Anémie hémolytique et photosensibilité chez un nourrisson
Hemolytic anemia and photosensivity in infant

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ABSTRACT

Congenital erythropoeitic porphyria (CEP) is a rare inherited metabolic disease which usually manifests in early childhood with severe cutaneous photosensivity , dark red urine and a variable degree of hematological involvement ranging from a mild hemolytic anemia to intrauterine hydrops fetalis. We report the case of a 4-month –old infant who was admitted for severe hemolytic anemia and red urines, she developed secondary severe cutaneous photosensitivity. The diagnosis of CEP was established on the basis of clinical symptoms and increased values of uroporphyrinogen and coproporphyrinogen in the plasma and urine.

Key words : congenital erythropoeitic porphyria; infant; physiopathology; management

INTRODUCTION :

Congenital eryhtropoeitic porphyria or Gunther disease, is one of the rarest of the porphyrias, with only about 150 reported cases to date [1].
The autosomal recessive disorder of porphyrin metabolism is due to the deficiency of uroporphynogen III cosynthase. The deficiency of this enzyme results in the accumulation of high amounts of uroporphyrin I and coproporhyrinogen I in all tissues with hematological involvement (hemolytic anemia and splenomegaly), severe cutaneous photosensivity and photomutilation , pink to dark discoloration of the urine , reddish –brown discoloration of teeth , also called erythrodontia , ocular complications and bone involvement. The only curative therapy for CEP is stem cell transplantation [2]. We report here a case of CEP in a 4-month- old -girl who was hospitalized for severe anemia associated to hematuria.

CASE REPORT :

A 4 month-old- girl who was full-term born vaginally without complications, was hospitalized to explore severe anemia and hematuria. She was the second child of un-related Tunisian parents. There was no family history of anemia and no consanguinity. She had a healthy sister who was aged 6 years.

Since birth, she has had red urines which was neglected by the parents, and at the age of 3 months, the parents remarked a pallor which worsened gradually.
On examination, a pallor and splenomegaly were noted without skin manifestations. We noted red urine. Urinalysis revealed hemoglobinuria. Her Laboratory investigations showed severe anemia (Hemoglobin: 6,4 g/dl, VGM : 78,4 fl, CCMH : 30,4g/dl) and elevated reticulocyte count (138000/mm3). Other investigations were done in order to evaluate this hemolytic anemia and they were normal: Hemoglobin electrophoresis, Pink test, quantitative G6PD test, negative direct antiglobulin test. Abdominal ultrasound found a splenomegaly and an infracentimetric gallbladder stone without renal abnormalities.
At the age of nine months, she developed skin ulcers with hypopigmentation scarring after sun exposure interesting particularly her face, hands and fingers. High concentrations of porphyrins in the urine and plasma (uroporphyrin, coproporphyrin I) confirmed the diagnosis of congenital erythropoetic porphyria. Molecular studies were not available in our country. Our patient was treated symptomatically (avoidance of sun or light exposure, sun pro-

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tection in summer, folate and vitamin D). Neither the parents, nor the sister was HLA class matched. After a follow up of two years, our patient has normal growth with multiples scars on the face and hands; she also had red urine, hypertrichosis and brown teeth (fig 1).

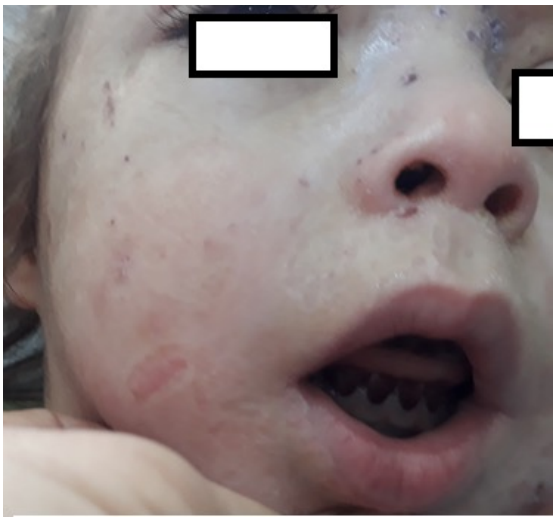

Figure 1 : hypopigmentation scarring and brown teeth

DISCUSSION :

CEP or Gunther's disease is one of the rarest porphyria's; it was first described in 1874 by Schultz [3] and was described in greater details by Gunther in 1911[4].

