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R E V I E W A R T I C L E

Porphyriya – The Vampiers Disease

Shaik Salma Sultana*, Sai Kiran Anem[1], Shaik Shafi[2]

Jagan's College of Pharmacy, Jangala kandriga, SPSR Nellore, Andhra Pradesh, India

A B S T R A C T

The Porphyrias are a group of seven rare genetic disorders. They are called the porphyrias because they cause accumulation of chemicals called porphyrins (purple-red pigments named from the Greek for purple); or the simpler chemicals (ALA and PBG), which are used by the body to make porphyrins. In each porphyria a specific enzyme, which is needed to complete each step on the pathway to produce Haem (a red pigment containing iron and porphyrin), is deficient. As a result these porphyrins accumulate causing severe medical problems. The type of porphyria varies according to the enzyme/step which is affected.

Keywords: Porphyria cutanea tarda, porphyria, plumboporphyria.

A R T I C L E I N F O

Corresponding Author
Shaik Salma Sultana
Jagan's College of Pharmacy, Jangala kandriga,
SPSR Nellore, Andhra Pradesh, India
MS-ID: WJPBT3580

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C O N T E N T S

1. Introduction

The name porphyria is from the Greek πορφύρα, porphyra, meaning "purple", a reference to the color of the urine that may occur during an attack**.**Porphyria is a group of relatively rare metabolic disorders. It is an inherited condition, meaning that an abnormal gene is passed on from one or both parents. It is not contagious and cannot develop through any other means. Porphyria affects blood composition. All forms of porphyria slow the production of heme, which is used in hemoglobin and other chemicals that transfer oxygen through the bloodstream. Heme is made from porphyrin, but people with porphyria are unable to fully convert porphyrin into heme. This means that porphyrin can accumulate in tissues and the blood, causing problems in the nervous system, skin, and other organs**.**

Types of Porphyria:

Table 1: Type of porphyria, the defficient enzyme responsible for the disorder

Type of Porphyria	Deficient Enzyme
Delta-aminolevulinate-dehydratase deficiency porphyria.	Delta-aminolevulinic acid dehydratase
Acute intermittent porphyria	Porphobilinogen deaminase
Hereditary coproporphyria	Coproporphyrinogen oxidase
Variegate porphyria	Protoporphyrinogen oxidase
Congenital erythropoietic porphyria	Uroporphyrinogen
Porphyria cutanea tarda	Uroporphyrinogen decarboxylase (~75% deffciency)
Hepatoerythropoietic porphyria	Uroporphyrinogen decarboxylase (~90% deffciency)
Erythropoietic protoporphyria	Ferrochelatase (~75% deffciency)

2. HistoryandEpidemiology

History: The disease was described at least as early as 370 BC by Hippocrates.The underlying mechanism was first described by Felix Hoppe-Seyle in 1871and acute porphyrias were described by the Dutch physician Barend Stokvis in 1889 The links between porphyrias and mental illness have been noted for decades. In the early 1950s, patients with porphyrias (occasionally referred to as "porphyric hemophilia") and severe symptoms of depression or catatonia were treated with electroshock therapy.

Epidemiology:

- The most common porphyria (PCT) has a prevalence of 1 in 10,000 people.
- The most common acute porphyria (AIP) has a prevalence of about 1 in 20,000 people.
- The most common erythropoietic porphyria (EPP) affects between 1 in 50,000 to 75,000 people.
- CEP is extremely rare, with prevalence estimates of 1 in 1,000,000 or less.
- Only six cases of delta-aminolevulinic acid dehydratase deficiency porphyria are documented.
- Porphyria can appear in childhood, as seen in EPP, but the onset is usually between the ages of 20 and 40 and it affects women more than men.

3. Signs and Symptoms

Acute porphyrias

Signs and Symptoms of Acute Porphyria May Include; Severe abdominal pain, Pain in your chest, legs or back**,** Constipation or diarrhea,Nausea and vomiting,Red or brown urine,Mental changes, such as anxiety, confusion, hallucinations.

