

## Favism in an Elderly Female Associated With Low Pulse Oximetry Saturation And A History of Normal Prior Consumption of Fava Beans

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### Abstract

**Background:** G6PD deficiency is common in Mediterranean countries and can cause favism, i.e. hemolysis after consumption of fava beans. Given the x-linked inheritance of the disease, favism is uncommon in female heterozygotes.

**Case report:** A 74-year-old female presented to the emergency department due to abdominal pain, jaundice and dark urine. The symptoms began after consumption of fava bean, despite uneventful consumption in the past. The patient was hypoxemic on pulse oximetry at presentation, despite normal saturation in concurrent arterial blood gas (ABG) analysis. Laboratory test revealed a negative-coombs hemolytic anemia. Further testing revealed reduced G6PD activity in the patient's blood (6.7U/g Hb, normal range 7-16). She was managed with intravenous hydration and transfusions, which resulted in resolution of the hypoxemia. She was discharged after a few days of in hospital stay with instructions to avoid fava beans and medications associated with hemolysis.

**Discussion:** The occurrence of favism in this elderly female, despite normal consumption of fava beans in the past, may be explained by the skewed X-chromosome inactivation with aging, resulting in a higher proportion of circulating red blood cells being G6PD-deficient. The low pulse oximetry saturation with normal ABG saturation may be explained by methemoglobinemia associated with favism.

**Keywords:** Favism, G6pd, Skewed X-Chromosome Inactivation, Female, Elderly, Methemoglobinemia, Hypoxemia, Hypoxia

### Introduction

G6PD deficiency is common in Mediterranean countries and is associated with favism, i.e., hemolytic anemia following consumption of fava beans [1]. Raw fava beans contain high concentrations of two  $\beta$ -glycosides, that undergo hydrolysis in the gastrointestinal tract releasing highly reactive redox compounds responsible for the oxidative damage of G6PD-deficient red blood cells [2].

Considering that it is an x-linked inherited disorder, favism is less common and less severe in women. However, G6PD deficiency should not be considered recessive, as favism can occur in heterozygous G6PD-deficient females [2]. X-chromosome inactivation in females results in a dual red-cell population with some red cells being normal and other being G6PD-deficient. Considering that X inactivation is a stochastic phenomenon, the proportion of G6PD-deficient red blood cells is highly variable, resulting in variable severity of hemolytic anemia in heterozygous females.

### Case report

A 74-year-old female presented to the emergency department due to abdominal pain, jaundice and dark urine. She had a history of arterial hypertension and the only medication she was taking were nebulolol 5mg and irbesartan/hydrochlorothiazide 300/25 mg. She denied having taken any new medication recently. She reported consumption of fava beans the night before the onset of her symptoms. However, she reported uneventful consumption in the past almost yearly. Nevertheless, she reported that her son had a confirmed diagnosis of G6PD deficiency.

At presentation she appeared icteric. She was afebrile with a blood pressure of 186/100 and a heart rate of 104 beats per minute. On pulse oximetry she had a saturation of 86% (confirmed with two different pulse oximeters). However, the arterial oxygen saturation in arterial blood gases (2 separate samples) was about 94%. Lung auscultation was normal, as was the rest of the physical examination. The chest x-ray was also normal. An ultrasound of the upper abdomen was also performed but was normal.

The laboratory tests were compatible with acute hemolytic anemia; hemoglobin 9.4 mg/dl, total bilirubin 8.4 mg/dl with conjugated bilirubin 1.25mg/dl and lactate dehydrogenase 582 U/l. The reticulocyte percentage at day 1 was 2.5% but rose to 25.4% at day 2 with a concurrent drop of the hemoglobin to 7.1 mg/dl. The urinalysis revealed hemoglobinuria (1+ trace on dipstick) with few red blood cells (3-4 red blood cells per high power field). The clotting times (prothrombin time, international normalized ratio and activated partial thromboplastin time) and platelet count were all normal. A direct-coombs test was negative. G6PD deficiency was confirmed with quantitative testing (enzyme activity 6.7U/g Hb, normal range 7-16).

