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G6PD Deficiency in Girls: About 2 Cases

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Abstract

Glucose-6-phosphate dehydrogenase (G6PD) deficiency, or Favism, is the most common erythrocyte enzymopathy in the world. It is a sex-linked genetic disorder, due to mutations in the G6PD gene (Xq28) and transmitted in an X-linked recessive manner. Hemizygous boys and homozygous girls fully express the deficiency, while in heterozygous girls, expression is variable, often absent or moderate. It can be responsible for severe neonatal jaundice and acute hemolytic crises when taking certain common drugs (some antimalarials, sulfonamides, analgesics), or during an infection.

Management aims to prevent hemolysis by informing patients about exogenous agents that can trigger crises. In this work we report two cases of female children of Moroccan nationality, with acute hemolytic anemia reported to be due to G6PD deficiency and followed at the Mohamed V military training hospital in Rabat.

This analysis helps to raise awareness among physicians of the need to consider G6PD deficiency in both boys and girls during a hemolytic crisis.

Keywords: *Hemolysis; Favism; G6PD; Girl*

Introduction

Glucose-6-phosphate dehydrogenase (G6PD) deficiency, or Favism, is the most common erythrocyte enzymopathy worldwide. It is a sex-linked genetic disorder, transmitted in a recessive manner. It is due to mutations in the G6PD gene (Xq28). Hemizygous boys and homozygous girls fully express the deficiency, while in heterozygous girls, expression is variable, often absent or moderate. It can be responsible for severe neonatal jaundice and acute hemolytic crises when ingesting certain foods (such as beans), taking certain common medications, or during an infection.

We report two cases of female children with acute hemolytic anemia related to G6PD deficiency and followed at the pediatrics department of HMIMV in Rabat.

Observations

Observation 1

16-month-old female infant, with no particular history, mixed breastfeeding since birth, diversified at the age of 6 months without incident, non-consanguineous parents, 2nd of a family of two with a healthy 7-year-old sister. Admitted to our department for anemic syndrome following the ingestion of beans. The clinical examination found a pale, tachycardic infant, respiratory stable and without hepatosplenomegaly. His biological examinations revealed: normochromic normocytic regenerative anemia with an Hb level of 8 g/dl, MCV: 74 fL, CCMH: 34%, reticulocyte level: 146000/mm, serum iron: 164 µg/dL, normal transaminases, normal ionogram, CRP 37 mg/L, alkaline phosphatase at 288 IU/L, total bilirubin: 28 mg/L, LDH: 1196 IU/L and haptoglobin < 0.08 g/L. The positive diagnosis was made by the enzymatic dosage of G6PD which returned to 8.4 U/gHb (N: 10 to 14.2). It is noted that the dosage of pyruvate kinase was normal. List of contraindicated medications and foods given to the parents. The outcome was favorable after transfusion of packed red blood cells.

Observation 2

4-year-old female child, with no significant history, exclusively breastfed, diversified diet at 6 months, non-consanguineous parents, 3rd of three siblings, in good health. Good height and weight development. Notion of taking beans 3 days before admission.

Admitted for asthenia associated with conjunctival pallor, cutaneous-mucosal jaundice and food vomiting, all developing in a context of apyrexia and preservation of the general condition. The clinical examination found a pale, tachycardic child, stable on the respiratory level and without hepatosplenomegaly. His biological examinations revealed: normochromic normocytic regenerative anemia with an Hb level of 6.2 g/dl, MCV: 75 fL, MCHC: 33%, reticulocyte level: 132000/mm, serum iron: 164 µg/dL, normal transaminases, normal ionogram, CRP 13 mg/L, alkaline phosphatase at 243 IU/L, total bilirubin: 60 mg/L, LDH: 934 IU/L and haptoglobin < 0.07 g/L. The etiological investigation, similar to the previous observations, found a G6PD deficiency at 7 U/gHb. The parents were informed of the diagnosis and the health record was completed. The evolution was favorable after transfusion.

Discussion

G6PD deficiency is due to a genetic abnormality in an enzyme involved in red blood cell metabolism. It catalyzes the first step of the pentose pathway and converts glucose 6-phosphate to 6-phosphogluconolactone, which classically hydrolyzes to 6-phosphogluconate [1].

This is a sex-linked genetic disease caused by an abnormal gene on the X chromosome (Xq28). Transmitted by mothers, boys always have G6PD deficiency if they carry a mutated G6PD gene whose clinical expression is variable. Girls, carrying two X chromosomes, can have a homozygous normal status, or a homozygous or heterozygous deficient status (Figure 1) [1].

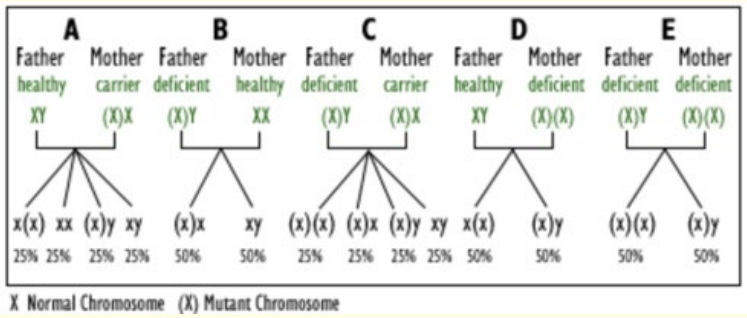

Figure 1: *Modes of transmission of G6PD deficiency.*

G6PD deficiency is a common condition, estimated to affect approximately 4 out of 1,000 people in the general population, with over 120 variants worldwide. The Mediterranean region, sub-Saharan Africa, the Americas (African and Hispanic populations), and Southeast Asia are the most affected regions.

