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Case Report

Glucose-6-phosphate Dehydrogenase Deficiency: A Case Report

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Abstract:

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common hereditary enzyme disorder and more than 200 million people have a deficiency in this enzyme. G6PD deficiency is an X-linked enzyme defect, and one of its main signs is the presence of hemolytic anemia. It is a worldwide important cause of neonatal jaundice and causes life threatening hemolytic crisis in childhood. At later ages, certain drugs such as anti-malarial drugs and fava beans cause hemolysis among G6PD deficiency patients. The frequency and severity is influenced by genetic and cultural factors. It is common in Mediterranean, African and some East Asian populations but rare in Bangladeshi peoples. Genetic counseling may be of benefit for patients and their families. Other treatment is symptomatic and supportive.

Key words: Hemolytic Anemia, Glucose-6-Phosphate Dehydrogenase Deficiency (G6PD).

Introduction:

Hemolytic anemia in certain susceptible individuals after ingestion of anti-malarial drugs was first reported in 1926. In the 1950s the cause of the hemolysis was considered to be inside the red cells. It has been proved that the cause of hemolysis is due to the decreased level of glucose-6 phosphatase dehydrogenase (G-6PD)) in the red cells. Now a days, G-6PD deficiency is the most common hereditary enzyme deficiency, causing hemolysis. Glucose-6-phosphate dehydrogenase (G6PD) deficiency affects over 200 million people around the world[1]. Its frequency is relatively high among African, Americans in the United States (13%) and populations in the Mediterranean (5 to 40%). G6PD deficiency is an X-linked enzyme defect, and one of its main signs is the presence of hemolytic anemia. Hemolysis may be triggered by infection and by drugs with oxidative properties, such as acetyl salicylic acid, vitamin K, chloramphenicol and antimalarial drugs[2]. G6PD present in neutrophils and erythrocytes is coded by the same gene[3], located in the Xq28 chromosome. Over 200 mutations have been reported[4]. Extremely low levels of G6PD (more than 5% below normal) in neutrophils may be observed in association with rare mutations, causing failure of oxidative metabolism and a consequent reduction in oxygen-dependent phagocytosis.

In the present article, we describe the case of a patient with increased G6PD deficiency in erythrocytes and recurrent infections.

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Case Report

A four years old girl was admitted at department of pediatrics of Faridpur Medical College Hospital, Faridpur because of fever, cough, and sputum for three days and gross hematuria for one day. She is the second girl of two sibling. Prior to this admission, she was admitted due to hemolytic anemia with acute tonsillitis one and half years back.

On admission, she looked actually ill, the conjunctivae were pale, the sclera were icteric and throat was infected. The lung sound was coarse and the liver and spleen were not palpable. The laboratory findings are as follows (Table-I): Hb 7.8 gm/dl, Hct 27.3%, reticulocyte count 3.6%, haptoglobin was under 37 mg/dl and there was a picture of hemolytic anemia. The chest X-ray showed pneumonic consolidation on left

lower lobe and the peripheral blood smear showed microcytic hypochromic anemia, nucleated RBCs, polychromasia, spherocytosis and anisocytosis. The bone marrow examination showed hyper-cellularity with M:E ratio of 1:1 and erythroid hyperplasia. On urinalysis, RBC was (++) and protein was (+++). The cold agglutinin test and Coombs' test were negative. On the G-6 PD Assay (Dye reduction test) by SIGMA kit, normal control was 30 minutes. However the patient time was prolonged to 6 hours. On the quantitative test for G-6-PD, normal value was 4.60 - 13.50 U/ g Hb but the patient's value was 2.11 U/ g Hb.

Table- I: Laboratory findings of G-6PD deficiency patient.

Investigations	Value
Hb (gm/dl)	7.8
Hct (%)	27.3
MCV (fl)	99.9
MCHC (gm/dl)	32.8
RDW (%)	13.3
Reticulocyte count (%)	3.6
Total bilirubin/Direct bil. (mg/dl)	3.4/0.4
Haptoglobin (mg/dl)	<37
SGPT/SGOT (U/dl)	119/22
Coombs test	Negative
G6PD Assay (U/g Hb)	2.11

Discussion:

Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency (G6PDD) is an inherited, sex-linked, metabolic disorder characterized by an enzyme defect that leads to the breakdown of red blood cells (hemolysis) upon exposure to stresses associated with some bacterial infections or certain drugs. A deficiency of this enzyme may result in the premature destruction of red blood cells (an acute hemolytic anemia or a chronic spherocytic type) when an affected individual is exposed to certain medications or chemicals, experiences certain viral or bacterial infections, and/or inhales the pollen of, or consumes, fava beans (favism). Glucose- 6-Phosphate Dehydrogenase Deficiency is inherited as an X-linked genetic trait[5]. It is a common inborn error of metabolism among humans. More than 300 variants of the disorder have been identified, resulting from mutations of the Glucose-6-Phosphate Dehydrogenase gene. The severity of symptoms associated with G6PD Deficiency may vary greatly among affected individuals, depending upon the specific form of the disorder that is present. Neonatal G6PDD is particularly dangerous to an infant. It is manageable if diagnose early, and screening for the disorder is common[6]. The role of the enzyme G6PD is to maintain the pathway to generate a chemical called glutathione, which in a particular form is an antioxidant. The antioxidant is necessary to protect the cell's hemoglobin and its cell wall (red cell membrane). If the level of antioxidant is too low, then the cell's hemoglobin will not bind oxygen (its main purpose); the cell wall will break allowing the cell contents, including the modified hemoglobin, to spill out[7].

