METABOLIC DISORDERS

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Medstudents' Homepage

Wilson's Disease

Definition

Wilson's disease, also called hepatolenticular degeneration, is a rare autossomal recessive inherited disease. It is primarly caused by an acumulation of copper in tissues all over the body, mainly in the liver, brain, kidneys and cornea.

Pathogenesis

The copper usually is excreted in the bile. In Wilson's disease, due to an unknown metabolic abnormality, this mechanism is impaired and takes to a progressive acumulation of copper in the organism. Positive copper balance produces a crescent acumulation of copper in the organism primarly in the liver. When the disease progresses and liver injury occurs the copper redistributes to others tissues. If the liver injury is acute the copper may be acutely released in the blood and cause hemolytic anemia. If liver injury is more cronic, the copper may acumulate in the brain and cause neuropsiquiatric symptoms. Also, by an not clear mechanism, the protein that carries copper in the blood, ceruloplasmin, is characteristically low.

Clinical Manifestations

The disease affects mostly young pacients, the median age being between 8 and 20 years. Any person with recurrent hepatic disease and unexplained neurologic symptoms should be investigated to have Wilson's disease. Liver disease occurs in half of the patients. It may be manifested in four ways: acute hepatitis, chronic active hepative hepatitis, cirrhosis and fulminant hepatitis. Recurrent episodes of liver disease may ocurr in a variable interval (months to years) until neurologic symptoms develop. Ultimately, all pacients develop cirrhosis. The fulminant liver injury may lead to sudden release of copper in the bloodstream and hemolytic anemia with negative coomb's test. This may be a life

threatening condition if not promptly corrected.

Neurologic manifestations may occur without liver disease and present in a large variety of ways, including resting and intention tremors, spasticity, rigidity and chorea. Dystonic signs include slowness of speech, unsteady gait, dystonic facies and posturing. Psiqiatric disturbances are present in majority of pacients with symptomatic disease, and include several forms of psychosis and neuroses. The Kayser-Fleischer ring denotes neurologic impairment and consists of copper deposition in the cornea. It presents as a greenwhish or golden brown ring around the cornea and is pathognomonic of Wilson's disease (figure 1).

Diagnosis

The classic diagnostic triad consists of : (1) Kayser-Fleischer rings, (2) low serum ceruloplasmin (< 20 mg/dl) and (3) increased amounts of amounts liver and urinary copper. The latter sign is also found in other diseases, like primary biliary cirrhosis. About 5 percent of patients with Wilson's disease presents with normal values of serum ceruloplasmin.

Treatment

Once diagnosis is firmly confirmed, treatment should start as soon as possible, either in symptomatic or assymptomatics patient. Total symptomatic recovery can be achived if intervention is made early. Otherwise death may not be prevented or recovery will be only partial.

Penicillamine is the drug of choice. It is given orally, in a amount of 1g/d divided in two doses. Response is quite slow and takes one year to maximum effect. Neurologic symptons may worse in the first months of treatment. After 14 days of penicillamine intake, patients often experiment some sensitivity effects, like fever, rash, lymphadenopathy, neutropenia and thrombocytopenia. Prednisone, 20 mg orally, is usually required to treat these reactions associated with penicillamine discontinuation. Late side effects include proteinuria, nefrotic syndrome, systemic lupus erythematosus, goodpasture's syndrome and chronic skin diseases. In these cases, penicillamine should be discontinued for a few months. Trientine or zinc are alternatives to penicillamine. Acute liver injury may not respond to therapy and require liver transplantation. Penicillamine tratment should be lifelong.

Bibliography:

1- SHEINBERG, IH: Wilson's disease, in Harrison's Principles of Internal Medicine, 13th ed. Mc Graw Hill, 1994.

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