



Glucose-6-Phosphatase Dehydrogenase Deficiency: Diagnosis at Presentation

Jaya Manchanda*, Ritu Gogia, Reena De, Prabhajyot Chopra

Department of Pathology, Star Imaging and Path Lab, New Delhi, India

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Abstract

Glucose-6-phosphate dehydrogenase (G6PD) deficiency, a most common enzyme deficiency worldwide, causes a spectrum of disease including neonatal hyperbilirubinemia with acute and chronic hemolysis. Persons with this condition also may be asymptomatic. This X-linked inherited disorder most commonly affects persons of African, Asian, Mediterranean or Middle-Eastern descent. Approximately 400 million people are affected worldwide. This is a case of a 37 year old man who presented with a typical clinical and haematological picture of favism. There was no initial difficulty in confirming G6PD deficiency because the enzyme concentrations were compatible with heterozygosity for G6PD deficiency. It is uncommon for the patient to present with low G6PD level at presentation; hence this case is being reported.

***Corresponding author:**

Dr Jaya Manchanda,
jaya87manchanda@gmail.com

Introduction

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is an inherited disease with a high prevalence in Africa, southern Europe, the Middle East, South East Asia and Oceania and in descendants of migrants from these areas. G6PD is a house-keeping enzyme that catalyzes the first step in the pentose phosphate pathway, providing reducing power in the form of nicotinamide adenosine dinucleotide phosphate (NADPH). This metabolic pathway is the only source of NADPH in erythrocytes and is therefore the mechanism by which the cell damage caused by oxidative stress is avoided [1,2]. Reduced concentrations of G6PD render red blood cells susceptible to haemolysis under conditions that occur when oxidant drugs are administered, fava beans are ingested or during infection.[1]

Case Report

A 37 year old man presented to the emergency department with few hour history of feeling restless, fatigued and severe abdominal pain associated with bouts of vomiting. He also noticed that he had yellowish discoloration of eyes and dark urine. He denied history of foreign travel or the usage of herbal medications or illicit drugs. On further questioning, he confessed consuming naphthalene balls 30 hours before his symptoms began. There was no history of neonatal jaundice and family history of jaundice or anaemia. On examination, his conjunctivae were pale and sclera icteric with mild pitting oedema of the ankles. His pulse was 104 beats/minute, regular with a blood pressure of 110/80 mm Hg. Oxygen saturation on room air was 100%. Examination of the cardiovascular, respiratory, and abdominal systems was normal. An ultrasound scan of the abdomen was normal. The serum of the patient showed evidence of hemolysis (Figure-1).



Figure1-Serum sample showing evidence of hemolysis

The patient's blood film at presentation showed micro-

cytic hypochromic cells with several polychromatic macrocytes and frequent irregularly contracted cells suggestive of oxidant induced red blood cell damage (blister cells) (Figure-2). Also noted 7 nRBCs/100WBCs. (Figure-3). Crystal violet staining showed presence of Heinz bodies (Figure-4). Haptoglobulins were absent from the serum on screening. LDH levels were increased and the urine sample (Figure-5) tested positive for hemoglobin.

While in hospital, the patient was transfused with six units of blood and his haemoglobin (Hb) rose to 14.7 g/dl. On admission, Hemoglobin was 6.4g/dl and the quantification of the serum levels of G6PD was 2.1 ug/Hb (normal range, 4.6–13.5 ug/ Hb) which rose to 6.7 ug/Hb when the tests were repeated the next day. Because of the classic clinical history, peripheral smear appearances and G6PD assay immediately after the acute hemolytic episode, a presumptive diagnosis of G6PD deficiency was made. The within range G6PD values the next day and low levels when the investigations were repeated six weeks later after presentation confirmed the diagnosis.

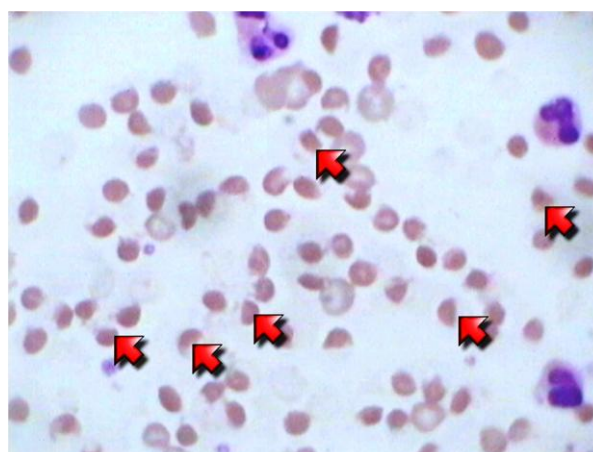


FIGURE 2-Peripheral smear show irregularly contracted cells (blister cells/hemi-ghost cells) as a result of oxidant damage.

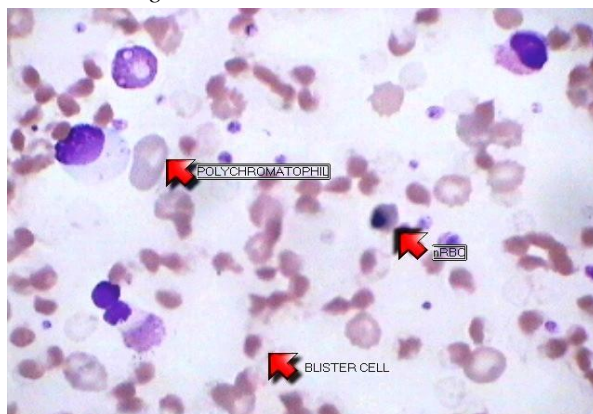


FIGURE 3- Peripheral blood picture shows nRBCs, polychromatophils and blister cells.