The severity of symptoms associated with G6PDD varies greatly from case to case, depending upon the form of the disorder that is present, and some people have no symptoms at all. When symptoms are present, they may include fatigue, pale color, shortness of breath, rapid heartbeat, jaundice or yellow skin color, dark urine and enlarged spleen.

In the relatively rare, severe, potentially life-threatening cases, symptoms include, in addition to those listed above, others such as: blood in the urine (hemoglobinuria), shock, kidney (renal) failure and congestive heart failure in which the heart is unable to pump blood effectively throughout the body. Most affected individuals, when exposed to fava beans, will experience severe episodes of hemolytic anemia due to such exposure.

Chromosomes, which are present in the nucleus of human cells, carry the genetic characteristics of each individual. Pairs of human chromosomes are numbered from 1 through 22, with an unequal 23rd pair of X and Y chromosomes for males, and two X chromosomes for females. Each chromosome has a short arm designated as "p" and a long arm identified by the letter "q." Chromosomes are further sub-divided into many bands that are numbered. For example, "chromosome 11p13" refers to band 13 on the short arm of chromosome 11[8].

Human traits, including the classic genetic diseases, are the product of the interaction of two genes, one received from the father and one from the mother. Glucose-6-Phosphate Dehydrogenase Deficiency is inherited as an X-linked trait. The responsible gene has been mapped to Xq28[9].

X-linked recessive disorders are conditions that are coded on the X chromosome. Females have two X chromosomes, but males have one X chromosome and one Y chromosome. Therefore, in females, disease traits on the X chromosome can be masked by the normal gene on the other X chromosome. Since males only have one X chromosome, if they inherit a gene for a disease present on the X, it will be expressed. Men with X-linked disorders transmit the gene to all their daughters, who are carriers, but never to their sons. Women who are carriers of an X-linked disorder have a 50 percent risk of transmitting the carrier condition to their daughters, and a 50 percent risk of transmitting the disease to their sons[10].

In X-linked dominant disorders, the female with only one X chromosome affected will develop the disease. However, the affected male always has a more severe condition. Sometimes, affected males die before birth so that only female patients survive.

In some affected individuals, episodes of Hemolytic Anemia due to G6PD Deficiency may result from exposure to certain drugs. Such episodes may also result in some affected individuals due to diabetic acidosis, certain viral and bacterial infections, and/or exposure to fava beans or certain derivatives of Vitamin K[11].

As mentioned above, Glucose-6-Phosphate Dehydrogenase Deficiency is one of the most common forms of enzyme deficiency and is believed to affect approximately 400 million people worldwide. The highest prevalence rates are found in Africa, New Guinea, the Middle East, certain parts of the Mediterranean, and certain areas in Asia. In these regions, the rate ranges from 5% to 25% of the population[12].

Over 400 variants of the disorder have been identified, resulting from different mutations of the Glucose-6-Phosphate Dehydrogenase (G6PD) gene. In the United States, the incidence of G6PDD is much higher among the Afro-American population than in other sectors. The frequency of a carrier state in which one partner carries a normal gene and the other carries an abnormal variant is as high as 24%. About 10%-14% of Afro-American males are affected. For example, two common variants occur in many African-American males. Approximately 20 to 25 percent have the near normal G6PD variant called "A+", while about 10 to 13 percent have another variant called "A-". Another relatively common G6PD variant is found particularly among individuals of Sephardic Jewish or Sardinian descent. In addition, another somewhat common variant is present among some individuals of southern Chinese descent. In many cases, the disorder is not diagnosed because most individuals do not experience serious symptoms unless they are exposed to certain drugs (usually oxidants) or other specific stressors[13].

If jaundice and anemia occur together, a diagnosis of G6PDD is suspected. The diagnosis is confirmed by blood tests that determine the volume of red blood cells circulating. Further supporting evidence may be had by means of tests that measure the intensity of the enzyme activity it self[14].

Glucose-6-Phosphate Dehydrogenase Deficiency is best managed by preventative measures. Individuals should be screened for the G6PD defect before being treated with certain drugs such as anti-malarial and other medications. People with G6PD Deficiency should not eat fava beans. If an episode of Hemolytic Anemia is due to the use of certain medication, the causative drug should be discontinued under a physician's supervision. If such an episode is due to an underlying infection, appropriate steps should be taken to treat the infection in question. Some cases may require the administration of oxygen to the patient. Other patients may need short-term treatment with fluids or even blood transfusions. Neonatal jaundice is treated by placing the infant under special lights that alleviate the jaundice[15].

Genetic counseling may be of benefit for patients and their families. Other treatment is symptomatic and supportive.

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