Gilbert syndrome

Gilbert-Meulengracht syndrome (Gilbert's disease, juvenile jaundice, intermittent hyperbilirubinemia) is a benign AR hereditary unconjugated hyperbilirubinemia with intermittent manifestations of jaundice. It is characterized by a chronic, small increase in unconjugated bilirubin in the serum without the presence of bilirubin in the urine, without hyperhemolysis, and without other signs of liver disease. It is usually diagnosed in adolescents, but manifests throughout life. It is more common in men than in women.

A typical manifestation is an **increase in the level of bilirubin** during starvation, mental stress, physical exertion, intercurrent infection, operations, injuries, excess alcohol, in premenstrual women. Conversely, a decrease in the bilirubin level occurs with excessive energy intake and after enzymatic inducers.

Clinical manifestations are defined as **mild isolated unconjugated hyperbilirubinemia**, mostly up to 80 µmol/l, rarely up to 100 µmol/l, without manifest hemolysis and without signs of other liver function disorders (except glucuronidation). The liver parenchyma is without macroscopic or microscopic changes.

Incidence: 3% of the population (some sources report 5-10%)

Etiology

It is a genetically determined **defect of bilirubin glucuronidation**, based on the reduced activity of the liver glucuronyltransferase UGTA1 (disorder of the TATAA box of the promoter region of the uridine diphosphoglucuronosyltransferase gene, reduced expression, AR, 10-12% of the population).

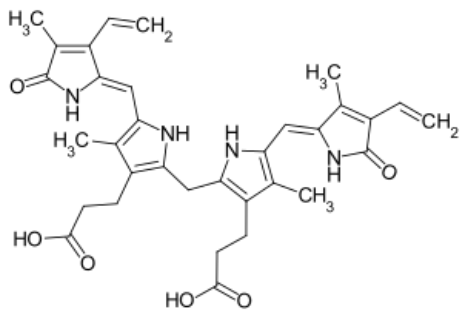
Clinical picture

The majority of those affected are completely free of difficulties, some patients suffer from **non-specific symptoms** - digestive difficulties, weakness, increased fatigue, poor ability to concentrate - difficulties are not correlated with the level of hyperbilirubinemia.

Diagnostics

Diagnosis is based on a careful history, physical examination, and the fact that individuals are virtually asymptomatic. In the laboratory, we repeatedly demonstrate fluctuating, isolated, unconjugated hyperbilirubinemia. Bilirubin levels are usually between 30-50 µmol/l

- Hyperbilirubinemia should be detected repeatedly - at least 3 times.
- During the follow-up period, only the bilirubin values and **no other laboratory** findings change.
- About a third of patients have periods when bilirubin is completely normal.
- The rise is often associated with infections, a fatty diet, starvation, alcohol consumption, physical exertion or premenstrual tension.



chemical structure of Bilirubin

During the diagnosis, we must rule out hemolysis, i.e. the blood count must be normal, including reticulocytes. Furthermore, liver tests are normal, negative HBsAg and anti HCV. A biopsy is usually not beneficial.

The fasting and phenobarbital tests are no longer used today due to their non-specificity.

- **fasting test:**
  - after 2 days we will reduce the energy intake to 400 kcal/day = 1680 J/day
  - there will be an increase in the level of bilirubin (usually by two to three times), and only the unconjugated fraction
- **phenobarbital test:**
  - administration of 200 mg phenobarbital/day
  - the level of bilirubin in the serum will decrease (enzyme induction principle)

Differential diagnosis

Diff. dg between Gilbert's syndrome and other hepatocyte involvement

- medical history – past infectious mononucleosis, contact with hepatitis
- serology, liver tests
- the presence of hepatosplenomegaly
- **post-infection states** have intermittently elevated conjugated bilirubin
- genetic examination

- it is also necessary to distinguish Wilson's disease, which also has neurological symptoms, copper in the urine, when we think of this diagnosis, we immediately do a liver biopsy - we find steatosis, a lot of copper in the liver solids, molecular diagnostics - it affects about 90%)
- α1-antitrypsin defect, which in children does not manifest itself in typical emphysema, but rather in repeated respiratory infections, molecular diagnostics are very profitable here)

Examination algorithm

1. blood count + reticulocytes
2. serum biochemistry
3. liver function - they are mainly reflected by the level of proteosynthesis - Quick, INR, aPTT, cholinesterase, which rises even with toxic liver damage, and prealbumin are sensitive, but they are also acute phase proteins
4. immunology – may be chronic jaundice, Ig, CIK, ANAb
5. ceruloplasmin, α1-antitrypsin, haptoglobin (hemolysis marker)
6. serology – VHA, VHB, VHC, EBV, CMV, HSV, toxoplasma
7. stool for parasites
8. sono of the liver, spleen, gall bladder

Diff. dg isolated unconjugated hyperbilirubinemia of the hepatic type

- low-score chronic hepatitis - difficult to distinguish without histology, often elevated aminotransferases
- Crigler-Najjar syndrome - AR hereditary
  - type I – severe hyperbilirubinemia with the risk of nuclear icterus
  - type II – mild hyperbilirubinemia
- posthepatic bilirubinemia

Therapy

Treatment is not necessary. We must warn the patient that this is a benign condition with an excellent prognosis. Furthermore, the patient must follow a light liver diet.

Links

Related articles

- Jaundice
- Juvenile hyperbilirubinemia
- Hyperbilirubinemia of newborns and infants

References

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