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Hematology

Diagnostic Orientation of G6PD Deficiency Anemia by Cytology: Two Case Reports

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Abstract | **Case Report**

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most frequent erythrocyte enzymatic disorder worldwide, due to an X-linked recessive mutation with a clear male predominance. It is a leading cause of hemolytic anemia. Although diagnosis is confirmed by enzymatic assay outside of hemolytic crises, cytological analysis of peripheral blood smears offers a rapid, accessible, and cost-effective diagnostic orientation. We present two pediatric cases—one typical and one atypical—where blood smear examination, highlighting specific morphological abnormalities such as ghost cells, bite cells, and Heinz bodies (after brilliant cresyl blue staining), provided strong diagnostic guidance. These cases underscore the crucial role of careful cytological examination in the diagnostic approach to hemolytic anemias.

Keywords: G6PD deficiency, Hemolytic anemia, Peripheral blood smear, Heinz bodies, Favism.

INTRODUCTION

Glucose-6-phosphate dehydrogenase (G6PD) deficiency, or favism, is the most common red blood cell enzymatic defect worldwide, affecting approximately 400 million individuals. It is caused by mutations in the G6PD gene located on the X chromosome, with a predominance in males due to its X-linked recessive inheritance. The disorder often remains clinically silent until a hemolytic crisis is triggered by oxidative stress, commonly after ingestion of fava beans or certain drugs.

The diagnosis is often suspected in the setting of acute hemolytic anemia with supporting clinical history. However, confirmation requires enzymatic assay, ideally performed after resolution of the crisis to avoid false negatives due to reticulocytosis. Cytological examination of a peripheral blood smear is a simple, inexpensive tool that can provide essential diagnostic clues. In this report, we present two pediatric cases illustrating the value of cytology in suggesting G6PD deficiency, even in atypical clinical settings.

CASE REPORTS

1. Case Report 1

A 4-year-old boy with no prior medical history presented with acute jaundice following ingestion of fava beans. Physical examination was notable for pallor and mild splenomegaly. Laboratory tests revealed:

- Hemoglobin: 6.5 g/dL
- White blood cells: 15,000/mm3
- Platelets: 480,000/mm3
- Reticulocytes: 8%
- Total bilirubin: 4.5 mg/dL (indirect predominance)

Peripheral blood smear (May-Grünwald-Giemsa) showed ghost cells and bite cells. After brilliant cresyl blue staining, numerous Heinz bodies were visible. G6PD enzymatic assay performed two weeks after the acute episode confirmed severe G6PD deficiency.

2. Case Report 2

A 12-year-old boy with no prior medical history presented with dark urine and anemia following a febrile diarrheal episode. He developed acute renal failure (creatinine 2.4 mg/dL) and was referred for suspicion of hemolytic uremic syndrome (HUS).

Laboratory tests revealed:

- Hemoglobin: 7.2 g/dL
- White blood cells: 14,500/mm3
- Platelets: 310,000/mm3
- Reticulocytes: 6.5%
- LDH: 980 U/L
- Direct Coombs test: Negative

However, peripheral smear did not reveal schistocytes, which are typically expected in HUS. Instead, ghost cells and bite cells were observed, with numerous Heinz bodies after brilliant cresyl blue staining. This morphological picture strongly suggested G6PD deficiency, later confirmed by enzymatic assay.