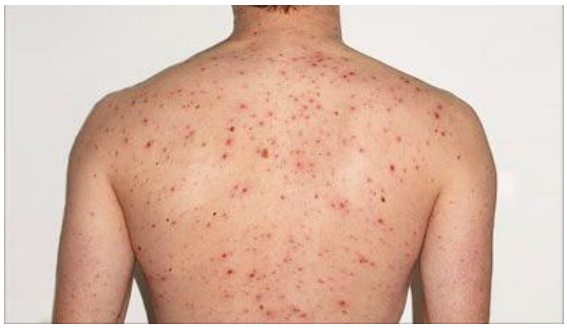

Fig 1: Symptoms of Porphyria affected body

Cutaneous porphyrias

Signs and Symptoms of Cutaneous Porphyria May Include: Sensitivity to the sun and sometimes artificial light, causing burning, Sudden painful skin redness (erythema) and swelling (edema), Blisters on exposed skin, usually the hands, arms and face**,** Fragile thin skin with changes in skin color (pigment)**,** Red or brown urine.

Causes[6]

Genitic forms:

Most forms of porphyria are inherited. Porphyria can occur if you inherit: A defective gene from one of your parents (autosomal dominant pattern) Defective genes from both parents (autosomal recessive pattern) Just because you inherit a gene or genes that can cause porphyria doesn't mean that you'll have signs and symptoms. You might have what's called latent porphyria, and never have symptoms. This is the case for most carriers of the abnormal genes.

Acquired forms:

Porphyria cutanea tarda (PCT) typically is acquired rather than inherited, although the enzyme deficiency may be inherited. Certain triggers that impact enzyme production such as too much iron in the body, liver disease, estrogen medication, smoking or excessive alcohol use can cause symptoms.

Pathophysiology of Porphyria[7]

Porphyrias present in 2 distinct syndromes,i.e., acute and chronic**.**

Acute porphyrias

The acute porphyrias are characterized by periodic acute attacks of neurovisceral symptoms and may stay occult for a long time. Four major disorders in this group are the Doss porphyria, acute intermittent porphyria, hereditary coproporphyria, and variegate porphyria. These porphyria syndromes are characterized by abdominal pain, neurologic deficits, psychiatric symptoms, and colored (red) urine.

Chronic porphyrias

The chronic porphyrias are dermatologic diseases that may or may not involve the liver and nervous system and do not present with acute attacks as described for the acute porphyrias above. These syndromes include congenital erythropoietic porphyria, erythropoietic porphyria, and porphyria cutanea tarda.

Other forms

[a] Doss porphyria / plumboporphyria:

Doss porphyria, also known as plumboporphyria (ALA dehydratase deficiency), is extremely rare. Abdominal pain and polyneuropathy are typical of this syndrome. Urinary ALA and coproporphyrin are markedly increased.

[b] Acute intermittent porphyria:

Acute porphyria attacks are brought about by uncontrolled upregulation of the ALA synthase enzyme. This can be precipitated by certain lipophilic drugs (see the Drugs to Avoid section), hypoglycemia ("the glucose effect"),and a deficiency of heme, the end-product of the heme pathway that acts as a negative feedback mechanism in normal circumstances.

[c] Erythropoietic porphyria:

Erythropoietic porphyria, the protoporphyrin molecule accumulates and can be excited by absorbing light energy. This causes the generation of free radicals and, thereby, photosensitivity of all tissues exposed to light.

[d]Porphyria cutanea tarda:

Porphyria cutanea tarda (PCT) is characterized by the defective uroporphyrinogen III decarboxylase enzyme. patients present with skin fragility, erosions, vesicles, bullae, and milia in sun-exposed areas of the skin.

[e]Congenital erythropoietic porphyria (Gunther's disease): Congenital erythropoietic porphyria, or Gunther's disease, is one of the least common porphyrias. It results from a deficient activity of uroporphyrinogen III synthase (URO-synthase).

Risk factors[8]

- Exposure to sunlight
- Certain medications, including hormone drugs
- Recreational drugs
- Dieting or fasting
- Smoking
- Alcohol use

4. Diagnosis

Diagnosis can be delayed because porphyria mimics the symptoms and signs of various other medical conditions such as Guillain-Barre syndrome, eczema, multiple sclerosis and irritable bowel syndrome.

Diagnostic tests may include,

- Physical examination
- Medical history
- Urine tests to check for elevated substances including porphyrins
- Blood tests to check for high levels of porphyrins in the plasma
- Stool sample to check for excreted porphyrins
- Genetic test.

Life Style Changes[10]

Depending on the type of porphyria, the following lifestyle changes will be recommended by your physician.

