

# CASE REPORT

## Seizure as the First Presentation of Glucose-6-Phosphate Dehydrogenase Deficiency in a 3-Year-Old Child

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*Afshin FAYYAZI MD<sup>1</sup>,*  
*Ali KHAJEH MD<sup>2</sup>,*  
*Hosein ESFAHANI MD<sup>3</sup>*

### Abstract

Seizure is a rare presentation for acute hemolysis due to G6PD deficiency. We report a previously healthy boy who presented initially with seizure and cyanosis and subsequently acute hemolysis, due to glucose-6-phosphate dehydrogenase deficiency (G6PD) and probably secondary methemoglobinemia, following the ingestion of fava beans.

**Keywords:** Seizure; Glucose 6 phosphate dehydrogenase deficiency; Acute hemolysis; Methemoglobinemia

### Introduction

Glucose-6-phosphate dehydrogenase (G6PD) is an intracellular protective enzyme against oxidative stress. Its reduced concentration renders erythrocytes susceptible to hemolysis under oxidative conditions such as ingestion of fava beans or certain drugs (1).

G6PD deficiency is characterized by acute hemolysis, hemoglobinuria, anemia and jaundice (2). Although elevated methemoglobin (metHb) levels have been observed during the hemolytic crisis (3), symptomatic methemoglobinemia as a clinical feature is a rare situation (1,2,4).

We report a 3-year-old boy who was admitted with seizure attack as the first presentation of acute intravascular hemolysis caused by fava ingestion.

### Case Presentation

A 3-year-old boy was brought to the emergency department with a history of two generalized tonic-clonic seizures. The first seizure occurred one day before and the second episode one hour before admission. The child was irritable, mildly pale and a bluish discoloration of the lips was noticed. He had a body temperature of 37°C. The nail beds were deeply cyanotic without clubbing. No focal deficit was noted in the neurologic examination. There was no abnormality in his cardiopulmonary examinations and any respiratory distress. Hepatosplenomegaly was not detected. He had normal psychomotor development. He did not have a prior history of seizure and the history of seizure in his family was negative too. In his past history the patient had no episodes of jaundice or hemolysis and any cardiopulmonary diseases. He ate a large amount of fava beans the night before his attack.

Oxygen saturation (SatO<sub>2</sub>), measured with pulse oxymeter varied between 60% and 65% and did not increase after application of 10 L/min oxygen via oxyhood. The first arterial blood gas analysis disclosed a pH of 7.39; PO<sub>2</sub> of 90 mmHg

1. Pediatric Neurologist, Hamedan University of Medical Sciences, Hamedan, Iran  
2. Pediatric Neurologist, Zahedan University of Medical Sciences, Zahedan, Iran  
3. Pediatric Hematologist, Hamedan University of Medical Sciences, Hamedan, Iran

Corresponding Author:  
Fayyazi A. MD  
Tel: + 98 914 3210149  
Email: Afshin\_fay@yahoo.com

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and bicarbonate of 14.8. On admission, the hemoglobin level was 9 g/dl and the white blood cell count was 24100 with 68% neutrophils. One drop of the patient's blood compared with the examiner's sample showed an abnormal brown color. Blood urea nitrogen, serum electrolytes, creatinine and bilirubin levels were within normal limits. The initial urine analysis was also normal. The chest X-ray, electrocardiogram and echocardiography were normal. The brain CT scan was normal. In later hours he looked icteric and passed dark cola colored urine and his pallor became more prominent. The hemoglobin level dropped to 7.5 g/dl, hemoglobinuria appeared and indirect bilirubin level rose to 4.2 mg/dl. Pronounced reticulocytosis with Heinz bodies developed in his peripheral blood (supravital stain). Ghost cells and fragmented RBCs were seen in Wright-stained peripheral blood smear. G6PD was normal in this stage. Conservative treatment with oxygen therapy, hydration and blood transfusion were performed which caused decrease of cyanosis on the third and cessation of hemolysis on the fourth day. The patient was discharged on the sixth day and was followed for several months. On admission, hemoglobin electrophoresis was reported normal and when repeated 4 months later, to find probably methemoglobinemia, showed the same result, but the G6PD level which was reported normal on admission, was announced abnormally low later.

### Discussion

Methemoglobin is an abnormal hemoglobin with oxidized iron from ferrous (Fe+2) to its ferric (Fe+3) state. MetHb is incapable of normal oxygen binding; consequently, shifting the oxygen-hemoglobin dissociation curve to the left. High concentrations of metHb in the blood may cause tissue hypoxia (5).

In physiological conditions, metHb levels are maintained less than 1% of the total hemoglobin by NADH-dependent cytochrome b5-methemoglobin reductase. This enzyme accounts for 99% of daily metHb reduction. If an exogenous oxidizing agent overwhelms this reducing system, metHb levels will increase (5).

Methemoglobinemia may be congenital or acquired. The acquired form is more common and may occur

after exposure to analgesics, antimalaria drugs and antibiotics as well as nitrite salts. Congenital enzyme deficiencies such as G6PD deficiency and abnormal variants of hemoglobin may also be reported as a cause of methemoglobinemia (6).

MetHb formation in favism is attributed to the excessive oxidative stress which cannot be reduced properly by the insufficient G6PD-dependent hexose monophosphate shunt (7).

Usually patients with methemoglobinemia have a normal PO<sub>2</sub> and a low oxygen saturation level (8) and measurement of SatO<sub>2</sub> with pulse oximetry is not reliable in methemoglobinemia patients (5).

Following exposure to fava beans, our patient experienced frank intravascular hemolysis that was diagnosed as G6PD deficiency afterwards. The patient was suspected of methemoglobinemia clinically, but this was not approved paraclinically.

Several reports have described the combination of methemoglobinemia and favism; however, it has not been reported whether symptomatic methemoglobinemia was found (4).

A similar case report demonstrated that symptomatic methemoglobinemia accompanied a favic crisis in a 1-year-old boy of Afghan origin with G6PD-deficiency (4).

Seizure disorders may be induced by acute symptomatic etiology such as hypoxia, trauma, hypoglycemia and fever, but G6PD and probably secondary methemoglobinemia is a very rare cause for seizure in children and physicians may mistake in diagnosis.

Our patient presented with seizure, lethargy, marked cyanosis in the early stage and jaundice, dark urine and pallor occurred later. He had G6PD deficiency and was treated with blood transfusion and hydration. If we consider that the patient had methemoglobinemia, methylene blue therapy may be helpful, but G6PD deficiency is a contraindication for this type of therapy. In conclusion, we present a patient with acute attack of intravascular hemolysis induced with G6PD deficiency, temporary cyanosis and seizure disorder. A prompt diagnosis and therapy is mandatory.

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