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CONGENITAL ERYTHROPOIETIC PORPHYRIA*

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Congenital erythropoietic porphyria, also known as Günther's disease, is the rarest type of porphyria. The disease was first described by Günther in 1911[1-3]. Up to 1979[2], less than 150 cases had been reported anywhere in the world. The disease is characterized by the onset, in infancy, of cutaneous photosensitivity, erythrodontia which is fluorescent under Wood lamp, splenomegaly, the excretion of red urine and the presence of excessive uroporphyrin and coproporphyrin in the blood, urine and stools[1-6].

The disease is a recessive autosomal disorder, that is often seen in children of consanguineous marriages[1-4,7].

Erythrodontia, cutaneous photosensitivity and red urine are due to excessive amounts of uroporphyrin I, a biologically useless isomer that cannot be converted to heme in human beings[1-3,6]. Studies with fluorescence microscopy have shown that the excess porphyrin is formed in red cell precursors in the bone marrow[8,9].

Anemia is a significant clinical feature of Günther's disease, although little is known about the pathogenesis of the anemia[7,10]. Kinetic studies have suggested that both shortened red blood cell survival and ineffective erythropoiesis play a role in the pathogenesis of the anemia[11,12]. Anisocytosis, poikilocytosis, polychromasia, basophilic stippling and nucleated erythrocytes appear to be fairly common features of the peripheral blood smears of patients with congenital erythropoietic porphyria[1,10]. Morphological abnormalities of the bone marrow have ranged from erythroid hyperplasia to degenerative changes in the erythropoietic cells[7,9,10].

The fundamental defect responsible for this disease has not yet been elucitated. It has been suggested that the increase of type I isomers in this disease results from an imbalance between the activity of uroporphyrinogen I synthetase and uroporphyrinogen III cosynthetase, with the former reaction relatively more active than the latter[2,3,13-15].

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It seemed worthwhile to present this case of a patient with the classical clinical and biochemical features of congenital erythropoietic porphyria since so few such cases have been fully reported.

Case Report

A.Y., a 17-month-old boy was admitted to the pediatric service of the Research Hospital of Atatürk University on account of his urine being red, his teeth being discolored a dirty brown and because there were lesions on the exposed parts of the body. It was learned that his urine had been red from birth, that his teeth had been a dirty brown when they first appeared and that he began to have vesiculo-bullous lesions of the skin on his arms and face following exposure to sunlight when he was one year old. It was noted that he was the child of a consanguineous marriage. He had three sisters. One of them died of a similar clinical condition at the age of three.

In the physical examination the boy was found to have hyperpigmented macules with mild scarring and vesiculo-bullous lesions on the dorsal aspects of the hands and also on the face (Figure 1). Moreover, the patient was extremely pale. The teeth were a dirty-brown and fluoresced under a Wood lamp (Figure 2). The liver was distinctly palpable 3 cm below the right costal margin and the spleen extended 5 cm below the left costal margin. The remainder of the physical examination findings

