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CASE REPORTS

A CASE OF FALSE HEMATURIA AND AN UNEXPECTED DIAGNOSIS

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ABSTRACT

Waterpipe tobacco smoking is becoming frequent worldwide with the prevalence increasing among youth. Glucose-6-phosphate dehydrogenase deficiency is the most common enzymatic disorder of red blood cells, predisposing patients to decreased resistance to oxidative stress, when exposed to certain toxic substances.

The authors present a case of a 17-year-old male patient, with no relevant past medical history, who presents to the pediatric emergency department complaining of "hematuria". Icteric sclera was identified on physical examination. Hemolytic anemia due to glucose- 6-phosphate dehydrogenase deficiency was found and a false hematuria was identified.

The present case report is intended as an alert to the waterpipe smoking as a possible cause of false hematuria. Given its prevalence, the diagnosis of G6PD deficiency should be considered in the presence of non-immune hemolytic anemia.

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False hematuria, Glucose-6-phosphate dehydrogenase deficiency, Waterpipe tobacco smoking.

Introduction

Adolescence is defined by World Health Organization (WHO) as people between 10 and 19 years and can now be understood as a dynamic period of brain development, with the remodeling of the brain reward system taking part in this period. Psychologically it is characterized by low resistance to peer influences and low risk perception, leading to an increase in risk taking behavior, including smoking, drugs, and alcohol consumption.[1]

Waterpipe tobacco smoking (WTS) is becoming prevalent worldwide and its prevalence is increasing dramatically among youth. In the past decade WTS has been associated with many chronic health effects such as lung cancer, chronic obstructive pulmonary disease, cardiovascular disease, and asthma. Waterpipe smoke contain toxic chemicals such as carbon monoxide, polycyclic aromatic hydrocarbons, volatile aldehydes, and addictive chemical nicotine.[2]

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common enzymatic disorder of red blood cells (RBC), caused by a genetic defect in the G6PD enzyme, which generates NADPH and protects RBCs from oxidative injury.[3] Consequently, G6PD deficiency patients have decreased resistance to oxidative stress, when exposed to certain toxic substances.[3]

The authors present a case of acute hemolysis in a 17-year-old male, without previous history of anemia or jaundice, who presents to the pediatric emergency department complaining of "hematuria".

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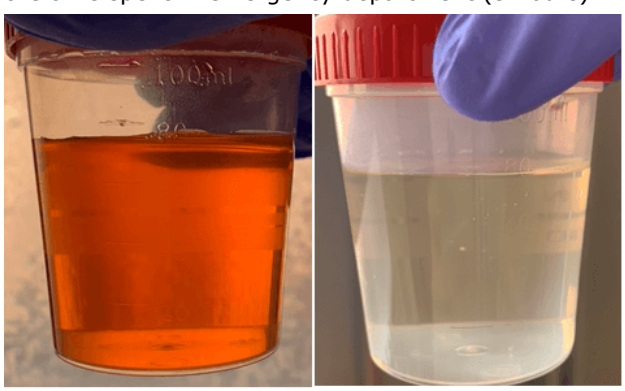
Case Report

A 17-year-old male patient, with no relevant past medical or family history, presented to the pediatric emergency department complaining of hematuria the past 12 hours. He denied dysuria, urgency, frequent urination, fever, or recent history of respiratory or gastrointestinal infections. A history of waterpipe smoking with red pigmentation tobacco (figure 1), the day before, was reported. He denied any other toxic consumptions. Physical examination revealed icteric sclera and was otherwise unremarkable. The urine analysis showed a red-orange pigmentation (figure 2), with no leukocytes, erythrocytes, nitrites, or bilirubin detection. Urine toxic screening and culture was also negative. The laboratory evaluation carried out showed hemoglobin 10.5 g/dL [11.5-18.0], hematocrit 0.306 L/L [0.370-0.540], VGM/MCV 98.1 fL [76.0-96.0], HGM/MCH 33.6 pg [27.0-32-0], reticulocyte count 2.2% [0.5-1.5%], platelets 284,000 cells/µL [130-400], leukocytes 5,0 x 10^9 cells/µL [4,0-11,0] with 48,7% neutrophils [40-74], total serum bilirubin 5.8 mg/dL [<1.2], conjugated bilirubin 0.52 mg/dL [<0.3], lactate dehydrogenase 358 IU/L [100-250], aspartate aminotransferase 19 IU/L [<40], alanine aminotransferase 19 IU/L [<50], C-reactive protein 1.98 mg/dL [<0.2], serum haptoglobin concentration 17.00 mg/dL [30.00-200.00], glucose 6 phosphate dehydrogenase 3.1 IU/gHb [7.90-16.30]. The direct and indirect coombs test were negative. Red blood cell morphology included rare spherocytes and polychromatophilic macrocytes. Hemolytic anemia due to a glucose 6 phosphate dehydrogenase deficiency diagnosis was suspected and confirmed after a low value of the enzyme repeated one month later after the hemolytic crisis (glucose 6 phosphate dehydrogenase 2.7 UI/gHb) . At this point the clinical history was reviewed and the consumption of fava-beans was identified two days before the onset of symptoms. In the absence of

