Normocytic Anemia: G6PD Deficiency (Glucose-6-Phosphate-Dehydrogenase Deficiency)

See online here

Glucose-6-phosphate-dehydrogenase-deficiency is an enzymatic disorder of erythrocyte metabolism. It is one of the most frequent congenital diseases and the most frequent enzymatic disease worldwide.

Epidemiology of G6PD Deficiency

G6PD deficiency is more common in people from the Mediterranean and Africa. X-linked and patients need to avoid factors that lead to the production of excess oxidants – some drugs and kidney beans.

Etiology and Pathogenesis of G6PD Deficiency

The cause of the disease can be a point mutation or a deletion in the glucose-6-phosphate-dehydrogenase-gene. It is X-chromosomal-recessively inherited. The mutation decreases the half-life of the enzyme (t_{1/2} = 13 days, normal 62). Usually, this leads to women to be conductors, while men become diseased.

The absence, or the lack of the enzyme in the erythrocytes, leads to production disorders of NADPH. However, without sufficient NADPH, the erythrocytes lack protection for oxidation. As a consequence, they are prematurely degraded. Hemolysis occurs.
Biochemistry of G6PD deficiency

Clinic of G6PD Deficiency

The clinical picture is not clear and mainly depends on the degree of the enzymatic defect or deficiency. While some patients do not show any or only slight discomforts, others suffer from partially **severe hemolytic crises** with severe pain conditions in the abdominal and back area. Also, fever and shivers are possible.

If infants suffer from the enzyme deficiency, they often show neonatal jaundice due to the impaired liver function.

Since the erythrocyte only possesses decreased or no protection against oxidation at glucose-6-phosphate-dehydrogenase-deficiency, increased oxidative stress can quickly lead to hemolytic crises. The consumption of bell beans alone can break through the existing protective barrier against oxidatively effective substances, which is why the disease has the epithet **favism**. Further, oxidative stress triggering factors are acute infections, medicaments like sulfonamides, ASS, vitamin-k-analogs, but also analgesics and antibiotics.
The pentose phosphate shunt is the only source of NADPH in RBCs. NADPH is required for the recycling of glutathione. Glutathione repairs oxidative damage. G6PD deficiency leads to oxidative damage, including hemoglobin precipitation (Heinz bodies) and membrane damage (bite cells). Heinz bodies are denatured hemoglobin. Bite cells are RBCs with membrane damage, partially consumed by macrophages. The damages RBCs are cleared in the spleen (bite cells).

G6PD deficiency is most common in patients of African and Mediterranean descent. It causes episodic hemolytic anemia (pallor, fatigue and jaundice) with oxidative stress, such as infection, oxidizing drugs (sulfonamides, nitrofurans and antimalarials) and fava beans.

**Diagnosis of G6PD Deficiency**
Since the blood count between the individual hemolytic crises can be inconspicuous, further tests for backup of the diagnosis can be made. The detection of decreased or absent glucose-6-phosphat-dehydrogenase-activity is evidence, preferably via a direct enzyme assay. Since contracted and fragmented cells can be seen in the blood smear during a crisis (bite cells and vesicular cells), this can also be used for diagnostics. Finally, Heinz bodies in the erythrocytes can be seen in the blood smear with supravital stain out of oxidized, denatured hemoglobin.

Therapy of G6PD Deficiency

A possible, already existing medication should be checked for tolerance. If an acute infection is present, it has to be treated. In severe cases, the blood transfusion can be performed. Infants with neonatal jaundice get phototherapy and exchange transfusions.

References

Begemann, Michael: Praktische Hämatologie, Stuttgart 1999 (11. Auflage)

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