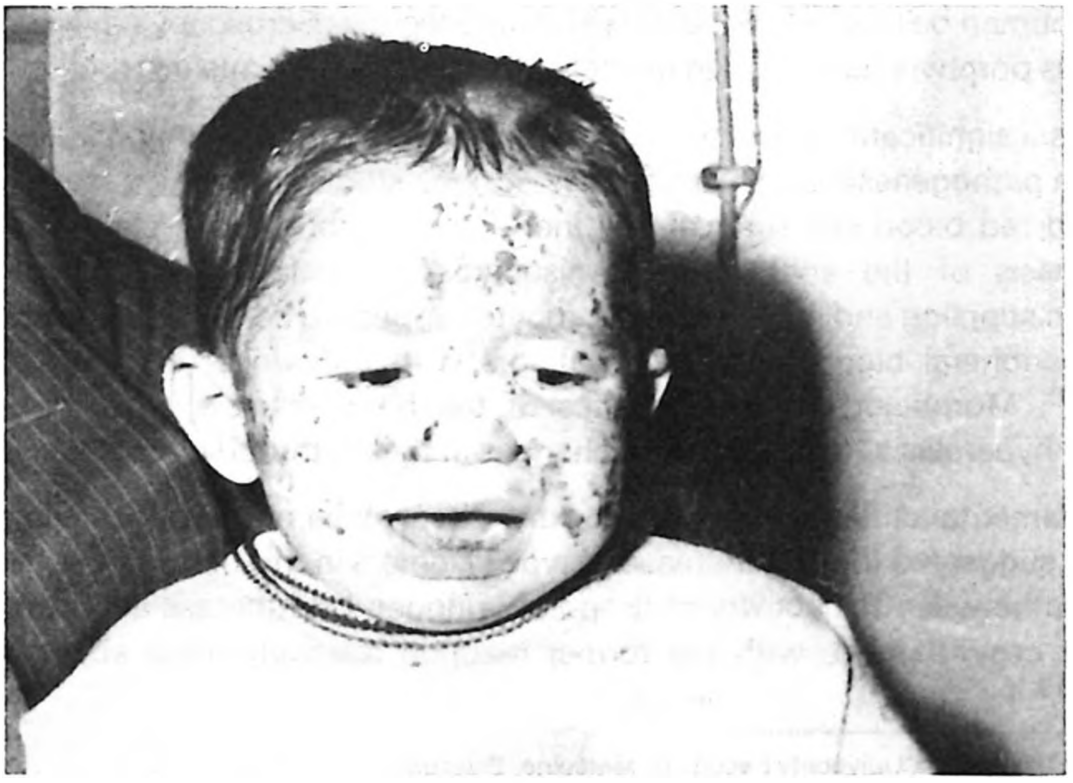

Figure 1

Skin lesions of the photosensitivity type in erythropoietic porphyria in a 17-month-old boy.

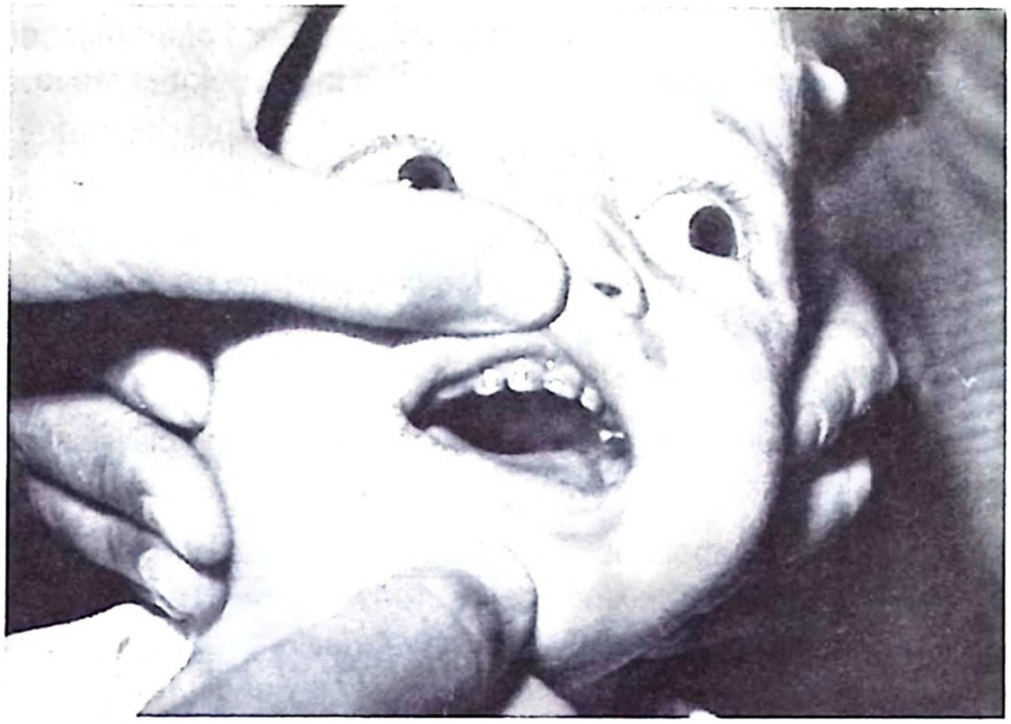

Figure 2

Erythrodontia in the same patient.