changes in the urine analysis, the red-orange-colored urine was associated to the consumption of the red colored tobacco, which resolved spontaneously in a period of hours. Fava beans, and possibly the waterpipe tobacco, were identified as triggers for the hemolysis. No treatment was implemented, and the patient was referred to a pediatric consultation, where instructions were given about the disease and potential triggers of the hemolytic crisis. Analytical reassessment was performed with normalization of blood count values. No new episodes of hemolysis were verified.

Figure 1. Waterpipe tobacco consumed by the patient.

Figure 2. Progression of urine pigmentation during the time spent in emergency department (3 hours).



Discussion

The authors present a case of an otherwise healthy, 17-year-old male patient, who presented to the pediatric emergency department with red-orange urine pigmentation and icteric sclera. The laboratory evaluation showed low hemoglobin and serum haptoglobin concentration with high reticulocyte count, lactate dehydrogenase, and total serum bilirubin, especially due to the unconjugated fraction. The direct and indirect coombs tests were negative, and the urinalysis was normal. These results gave rise to the suspicion of a non-immune hemolytic anemia. Due to its prevalence, the hypothesis of G6PD deficiency was suspected, being afterwards confirmed by a low result of the enzyme activity.

False hematuria is defined by urine pigmentation whose cause may be due to endogenous substances (urates, bile pigments), drugs (rifampin, phenytoin), or food (beets, rhubarb, senna).[4]

Waterpipe tobacco contains numerous carcinogens and toxicants, such as tobacco-specific nitrosamines, polycyclic aromatic hydrocarbons (PAH) (e.g., benzo[a]pyrene, anthracene), volatile aldehydes (e.g. formaldehyde, acetaldehyde, acrolein), aromatic amines, benzene, nitric oxide, and heavy metals (arsenic, chromium, lead).[2,5] Due to lack of legislation, many of these compounds are not identified on tobacco packaging labels, making it difficult to identify the different components.

G6PD deficiency is the most common enzymatic disorder of RBC, is an X-linked recessive disorder with a male predominance, and an incidence of 400 million individuals worldwide, with a high prevalence in persons of African, Asian, and Mediterranean descent.[3,6] Over 200 G6PD different mutations have been described, with approximately one-half described as polymorphic mutations, affecting amino acid residues throughout the enzyme, and decreasing the stability of the enzyme in the red cell. The remaining mutations have been described has sporadic mutations.[7,8] G6PD is expressed in all tissues where it catalyzes the first reaction in the pentose phosphate pathway which generates reduced NADPH.[8,9] G6PD deficiency patients have decreased resistance to oxidative stress, and in presence of some triggers such as fava beans, infections and some medications and toxic substances, hemolytic reaction can occur.[3,6] WHO has classified the different G6PD variants according to the magnitude of the enzyme deficiency and the severity of hemolysis. Class I variants have severe enzyme deficiency and chronic hemolytic anemia, classes II and III have intermittent hemolysis associated with some triggers, and classes IV and V are of no clinical significance.[6]

The management of G6PD deficiency is based on the avoidance of oxidative stress to RBC to prevent hemolytic crisis. When hemolysis does occur, the inciting agent should be removed as soon as possible. In some patients with acute intravascular hemolysis and severe anemia aggressive hydration or transfusion may be necessary.[6]

This case highlights several important topics. On the one hand, when a patient presents with red colored urine, it is mandatory to exclude false hematuria,

considering its many potential causes, some of them rare as happened in the presented case, where the toxins present in waterpipe tobacco, were responsible for the change in urine color. On the other hand, in the presence of a first episode of hemolytic anemia, G6PD deficiency should be considered, and the possible triggers identified. For this purpose, a complete medical history must be taken. In the presented case, the consumption of fava beans (a known trigger for hemolytic crisis in G6PD deficiency) was identified. However, the toxins present in the waterpipe tobacco could also be assumed as a possible co-trigger in our case, although there haven't been identified any associations in literature to date between waterpipe tobacco smoking and hemolysis in individuals with G6PD deficiency. Finally, it is important to remind clinicians dealing with adolescent patients, to consider the possibility of toxic substances' consumption and to warn them about the associated risks.

Compliance with Ethical Standards

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Conflict of Interest: None

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