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Artículo original

Hereditary porphyrias: A prospective, 28-year, single institution experience

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RESUMEN

Antecedentes: hay muy poca información sobre porfirias hereditarias en México. En la literatura internacional solo hay cuatro trabajos, escritos por autores mexicanos, publicados sobre el tema.
Objetivo: analizar la experiencia obtenida en un lapso de 28 años en los Laboratorios Clínicos de Puebla, con los estudios de laboratorio orientados a diagnosticar y a clasificar las porfirias hereditarias.
Material y métodos: entre octubre de 1983 y septiembre de 2010 se diagnosticaron y clasificaron casos de porfiria hereditaria empleando los siguientes métodos: desaminasa del porfobilinógeno en sangre, acido delta-amino levulínico en orina, deshidratasa de ácido delta-amnolevulínico en sangre, porfobilinógeno en orina, uroporfirinas en orina, coproporfirinas en orina, porfirinas fecales y protoporfirina libre en eritrocitos.
Resultados: se identificaron 147 casos de porfiria hereditaria empleando las pruebas antes descritas:

	n	*%*
Porfiria aguda intermitente	59	40
Porfiria variegata	36	25
Porfiria eritropoyética	22	15
Coproporfiria	17	12
Porfiria cutánea tarda	8	5
Protoporfiria	5	3
	147	

Conclusiones: se trata de la serie más grande informada en el país de porfirias hereditarias. La distribución de las variedades no es diferente de la informada en otros sitios del mundo.
Palabras clave: porfirias, Puebla, México.

ABSTRACT

Background: There is very little information about the hereditary porphyrias in México; only four papers by Mexican authors on the topic could be identified.
Objective: To analyze the 28-year experience in the diagnosis and classification of hereditary porphyrias in a single institution in México (Laboratorios Clínicos de Puebla).
Material and methods: Between October 1983 and September 2010, the diagnosis and classification of the hereditary porphyrias was done using the following assays: Blood porphobilinogen deaminase, urine delta aminolevulinic acid, blood delta aminolevulinic dehydratase, urine porphobilinogen, urine uroporphyrins, urine coproporphyrins, fecal porphyrins and red blood cell free protoporphyrins.
Results: One hundred and forty seven cases of hereditary porphyrias were identified and classified:

	n	*%*
Acute intermitent porphyria	59	40
Variegate porphyria	36	25
Erythropoietic porphyria	22	15
Coproporphyria	17	12
Porphyria cutanea tarda	8	5
Protoporphyria	5	3
	147	

Conclusions: This is the largest series of patients with porphyria described in México; the distribution of the variants is not different of that informed from other places in the world.
Key words: Porphyrias, Puebla, México.

Hereditary porphyrias are a group of metabolic disorders of the *haem* biosynthesis pathway, characterized by acute neurovisceral symptoms, skin lesions, or both. Every porphyria is caused by abnormal function of a separate enzymatic step, resulting in a specific accumulation of *haem* precursors. Acute porphyrias present with acute attacks, typically consisting of severe abdominal pain, nausea, constipation, confusion, and seizure, and can be life-threatening. Cutaneous porphyrias present with either acute painful photosensitivity or skin fragility and blisters. Infrequent recessive porphyrias usually manifest in early childhood with either severe cutaneous photosensitivity and chronic hemolysis or chronic neurological symptoms with or without photosensitivity. Diagnosis is essential to enable specific treatments to be started as soon as possible. Screening of families to identify carriers is crucial to decrease risk of overt disease of acute porphyrias through counselling about avoidance of potential precipitants.

The experience in diagnosing, classifying and treating porphyrias in México is very limited, and only three papers have been published on the topic by Mexican physicians.[2-4] We report here the 28-year experience in the diagnosis of porphyrias in Mexico of a single institution which is currently a national referral center for the diagnostic approach of these inherited disorders.

MATERIAL AND METHODS

Patients. All consecutive patients with an abnormal result in at least one of the porphyria tests (*vide infra*), obtained in *Laboratorios Clínicos de Puebla* (Clínica Ruiz, Puebla, México) between October 1983 and September 2010 were prospectively included in the study.