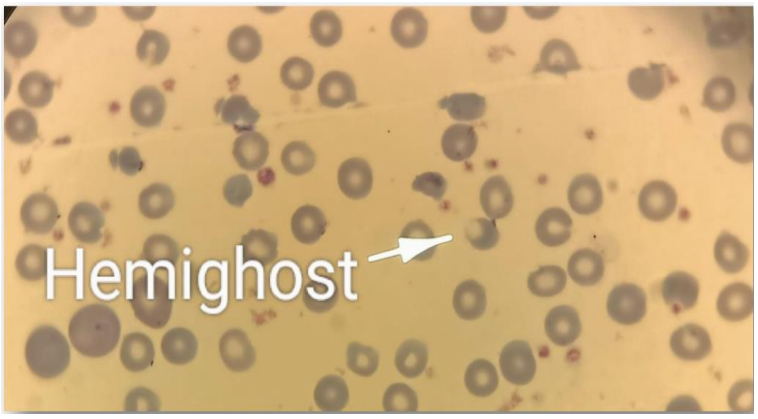

Figure 1: Hemighost

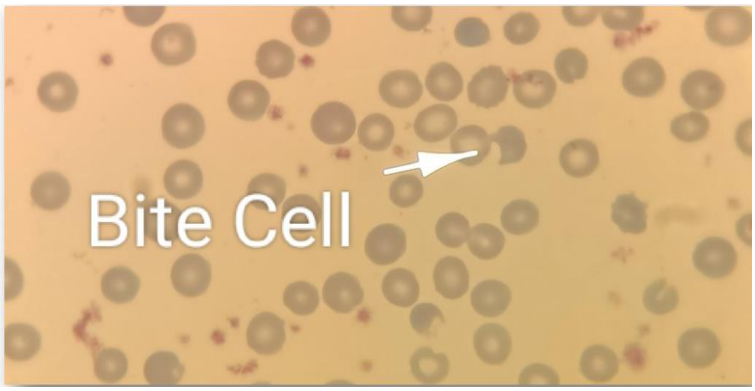

Figure 2: Bite Cell

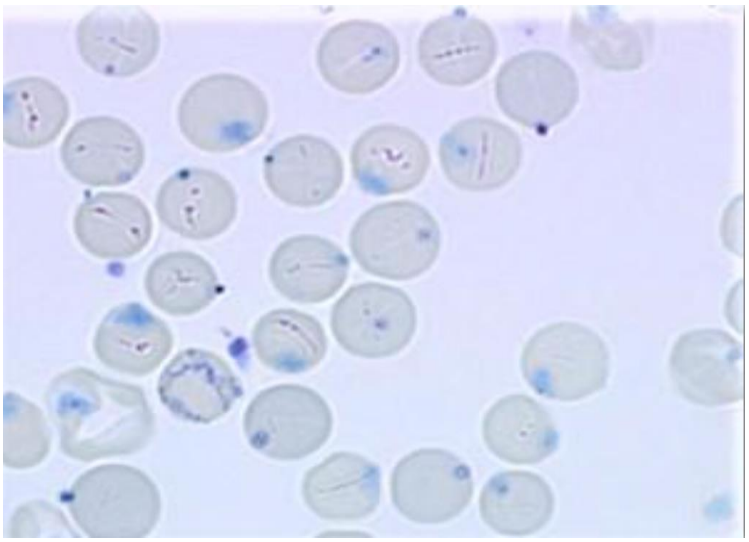

Figure 3: Heinz Body

DISCUSSION

G6PD deficiency is a common enzymopathy with significant clinical implications [1]. Its diagnosis relies on enzymatic assay, but this may be unreliable during hemolytic crises due to the predominance of young erythrocytes with normal enzyme activity.

In such contexts, cytological examination becomes a valuable tool [2]. Morphological features including ghost cells (partially or completely empty

RBCs due to membrane damage), bite cells (resulting from macrophagic removal of Heinz bodies), and Heinz bodies themselves (denatured hemoglobin aggregates) provide vital diagnostic clues.

Our observations highlight the crucial importance of a well-executed peripheral blood smear, using both May-Grünwald-Giemsa and brilliant cresyl blue stains. These findings not only supported the suspicion of G6PD deficiency but also redirected the diagnostic approach in atypical presentations (as in case 2 initially considered HUS) [3,4].

A key limitation of cytology is its dependence on the observer's experience. Nonetheless, in resource-limited settings or during emergency presentations, its utility remains high [2].

CONCLUSION

Careful examination of peripheral blood smears can play a pivotal role in the early orientation toward G6PD deficiency, even in the absence of typical clinical triggers. We recommend incorporating blood smear cytology as a routine step in the diagnostic workup of hemolytic anemia, especially in pediatric patients.

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