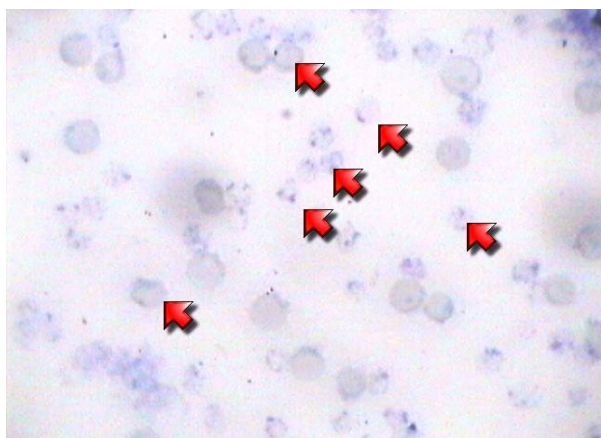


FIGURE 4- Crystal violet staining shows presence of Heinz Bodies



Figure 5-Cola colored Urine at presentation

Discussion

G6PD deficiency is the most common enzyme disorder and is distributed throughout the world affecting more than 200 million people.[5] In India, G6PD deficiency was reported more than 30 years ago and the frequency varies from 0 to 15% in different caste, ethnic, and tribal groups [6]. G6PD is the house keeping enzyme that is vital for the life of every cells. It converts glucose-6-phosphate to 6-phosphogluconolactone which is the first step in the hexose monophosphate (HMP) pathway and reduces the cofactor nicotinamide-adenine dinucleotide phosphate(NADP) to NADPH. G6PD deficiency affects every cell in the body but its primary effects are haematological.[4] This is because, in red cells, the HMP pathway is the only source of NADPH which is necessary to protect the cell and its hemoglobin from oxidation. Glutathione(GSH) repairs red cells when they are attacked by oxidative stress and is synthesized in red cells. Glutathione reductase and Glutathione peroxidase mediate the redox cycle of GSH and are closely related to G6PD.[5] G6PD is coded by genes located on X-chromosome. Inactivation of X-chromosome is essentially random during embryonic development and in heterozygous females, and the enzyme activity is inter-

mediate between that of deficient males and normal males.[7] The enzyme activity of homozygous females is as deficient and susceptible to oxidant drugs as to heterozygous males. The normal G6PD enzyme is genetically polymorphic and B form(G6PD B) is the most prevalent in all population groups. The A form (G6PD A) also has normal enzyme activity which has faster electrophoretic mobility and is common in some African populations. A large number of G6PD Variants are known and they are identified by the differences in enzyme activity, Michaelis constants(K_m) for Glucose-6-Phosphate, electrophoretic mobility, heat stability and pH optima. G6PD variants have been classified into 5 groups on the basis of 3 major criteria: clinical manifestation, enzyme activity and electrophoretic mobility. (Table 1). The common pathological variant are in class II and III.[8]

Class	Level of deficiency	Enzyme activity	Prevalence
I	Severe	<10% enzyme activity Chronic nonspherocytic hemolytic anemia in the presence of normal erythrocyte function	Uncommon; occurs across populations
II	Severe	<10% enzyme activity with intermittent hemolysis	Varies; more common in Asian and Mediterranean populations
III	Moderate	10–60% enzyme activity Hemolysis with stressors only	10% of black males in the United States
IV	Mild to none	60–150% enzyme activity No clinical sequelae	Rare
V	None	>150% percent of normal No clinical sequelae	Rare

G6PD - Glucose-6-phosphate dehydrogenase

The consumption of naphthalene balls prior to the episode of acute hemolytic attack explained the reason for its occurrence. Our objective for this case report is to encourage G6PD Deficiency screening not only to safeguard patients in clinical trials but also to better characterise and quantify drugs with hemolytic potential so that drugs can be used safely in public health settings.

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Competing Interests

None declared.

References

1. Beutler E: G6PD deficiency. *Blood* 1994, 84:3613-3636.
2. Luzzatto L, Mehta A, Vulliamy T: Glucose-6-phosphate dehydrogenase deficiency. In *The Metabolic and Molecular Basis of Inherited Disease* 8th edition. Edited by: Scriver ChR, Beaudet AL, Sly WS, Valle D. New York: McGraw Hill; 2001:4517-4553.
3. Seifert G, Sobin LH. The World Health Organization's Histological Classification of Salivary Gland Tumors. *Cancer* 1992;70:379-85.
4. Beutler E: Glucose-6-Phosphate Deficiency. *N Engl J Med* 1991; 324:169-174
5. Srivastava SK, Beutler E: Glutathione metabolism of the erythrocyte. The enzymatic cleavage of glutathione-hemoglobin preparations by glutathione reductase. *Biochem J* 119:353-361, 1970
6. Baxi AJ. G6PD deficiency. A note on the distribution of gene frequency in India. *Proc. 1st conf. Ind. Soc. Hum. Genet. Vol. 1 Human population genetics in India. Ms. Orient Longman Ltd.* p 60 1974.
7. Jandle JH: Heinz body hemolytic anemia. In Jandle JH, ed. *Blood; Textbook of Haematology* 1st ed. Boston/Toronto. Little, Brown and Company 1987, 335-350.
8. Beutler E: Glucose-6-Phosphate Deficiency. IN Stanbury JB et al. ed. *The metabolic basis of inherited disease*, 3rd ed. New York, McGraw Hill, 1972.