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Laboratory studies. The table 1 summarizes the laboratory studies performed to both diagnose and classify the hereditary porphyrias in *Laboratorios Clínicos de Puebla*. Examination of urine for excess porphobilinogen is the essential first-line test for patients with a suspected attack of acute porphyria. Measurement of 5-aminolaevulinic acid is not essential to establish the diagnosis but can be helpful for differentiation of the disorder from other metabolic causes of abdominal pain, eg, lead poisoning or the rare 5-aminolaevulinic acid dehydratase porphyria. Urinary porphobilinogen and 5-aminolaevulinic acid are increased in all three acute hepatic porphyrias (acute intermittent porphyria, hereditary coproporphyria, and variegate porphyria) although the concentrations are higher and longer lasting in acute intermittent porphyria than in the other two types (hereditary coporphyria and variegate porphyria). Measurement of urinary porphyrins is unhelpful and specific coproporphyrinuria in many common disorders. With a recorded porphobilinogen overexcretion, treatment can be started immediately, with further laboratory investigations used to define the porphyria type in the proband. For diagnosis of the type of acute porphyria in the proband, plasma fluorescence emission spectroscopy is a first-line test because a peak at 624-628 nm establishes the diagnosis of variegate porphyria. However, it does not distinguish acute intermittent porphyria from hereditary coproporphyria, for which the emission peak at 620 nm is usually present for both types. Urinary porphyrin analysis alone is not sufficient for discrimination. Total fecal porphyrin concentration is increased in variegate porphyria, with

Table 1. Laboratory tests conducted at *Laboratorios Clínicos de Puebla* to both diagnose and classify hereditary pophyrias

Test	*Method*	*Reference*
Blood porphobilinogen deaminase	Spectrophotometry	3
Urine delta aminolevulinic acid	Spectrophotometry	5
Blood delta aminolevulinic dehydratase	Spectrophotometry	6
Urine porphobilinogen	Spectrophotometry	5
Urine uroporphyrins	Spectrophotometry	7
Urine coproporphyrins	Spectrophotometry	7
Fecal porphyrins	Ultraviolet observation	7
Red blood cell free protoporphyrins	Spectrophotometry	8

protoporphyrin concentrations (protoporphyrin IX) greater than those for coproporphyrin whereas it is usually normal in acute intermittent porphyria. Total fecal porphyrin concentration is raised in hereditary coproporphyrin as the main a ratio of isomer III to isomer I greater than 2. A 50% decrease of porphobilinogen-deaminase activity can positively identify acute intermittent porphyria patients.[3]

RESULTS

A total of 147 patients with an hereditary form of porphyria were identified in this 28-year period; only one case of acquired porphyria in the setting of pancreatic carcinoma was identified. The table shows the distribution of these findings. It is clear hat the most frequent form of porphyria identified in this single-institution experience was acute intermitent porphyria, followed by variegate porphyria (see table 2).

Table 2. Classification of the 147 cases of hereditary porphyrias prospectively identified in *Laboratorios Clínicos de Puebla* along a 28-year period (n = number of cases)

Porphyria	*n*	*%*
Acute intermitent porphyria	59	40
Variegate porphyria	36	25
Erytrhropoietic porphyria	22	15
Coproporphyria	17	12
Porphyria cutanea tarda	8	5
Protoporphyria	5	3
	147	

DISCUSSION

Porphyrias are still underdiagnosed, but when they are suspected, and dependent on clinical presentation, simple first-line tests can be used to establish the diagnosis in all symptomatic patients. Since our laboratory has become a national reference center for the diagnosis of these inborn errors of metabolism, the clinical information about the patients is not fully available. Samples are received in our facilities and results are provided to the referring physicians who engage into therapeutic activities which are not available to us. The distribution of the variant of the inherited porphyrias in México which we have identified is not significantly different than those described in other populations.[1] These data indicate that hereditary porphyrias are not infrequent in México and that these diseases should be borne in mind in cases characterized by acute neurovisceral symptoms, skin lesions or both. Further studies about the distribution of these inborn errors of metabolism in our country are needed.

REFERENCES

1. Puy H, Gouva L, Deybach JC. Porphyrias. Lancet 2010;375(9718):924-937.
2. Sánchez-Anzaldo FJ, Ruiz-Argüelles GJ, Ortiz López R. Erythropoietic protoporphyria. Description of the first case identified in Mexico. Sangre (Barc). 1987;32(2):236-242.
3. Vázquez-Prado J, Sánchez-Anzaldo FJ, Ruiz-Argüelles GJ, Marín-López E, Lobato-Mendizábal E. A modified spectrophotometric assay for porphobilinogen deaminase: its application in the detection of both carriers and patients with acute intermittent porphyria. J Inherit Metab Dis. 1995;18(1):66-71.
4. Jara-Prado A, Yescas P, Sánchez FJ, Ríos C, Garnica R, Alonso E. Prevalence of acute intermittent porphyria in a Mexican psychiatric population. Arch Med Res. 2000;31(4):404-8.
5. Talman EL. Standard methods of clinical chemistry. Maryland: Academic Press, 1958; pp: 137-146.
6. David Glick [editor]. Methods of biochemical analysis, volume 8. New York: Interscience Publishers, 1960; pp: 221-293.
7. Tietz NW. Química clínica moderna. 1.ª ed. Ciudad de México: Editorial Interamericana, 1972; pp: 137-146.
8. Bauer JD, Ackerman PG, Toro G. Bray's clinical laboratory methods. St. Luois: Mosby Company, 1968; pp: 41-45.