were unremarkable. As for the laboratory findings, Hb was 6,8 gm/dl, WBC was 12500/mm^3 with 45% bands, 30% polymorphonuclear leukocytes, 6% monocytes, 19% lymphocytes, RBC 2,7 million/mm^3, hematocrit 22%, reticulocyte 6,5%, platelets 124.000/mm^3, and the erythrocyte sedimentation rate was 60 mm in the first hour (Westergren). The peripheral blood smear showed that there was anisocytosis, poikilocytosis, polychromasia and leptocytosis. Occasional nucleated red blood cells were seen. There was normochromic anemia: MCV 81 μ^3, MCH 25,2 $\gamma\gamma$, MCHC 31%. The Coomb's test was negative. Osmotic fragility of the red cells was normal. Bone marrow studies showed a mild normoblastic erythroid cell hyperplasia. The serum iron concentration, the total iron binding capacity and transferrin saturation were all normal. The urine was red in color. The urine sediment was unremarkable. While the total porphyrin in the urine was (+ + +), uroporphyrin was (+ +), coproporphyrin was (+ +) and urobilinogen was negative. The daily excretion of uroporphyrin was 229,25 μgm (the normal being 5-30 μgm) [16]. In the stools, porphyrin was (+) but chlorophyll was (−).

Discussion

The history and clinical findings of the patient pointed to the fact that this was a typical case of congenital erythropoietic porphyria.

The mode of inheritance of this disease is autosomal recessive. The history of consanguinity in the parents together with the possible presence of a similar disease in a sibling are findings that are quite in keeping with this mode of inheritance.

The typical clinical findings of the patient after birth are similar to those of other cases in the literature[3,4,17-19]. However, a few cases occurring in adulthood, without features suggesting a porphyria, have been reported[12,19,20]. Not all porphyrias are hereditary. Some cases of acquired porphyrias due to hexachlorobenzene have been reported, but Doğramacı[21] has later shown that these may have been predisposed genetically.

The clinical findings of our patient were similar to those of the classical reports but the patient had no alopecia or hypertrichosis.

The most characteristic metabolic abnormality of the disease is the greatly increased urinary excretion of uroporphyrin I and coproporphyrin I[1-3,7]. This pattern of urinary porphyrin excretion is demonstrated both quantitatively and qualitatively. The presence of porphyrins in the stools is demonstrated only qualitatively.

The abnormal morphological findings in the peripheral blood of our patient included anisocytosis, poikilocytosis, polychromasia and, rarely, nucleated erythrocytes, and reticulocytosis. Abnormalities in the bone marrow included erythroid hyperplasia. All these abnormalities had previously been noted in patients with congenital erythropoietic porphyria and suggest a hemolytic process. The patient did not have jaundice and his serum bilirubin was normal. Very few instances of jaundice have been reported in conjunction with congenital erythropoietic porphyria.

The findings of a normal osmotic resistance in the erythrocytes and the fact that the Coomb's test did not come out positive are, as reported previously, suggestive of an intracorpuscular defect.

This form of porphyria is clinically and laboratory distinguishable from the other forms of porphyria.

Most of the porphyrias have a dominant inheritance, except congenital erythropoietic porphyria[2,4,7]. Erythropoietic protoporphyria usually manifests itself in childhood[7]. In this disease, skin lesions are usually less severe, hemolytic anemia is rare; erythrodontia is absent; the urinary excretion of uroporphyrin and coproporphyrin is not increased, and the color of the urine is normal[4,7]. Clinical symptoms of hepatic porphyria are rare before puberty and, in contrast to the erythropoietic form, neurological manifestations are frequently to be observed. There is, however, no increase of porphyrin precursors in the urine; further, hemolitic anemia is not found in conjunction with hepatic porphyrias[2,3,7].

Since there was no excessive hemolysis, the patient was given neither steroid therapy nor a splenectomy for the effects of these on the disease are variable:

Bhutani et al[6] noted that following splenectomy, the sensitivity of the skin to light was reduced although the metabolic abnormality remained unchanged. Aldrich et al[17] reported that after splenectomy, patients with hemolytic anemia and porphyrinuria improved. On the other hand, Gray and Neuberger[22], found no improvement in the hematological picture or the cutaneous photosensitivity of their patients following splenectomy.

In the treatment of anemia, prednisone therapy has been seen to be beneficial in some cases but not in others[24]. It has also been reported that hematin, given intravenously, is often successful in reducing the porphyrin level in urine, plasma and erythrocytes[25].

Summary

In this report a typical case of congenital erythropoietic porphyria is presented and compared with the findings of other cases of porphyria reported in the literature.

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