WHO has established a classification of G6PD variants based on the value of activity compared to normal (Table 1). Moderate deficiency or class I (residual erythrocyte G6PD activity 10 to 40%), intermediate deficiency or class II (activity less than 10%) and severe deficiency or class III (activity less than 1%). Types IV, variants with normal activity, and type V which correspond to an overactivated enzyme, have no significance in pathology. Classes II and III are at risk of acute hemolytic accident in oxidative stress (dietary or drug) and neonatal jaundice. Class I is very rare with hemolytic anemia chronic non-spherocytic corpuscular disease present from birth [2].

Deficit class	Type of deficit	Residual erythrocyte G6PD activity
Class I	Severe deficit	< 1%
Class II	Intermediate deficit	< 10%
Class III	Moderate deficit	10 to 40%

Table 1: *WHO classification of G6PD deficiencies.*

The mutation responsible for G6PD deficiency replaces the amino acid Val431 with glycine, which destabilizes the molecule [3]. Early in embryonic development in females, one of the X chromosomes is inactivated. Thus, the expression of genes linked to X chromosome inactivation is random and depends on cellular selection [4]. There is a slight phenotypic difference in G6PD deficiency in women, which may be due to an *in vivo* interaction between two cell populations or to a common phenotypic variation, explaining the mildly symptomatic and asymptomatic forms [1]. Indeed, X chromosome inactivation may not be random or may be preferential, leading to phenotypic variation in G6PD activity in females [1]. Mothers of boys with type I deficiency are heterozygous carriers of the mutant but have normal G6PD activity because red blood cells expressing the mutated X are destroyed before entering the bloodstream.

Hemolysis occurs a few hours to three days after ingestion of certain foods (such as beans), taking certain common medications (certain antimalarials, sulfonamides, analgesics), or during an infection. Hemolysis can be very sudden with anemia of less than 5g of regenerative Hb/dl, jaundice, splenomegaly and abdominal pain. G6PD deficiency can manifest in girls from the neonatal period [1]. Hyperbilirubinemia, the main clinical manifestation in the neonatal period, can be severe with the risk of nuclear jaundice [5,6]. When a G6PD deficiency is discovered in a newborn, a family investigation is essential to screen the parents and siblings, leading to information and a broader family investigation. Nowadays, it is recommended to include girls in neonatal screening programs for G6PD deficiency and should be systematic in populations at risk. Our two patients did not have neonatal jaundice.

Diagnosis is based on the quantitative spectrophotometric assay of erythrocyte enzymatic activity, which remains the reference test. It determines the degree of severe or moderate deficiency according to the percentage of enzymatic activity measured as well as partial deficiencies with an efficiency of 80%. Screening in heterozygous girls is complex. Heterozygosity may not be detected by quantitative screening techniques. G6PD activity assay may be falsely normal, especially in cases of high reticulocytosis [7]. Only the molecular technique by PCR would make it possible to distinguish deficient girls by highlighting genetic mutation(s) on the DNA [8]. Molecular diagnosis is also useful in cases of blood transfusion preventing enzymatic dosage.

The presence of Heinz bodies sought on the smear by staining with cresyl blue or methyl violet, the presence of ghost red blood cells or even bitten or pinched red blood cells are suggestive.

Management aims to prevent hemolysis by informing patients about exogenous agents that can trigger crises. Some are dangerous, others are contraindicated, except in the absence of alternative treatment and then, under strict medical supervision. Finally, some are only dangerous if the usual daily dose is exceeded. The prognosis depends on screening, because it allows to be well aware of dangerous drugs and foods and to do everything to avoid them, thus avoiding acute hemolytic anemia.

Conclusion

G6PD deficiency is the most common erythrocyte enzymopathy in the world, can affect both sexes. It can be responsible for acute hemolytic accidents and severe hyperbilirubinemia in the neonatal period, indicating in family survey to screen asymptomatic parents and siblings.

Consent

In accordance with international or academic standards, written parental consent was collected and preserved by the authors.

Ethics Approval

In accordance with international or academic standards, written ethical approval was obtained and maintained by the authors.

Correspondence of Interests

The authors declare that they have no conflicts of interest to report.

Bibliography

1. Renaulta A., *et al*. "G6PD deficiency in girls with neonatal revelation. Review of 4 clinical cases". *Archives of Pediatrics* 24.9 (2017): 865-871.

2. WHO Working Group. "Glucose-6-phosphate dehydrogenase deficiency". *Bulletin of the World Health Organization* 67.6 (1989): 601-611.

3. Naylor CE., *et al*. "Glucose 6-phosphate dehydrogenase mutations causing enzyme deficiency in a model of the tertiary structure of the human enzyme". *Blood* 87.7 (1996): 2974-2982.

4. Sara TO Saad and Fernando FC. "Mild hemolysis in a girl with G6PD Sumaré (class I variant) associated with G6PD A-". *Blood Cells, Molecules, and Diseases* 30.3 (2003): 238-240.

5. Zangen S., *et al*. "Fatal kernicterus in a girl deficient in glucose-6-phosphate dehydrogenase: A paradigm of synergistic heterozygosity". *Journal of Pediatrics* 154.4 (2009): 616-619.

6. Herschel M., *et al*. "Hemolysis and hyperbilirubinemia in an African American Neonate heterozygous for Glucose-6-phosphate dehydrogenase deficiency". *Journal of Perinatology* 22.7 (2002): 577-579.

7. Watchko JF. "Hyperbilirubinemia in African American neonates: clinical issues and current challenges". *Seminars in Fetal and Neonatal Medicine* 15.3 (2010): 176-182.

8. Kaplan M and Hammerman C. "Neonatal screening for Glucose-6-phosphate dehydrogenase deficiency: biochemical versus genetic technologies". *Seminars in Perinatology* 35.3 (2011): 155-161.

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