The disease results from decreased activity of uroporphyrinogen III cosynthase (UROS), the fourth enzyme of heme biosynthesis pathway, which normally converts hydroxymethylbilane (HMB) to uroporphyrinogen III. HMB accumulates and condenses spontaneously to uroporphyrinogen I which in turn can be decarboxylated to coproporphyrinogen I. Both uroporphyrinogen I and coproporphyrinogen I accumulate in the bone marrow, erythrocyte, plasma, bones and teeth where they are metabolized to uroporphyrin I and coproporphyrin I and are excreted in feces and urine [2,5].

CEP usually manifests in early childhood with diverse clinical symptoms of variable severity. The first manifestation is often pink to dark red discoloration of the urine, which can be confused with hematuria. Hemolytic anemia is common and can be mild to severe, requiring chronic blood transfusions [5]. Secondary splenomegaly may develop as a consequence of hemolytic anemia which can worsen the anemia and can also lead to leukopenia and thrombocytopenia. During her follow up, our patient had mild anemia (9- 10 g/dl) and she required only two blood transfusions.

Cutaneous photosensivity is present at birth or early infancy; it's characterized by blistering and increased friability of the skin over light exposed areas (face, hands and fingers), hypertrichosis of the face and extremities may occur. Our patient developed skin manifestations at the age of nine months; it may be due to the absence of sun exposure during the first months of her life.

Deposition of porphyrins in different tissues, may lead to corneal ulcers and scarring, which can ultimately lead to blindness [5], reddish-brown color of teeth, termed erythrodontia and bone loss. Vitamin D deficiency can occur in patients with CEP because of the avoidance of sunlight.

The diagnosis of CEP is supported by biochemical testing (elevated uroporphyrin I and coproporhyrin I levels in erythrocytes, plasma, urine and feces and / or decreased (URO)- synthase activity in erythrocytes) and confirmed by molecular studies [5].

The diagnosis in our patient was established on the basis of clinical symptoms and markedly increased values of urinary uroporphyrin I and coproporphyrin I.

To date , no curative therapy is known, preventive measures include absolute avoidance exposure of sunlight and skin trauma , sun protection, blood transfusion if severe anemia, splenectomy to decrease anemia and thrombocytopenia . The most effective treatment, described in the literature, was bone marrow transplantation [2].

CONCLUSION :

CEP porphyria is a rare inherited disorder; it must be considered in children presenting haemolytic anemia and skin manifestations. The management of CEP is difficult because of the multi-organ impairment.

Disclosure of interest

The authors declare that they have no competing interest

REFERENCES :

[1] Wiederholt T, Poblete-Gutiérrez P, Gardlo K and al. Identification of mutations in the uroporphyrinogen III cosynthase gene in german patients with congenital erythropoeitic porphyria. Physiol.Res 55: S85-S92, 2006.

[2] Shaw PH, Mancini AJ, Mc Connell JP, Brown D, Kletzel M. Treatment of congenital eythropoeitic porphyria in children by allogeneic stem cell transplantation: a case report and review of the literature

[3] Shultz JH. Ein Fall von pemphigus leprosus, compliciert durch Lepra visceralis. Greisfswald 1874:863

[4] Gunter H. Die haematoporphyriae. Deutsche Arch Klin Med 1911;105:89-146

[5] Erwin A, Balwani M, Desnick RJ; porphyrias consortium of the NIH-sponsored Rare diseases clinical Research Network. Congenita Erythropoeitic porphyria. 2013Sep 12