The patient was managed with intravenous hydration and red blood cell transfusions. The pulse oximetry saturation normalized after resolution of the hemolysis. The patient was discharged after 4 days of in-hospital stay with instructions to avoid fava beans and medications associated with hemolysis in G6PD deficient patients.

## Discussion

Two findings were interesting in this case; 1) our patient, an elderly heterozygous female, developed favism with severe hemolysis despite uneventful consumption of fava beans in the past. 2) The pulse oximetry saturation was much lower compared to the arterial blood gas oxygen saturation, and this finding resolved after the blood transfusion and resolution of the hemolysis.

Some studies have noted an increased prevalence of G6PD deficiency in elderly females compared to younger females [3, 4]. This finding has been attributed to skewed X-chromosome inactivation with aging, resulting in a larger proportion of G6PD-deficient red blood cells [3,4]. This is the most likely explanation in our patient, considering the uneventful prior consumption of fava beans in the past, although it is likely that our patient had subclinical episodes of hemolysis after consumption of fava beans in the past. Of note is that the severity of hemolysis in favism is dose-dependent (relevant to the amount of  $\beta$ -glycosides consumed). Therefore, several other factors may affect the severity of hemolysis after fava beans consumption (2): 1) the amount of fava beans consumed, 2) Raw fava beans cause more severe hemolysis (because cooking and roasting causes degradation of the glycosides), 3) Certain cultivars of fava beans have a higher content of glycosides.

Finally, the discordance of pulse oximetry with arterial blood gases suggests the presence of abnormal hemoglobin. Methemoglobinemia is a typical cause of a lower oxygen saturation on pulse oximetry [5]. Indeed, previous case reports have described patients with significant methemoglobinemia as a result of severe oxidative-hemolysis in patients with G6PD deficiency [6,7].

In conclusion, favism should be considered in the differential diagnosis of acute hemolytic anemia in elderly females even if the patient reports normal consumption of fava beans in the past. In cases of severe hemolysis, hypoxemia on pulse oximetry with normal arterial oxygen saturation may occur due to oxidation-induced methemoglobinemia. This finding resolves quickly after resolution of the hemolysis.

## References

1. Nkhoma ET, Poole C, Vannappagari V, Hall SA, Beutler E (2009) The global prevalence of glucose-6-phosphate dehydrogenase

deficiency: a systematic review and meta-analysis. *Blood cells, molecules & diseases* 42:267-278.

2. Planche T, Wilcox M (2011) Reference assays for *Clostridium difficile* infection: one or two gold standards? *Journal of clinical pathology* 64: 1-5.
3. Au WY, Lam V, Pang A, Lee WM, Chan JL, et al. (2006) Glucose-6-phosphate dehydrogenase deficiency in female octogenarians, nanogenarians, and centenarians. *J Gerontol A Biol Sci Med Sci* 61: 1086-1089.
4. Au WY, Ma ESK, Lam VMS, Chan JLC, Pang A, et al. (2004) Glucose 6-phosphate dehydrogenase (G6PD) deficiency in elderly Chinese women heterozygous for G6PD variants. *American Journal of Medical Genetics* 129: 208-211.
5. Wright RO, Lewander WJ, Woolf AD (1999) Methemoglobinemia: etiology, pharmacology, and clinical management. *Annals of emergency medicine* 34: 646-656.
6. Hassan KS, Al-Riyami AZ, Al-Huneini M, Al-Farsi K, Al-Khabori M (2014) Methemoglobinemia in an elderly patient with glucose-6-phosphate dehydrogenase deficiency: a case report. *Oman medical journal* 29: 135-137.
7. Schuurman M, van Waardenburg D, Da Costa J, Niemarkt H, Leroy P (2009) Severe hemolysis and methemoglobinemia following fava beans ingestion in glucose-6-phosphatase dehydrogenase deficiency: case report and literature review. *Eur J Pediatr* 168:779-782.

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