PBGD is not enough for clinical manifestation; there must be a presence of provoking factors: medications (inductors of P450 cytochrome oxidase), fasting, hormones (progesterone), smoking, alcohol, or metabolic stress (infection, surgery, psychological stress) [1].

Diagnosis is based on clinical presentation and a high level of urine porphobilinogen. The most relevant thing is the high level of clinical suspicion [9, 10].

Treatment consists of the following steps: review all medications and discontinue any that can exacerbate acute porphyria, restore energy balance using an enteral route if possible, if not, apply dextrose in the dose of 300–400 g/day i.v., hemin 3–4 mg/kg i.v., given once a day for four days in order to prevent future attacks (treat intercurrent infections and other diseases promptly) [11, 12].

Chronic complications are hepatocellular carcinoma and renal failure [13, 14].

## Conclusion

AIP is capable of mimicking a wide variety of medical conditions. It is important to have a high index of clinical suspicion and then, with a relatively simple biochemical test, confirm the diagnosis of AIP. Specialized care and prevention of future attacks are cornerstones of favorable outcomes. Nevertheless, we need more research in the future in order to obtain new therapeutic opportunities and detect parameters for monitoring the effects of therapy and prediction of outcome.

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