A 5-year-old child with hemolytic anemia caused by glucose-6-phosphate dehydrogenase deficiency: a case report

Bambang Edi Susyanto*, Gina Puspita1, Suryanto2

INTRODUCTION

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is a hereditary enzymatic defect of red blood cells in humans. Glucose-6-phosphate dehydrogenase (G6PD) deficiency is caused by mutations located at Xq28, consisting of 13 exons and 12 introns as G6PD gene. G6PD has a role in regulating the oxidation of the pentose phosphate pathway (PPP). G6PD is an enzyme that catalyzes the conversion of glucose-6-phosphate (6-PG) to ribulose 5-phosphate (Ru5P) and produces nicotinamide adenine dinucleotide phosphate (NADPH). Ru5P has the function of inhibiting the synthesis of nucleic acids. NADPH plays as converting oxidized glutathione (GSSG) to reduced glutathione (GSH). Glutathione reductase is essential for cellular antioxidants. NADPH is also necessary for reactive oxygen space synthesis. Consequently, defect in the G6PD enzyme induced more susceptibility to oxidative stress in the red blood cell.2

The global prevalence of G6PD deficiency is about 4.9% correlated with ethnicity in population and endemic malaria areas, including Africa, Mediterranean Europe, South-East Asia, and Latin America.6 In Indonesia, the prevalence of G6PD is relatively high. A few types of research showed the prevalence of G6PD in the various province in Indonesia, including 14% among males in Central Java, 6.2% among males in Flores, and 8% among males in Sumba Island.4

The G6PD deficiency is an X-linked recessive defect that exhibits several clinical manifestations as jaundice, hemolytic anemia, splenomegaly, and hemoglobinuria.7 The most common of caused hemolytic in G6PD deficiency by excessive ingestion of fava bean (favism) as an effect of some toxic items of fava beans, for instance, divicine, isouramil, and convicine.5 Moreover, the others cause of hemolytic in G6PD as induced by the drug of malaria and infection-induced hemolytic.4 This report is aimed to describe the diagnosis and treatment of a child who appears with acute hemolytic anemia due to favism.

CASE REPORT

We present a case report of a 5-year-old boy with G6PD deficiency from PKU Muhammadiyah Gamping Hospital, Yogyakarta. The child's mother gave written informed consent. The boy presented to the emergency department with a chief complaint of pale and fatigue since a day before admission in PKU Muhammadiyah Gamping Hospital. No family history of hemolytic anemia or parental consanguinity. He appeared icteric and with severe anemia. We found that he consumed fava beans twelve hours prior to the onset of the symptoms was reported. The laboratory findings were as follows: Hb 4.9 g/dl, total bilirubin 6.17 mg/dl, indirect bilirubin 5.49 mg/dl and a negative Coomb's test result then obtained. The patient then is transfused with PRC, and the level of Hb became 9.2 g/dl and total bilirubin 0.2 mg/dl. The blood smear result was met hemolytic anemia and bacterial infection. The level of G6PD result obtained four days after was low, 7.5 U/gr Hb (10.0-14.2).

Conclusion: The severe hemolytic anemia in the patient was proven caused by G6PD deficiency.

Keywords: fava bean, G6PD deficiency, hemolytic, severe anemia.


ABSTRACT

Introduction: Glucose-6-phosphate dehydrogenase (G6PD) is an enzyme that plays an essential role in the human body cell. It is found in the cytoplasm of cells and functions to prevent cellular damage from reactive oxygen species. G6PD deficiency can be highly variable in its clinical presentation. It can cause acute or chronic hemolytic anemia and hyperbilirubinemia. Severe hemolytic can cause mortality in children. So, it is crucial to be aware during the diagnosis of hemolytic anemia at any age. The hemolytic occurred is usually precipitated by exposure to medication or intake of fava bean. This report is aimed to describe the diagnosis and treatment of a child who appears with acute hemolytic anemia due to favism.

Case description: A 5-year-old boy came to the emergency department with a chief complaint of pale and fatigue since a day before admission in PKU Muhammadiyah Gamping Hospital. No family history of hemolytic anemia or parental consanguinity. He appeared icteric and with severe anemia. We found that he consumed fava beans twelve hours prior to the onset of the symptoms was reported. The laboratory findings were as follows: Hb 4.9 g/dl, total bilirubin 6.17 mg/dl, indirect bilirubin 5.49 mg/dl and a negative Coomb’s test result then obtained. The patient then is transfused with PRC, and the level of Hb became 9.2 g/dl and total bilirubin 0.2 mg/dl. The blood smear result was met hemolytic anemia and bacterial infection. The level of G6PD result obtained four days after was low, 7.5 U/gr Hb (10.0-14.2).