- Abstaining from alcohol.
- Avoiding those drugs that may trigger an attack.
- Avoiding any damage or injury to the skin.
- Staying away from sunlight as much as possible and using sunscreen whenever outdoors.
- Learn what could trigger symptoms
- Wear a medical alert bracelet or necklace

Prevention[11]

Primary Prevention:

Generally, a well-balanced diet containing enough calories to maintain body weight and 60% to 70% of total calories as carbohydrate is recommended. Cyclic attacks in women can be prevented by giving a gonadotropin-releasing hormone (GnRH) analog, which should be started during days 1 to 3 of the menstrual cycle.

Secondary Prevention:

Prevention of further attacks requires education of patients and their family members and physicians.Precipitating factors should be identified and avoided. Medical alert bracelets and wallet cards can remind patients and medical personnel of the diagnosis when other illnesses develop and during emergencies.

Managment[12]

Acute porphyria

[a] Carbohydrates and heme:

A high-carbohydrate diet is typically recommended; in severe attacks, a dextrose 10% infusion is commenced, which may aid in recovery by suppressing heme synthesis, which in turn reduces the rate of porphyrin accumulation.

[b] Symptom control:

Pain is severe, frequently out of proportion to physical signs, and often requires the use of opiates to reduce it to tolerable levels. Pain should be treated as early as medically possible. Nausea can be severe; it may respond to phenothiazine drugs but is sometimes intractable

[c] Early identification:

It is recommended that patients with a history of acute porphyria, and even genetic carriers, wear an alert bracelet or other identification at all times.

[d] Seizures:

Seizures often accompany this disease. Most seizure medications exacerbate this condition. Treatment can be problematic: barbiturates especially must be avoided. Some benzodiazepines are safe and, when used in conjunction with newer anti-seizure medications such as gabapentin, offer a possible regimen for seizure control.

Erythropoietic porphyria:

These are associated with accumulation of porphyrins in erythrocytes and are rare. The pain, burning, swelling, and itching that occur in erythropoietic porphyrias generally require avoidance of bright sunlight. Most kinds of sunscreen are not effective, but SPF-rated long-sleeve shirts, hats, bandanas, and gloves can help.

5. Treatment

Treatment – acute porphyria

Treatment may include: Pain medication Addressing the underlying cause – for example, prescribing antibiotics to treat an infection or ceasing a particular medication Medication called ‘hematin’, which is a type of heme the body can use Intravenous fluids and glucose Admission to hospital in severe cases [25].

Treatment – cutaneous porphyria

Treatment may include: Oral administration of activated charcoal, which helps to absorb excess porphyrins Daily supplementation with beta-carotene (vitamin A) as part of long-term treatment.

Porphyria Herbal Cure Treatment

Porphyria Herbal Cure Treatment combined with preventive measures, can in this manner go far in effectively regarding intense porphyria and also dealing with the medical condition on a long long-term basis. Herbs Solutions By Nature recommend ‘’ Phrenaton‘’ made with herbal extract it’s safe and effective in Porphyria Treatment without surgery.

Medical treatment

Therapeutic phlebotomy reduces iron stores, which improves heme synthesis disturbed by ferro-mediated inhibition of uroporphyrinogen decarboxylase (UROD). The goal of therapy is to reduce serum ferritin levels to the lower limit of the reference range.Venesections may be scheduled at intervals ranging from a unit of whole blood removed twice weekly to every 2-3 weeks as tolerated by the patient. Care should be taken to not induce anemia (hemoglobin < 10-11 g/dL). Phlebotomy is the preferred therapy for individuals with a heavy iron burden.

Efficacy of antihepatitis C therapy appears to be enhanced if hepatic siderosis is first reduced by phlebotomy. For patients in whom phlebotomy is not convenient or is contraindicated or for patients with relatively mild iron overload, oral chloroquine phosphate (125-250 mg PO twice weekly) or hydroxychloroquine sulfate (100-200 mg PO 2-3 times/wk)

6. Conclusion

In short, porphyria does not occur merely due to genetic factor, it will only trigger in the presence of both genetic and environmental factor. The treatment depends on the symptoms of porphyria that the patients have. Although porphyria usually cannot be cured, certain lifestyle changes may help to manage it. Undeniably, in most cases, people with AIP are capable of leading a normal healthy life. Despite that, they should be persistent in controlling their lifestyle, alcoholism and smoking must be avoided. Based on the case studies, it shows that patients with AIP are able to recover and lead a normal life after receiving the treatments. As an individual become older, the chance of experiencing acute attack reduces. However, the acute attack will still remain with the person and will not disappear in one's whole life.

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