Coexistence of Hereditary Coproporphyria and Epilepsy:
Coproporphyrinogen Oxidase Deficiency in Liver and Kidney

M. Doss*, R. von Tiepermann, and K.-H. Pflüger

Clinical-Biochemical Research Department and Medical Clinic of the University Hospital, Faculty of Medicine of the Philipp University, Deutschhausstr. 17½, D-3550 Marburg, Federal Republic of Germany

Summary. An acute hepatic porphyria of the hereditary type was found in a 28-year-old woman with tetraplegia and respiratory paralysis, who had had epilepsy diagnosed 6 years previously. The diagnosis of porphyria was established by high excretion of urinary δ-aminolevulinic acid, porphobilinogen and coproporphyrin III as well as of biliary coproporphyrin III. Coproporphyrinogen oxidase activity was decreased in liver and kidney, whereas δ-aminolevulinic acid synthase activity was much increased. The patient had been ill for the past 12 years: neurologic-psychiatric, gastroenterologic, gynecologic, and urologic diagnoses were made and followed by corresponding therapeutic measures including nine operations.

Key words: Porphyria acute hepatic – Coproporphyria hereditary – Coproporphyrinogen oxidase – Epilepsy – Tetraplegia


Introduction

Hereditary coproporphyria (HCP) is an autosomal dominant inherited disorder characterized by an abnormal hepatic and renal excretion of coproporphyrin and

* Corresponding author
deficient activity of the mitochondrial enzyme coproporphyrinogen oxidase [6, 12, 26]. It belongs, together with acute intermittent porphyria (uroporphyrinogen synthase deficiency) [25] and variegate porphyria (protoporphyrinogen oxidase deficiency) [5], to the group of acute hepatic porphyrias. These are essentially regulatory disorders at the molecular level [9] and have characteristic features: drug idiosyncrasy, acute clinical syndrome with abdominal, cardiovascular, neurologic and psychiatric symptoms [29], enhanced urinary excretion of porphyrins and their precursors and, in variegate porphyria and coproporphyria, elevated fecal porphyrin excretion [10], together with enhanced inducibility of hepatic δ-aminolevulinic acid synthase due to partial enzyme deficiencies in the biosynthetic sequence, favorable response to glucose, hematin and propanolol [28], and persistence of latent phases [29]. The case with “kongenitaler Porphyrinurie mit Koproporphyrin in Urin und Stuhl” reported by Hijmans van den Bergh was probably the first observation and recognition of this disease [17]. Later on, Watson and co-workers [30] in their studies on coproporphyrin described in 1949 two patients suffering from “idiopathic coproporphyrinuria”, who probably both represent HCP cases in the subclinical phase. On the basis of family studies the disturbance was recognized as a hereditary porphyria by Goldberg and colleagues [14]. There then followed further reports on the occurrence of hereditary coproporphyria in Sweden [16], Denmark [20], South Africa [7], USA [31], France [26] and Germany [11]. Coexistence of acute hepatic porphyrias and epilepsy is rare. An association of HCP with epilepsy has only been found in one child so far [18]. We report a case of hereditary coproporphyria in a young woman with epilepsy and complex clinical history. Coproporphyrinogen oxidase deficiency could be demonstrated in liver and kidney.

Case Report

A 28-year-old female patient with tetraplegia and respiratory paralysis was admitted 1980 to the intensive care unit from another hospital. Inquiry revealed previous abdominal complaints, with nausea and vomiting as well as muscle weakness. The patient was unconscious and had to be respired; blood pressure was 140/80 mm Hg, pulse 110/min. Screening tests for porphobilinogen and porphyrins [8] were positive in the red-coloured urine sample. Differential diagnostic analyses produced results which were characteristic of HCP (Table 1). From other clinics and doctors we learned that the patient had been almost permanently ill and unable to work for the past 12 years. The “diagnoses” were made in clinics and out-patient-departments by physicians, especially specialists in gastroenterology, cardiology, gynaecology, neurology and psychiatry, surgery, urology and orthopaedics, radiology and clinical pathology during a period of 12 years are presented in Table 2, and largely represent the possible spectrum of wrong diagnoses in acute hepatic porphyria [10]. Owing to the recurrent abdominal symptoms, the patient had had several operations performed by gynaecologists and urologists, including an ophorohysterectomy and nephropexy. In 1974 discharges were found repeatedly by EEG; epilepsy was diagnosed and was treated with carbamazepine and primidone. In summary, the patient had been ill for the past 12 years, and had been treated in 14 different hospitals more than 20 times, where gastrointestinal, neurologic-psychiatric, gynaecologic and urologic diagnoses were made (Table 2): these were followed by therapeutic measures, including 9 operations.

Urinary porphyrin and precursor excretion was greatly elevated (Table 1). Under ultra-violet light the bile was a lustrous and fluorescent colour and contained an extremely high concentration of coproporphyrin isomer III (Table 1). A feces sample could not be obtained. The