Conclusion: The severe hemolytic anemia in the patient was proven caused by G6PD deficiency.
DISCUSSION

Our patient presented in the emergency room with severe anemia and jaundice. We suspected hemolytic anemia based on the presence of anemia, jaundice, and indirect hyperbilirubinemia. The result of the peripheral blood smear supported hemolytic anemia and bacterial infection. The presence of indirect hyperbilirubinemia supported the presence of hemolytic. Hemolytic anemia is caused by the destruction of red blood cells due to an inherent abnormality of the cell, environmental factor, or both. The clinical manifestation of hemolytic anemia was hemolysis such as jaundice, splenomegaly and hemoglobinuria. Classification of hemolytic anemia divided by immune-mediated (alloimmune or autoimmune), membrane defect (spherocytosis and elliptocytosis), enzyme defect (G6PD deficiency and pyruvate kinase deficiency), and hemoglobin defect (sickle cell diseases and thalassemia). In G6PD diseases, the activity of immature RBC is more significant than older RBC. Thus, it could be an effect for increasing the activity of reticulocytosis. The G6PD deficiency is X-linked recessive with the mutation resulting in a low functional G6PD. Male has more frequent occurrences and more severe clinical manifestation than females because males have only one X chromosome and females with two X chromosomes. There is no history of his family with G6PD. We did not check for mutation in this case.

Furthermore, because the anemia was severe for the first time and there were no other suspicious causes such as blood transfusion or malaria, we suspected G6PD enzyme deficiency as the cause of the hemolytic anemia. G6PD enzyme level was obtained four days following the exam and confirmed the diagnosis of G6PD deficiency. The patient’s blood G6PD levels were reported low at 7.5. A negative coombs test indicates that hemolysis occurs not due to an antigen-antibody reaction but due to a corpuscular factor, in this case, G6PD deficiency.

The investigation for the cause of hemolysis in this patient yielded a history of fava bean intake. No other hemolytic risk factors were identified in this patient. From the literature, the most common etiology of G6PD was favism. Luzzato and Arese reported that the incidence of favism in Sardinia, Italy, is estimated at 1.2 cases per 10,000 population yearly. Acute hemolytic anemia in favism usually occurs around 24 hours after ingestion of the fava beans.

The favism in G6PD is caused by red cell destruction with a complex process. Divicine, isouramil, and convicine

![Figure 1. Peripheral blood smear of the patient at first presentation.](image)

<table>
<thead>
<tr>
<th>Table 1. Laboratory examination before and after treatment.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameters</td>
</tr>
<tr>
<td>------------------------------------</td>
</tr>
<tr>
<td>Hemoglobin</td>
</tr>
<tr>
<td>Erythrocytes</td>
</tr>
<tr>
<td>Hematocrit</td>
</tr>
<tr>
<td>Leucocyte</td>
</tr>
<tr>
<td>Platelets</td>
</tr>
<tr>
<td>Total bilirubin</td>
</tr>
<tr>
<td>Indirect bilirubin</td>
</tr>
<tr>
<td>Direct bilirubin</td>
</tr>
<tr>
<td>Coombs test</td>
</tr>
</tbody>
</table>
CASE REPORT

contained in fava beans pass into the intestinal epithelium enter the blood. They built reactive oxygen species (ROS) such as superoxide anion, rapidly oxidizing NADPH and glutathione. In people with normal G6PD, reactive oxygen species are detoxified by catalase and by glutathione peroxidase. However, a patient with G6PD deficiency was unable to reverse glutathione depletion and undergo severe oxidative damage. The oxidative damage induced damaged red cells to develop to hemolysis intra and extravascular. The effect of hemolysis in favism was implied by the term ictero-hemoglobinuric favism.

The patient has obtained a packed red blood cell transfusion and antibiotic for the management. Literature reported that therapy for G6PD in mild cases is based on symptomatic and hydration. An emergency case like acute hemolytic anemia requires blood transfusion for management.\textsuperscript{9,10} Nutritional education in this patient is to avoid consuming the fava bean and other beans that constituents divicine, isouramil, and convicine such as bell beans, horse beans, pigeon beans, silkworm beans, and tick beans. Studies reported that patients with G6PD deficiency have high consumption antioxidants for nutrient supplementation like iron, folic acid, vitamin E, selenium, and food with rich L-cysteine and α-lipoic acid. Splenectomy is not recommended for therapy in G6PD.\textsuperscript{5,11} There is still some limitation in our approach for this patient. In our case, we did not assess the mother’s G6PD level and did not assess the G6PD gene for any possible mutation using molecular analysis. Those assessments are needed for further investigation.

CONCLUSION
We have reported the case of a 5-year-old boy with severe acute anemia and proved to be hemolytic anemia due to deficiency of the G6PD enzyme.

CONFLICT OF INTEREST
No conflict of interest.

FUNDING
Not Applicable.

ETHICS APPROVAL
Informed consent was obtained from the patient parents before the case report was written

AUTHOR CONTRIBUTION
Two first authors are pediatricians in PKU Muhammadiyah Gamping Hospital, involved since the early phase of patient management; the third author is a clinical pathologist, to whom the first two authors consulted the aspect of hematology laboratory.

ACKNOWLEDGMENTS
We want to thank PKU Muhammadiyah Gamping Hospital for the patient care setting.

REFERENCES