Wilson's Disease Symptoms

Wilson disease is an autosomal recessive disorder due to a mutation in the ATP7B gene on chromosome 13, causing a failure to incorporate copper into ceruloplasmin and impaired copper excretion into bile. This disease is characterized by marked accumulation of copper in tissues and organs to toxic levels, including the liver, brain and eye. Normally, copper is absorbed in the small intestine and transported to the liver where it is incorporated into enzymes and bound to apoceruloplasmin to form ceruloplasmin. Ceruloplasmin can be secreted into the blood while excess copper is transported into bile to be excreted. A mutation in the ATP7B gene leads to a decrease in copper transport into bile, impairs its incorporation to ceruloplasmin and also decreases ceruloplasmin secretion into the blood causing accumulation of copper in the liver and decreased ceruloplasmin levels. The excess copper in the liver causes toxic injury via the production of reactive oxygen species and non ceruloplasmin bound copper enters the systemic circulation and can cause hemolysis of red blood cells and pathologic changes in the brain, cornea, kidneys, and joints. Penicillamine is a copper chelator that can be used in the treatment of Wilson disease.



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Cirrhosis

C-roses-on-liver

Mutation of the ATP7B gene leads to defective copper transport and excretion, resulting in toxic accumulation of copper in the liver. The buildup of excess copper generates reactive oxygen species (ROS), causing oxidative stress, lipid peroxidation, and mitochondrial damage, which lead to hepatocyte injury and apoptosis. Chronic inflammation and ongoing liver damage can result in progressive fibrosis, eventually leading to cirrhosis. As liver function deteriorates, copper spills into the bloodstream, contributing to systemic toxicity, hemolytic anemia, and neurological symptoms. If left untreated, severe liver dysfunction may progress to acute liver failure, necessitating liver transplantation.

Hepatocellular Carcinoma

Liver Car-gnome

Toxic accumulation of copper in the liver produces reactive oxygen species leading to liver damage. Chronic inflammation of the liver can predispose individuals to develop hepatocellular carcinoma.

Basal Ganglia Degeneration

Bass Guitar

In the brain, toxic copper accumulation primarily affects the basal ganglia, especially the putamen, leading to neuronal degeneration and gliosis. Damage to these motor control centers results in various movement disorders, including dystonia, tremors, chorea, and rigidity. The involvement of the basal ganglia can also cause a Parkinson disease-like syndrome, characterized by bradykinesia, rigidity, and postural instability. In addition to motor dysfunction, copper toxicity contributes to neuropsychiatric manifestations such as personality changes, depression, cognitive impairment, and, in severe cases, psychosis. MRI findings in Wilson disease often show characteristic "face of the giant panda" and basal ganglia hyperintensities, reflecting copper-induced damage.

Dementia

Demented-D-man

Toxic accumulation of copper in the brain can lead to early-onset dementia in patients with Wilson disease, often accompanied by psychiatric symptoms (such as depression, personality changes, and psychosis), movement disorders (including dystonia, tremors, and parkinsonism), and cognitive impairment. This occurs due to defective hepatic copper excretion caused by ATP7B gene mutations, leading to excessive copper deposition in the basal ganglia and other brain regions.

Dyskinesia

Disc-kite

Dyskinesia is a movement disorder characterized by involuntary movements (such as tremors, chorea, dystonia, and rigidity) and diminished voluntary movements (bradykinesia). It is a common neuropsychiatric manifestation of Wilson disease, resulting from toxic copper accumulation in the basal ganglia. Patients with Wilson disease may exhibit parkinsonian features, orofacial dyskinesia, and gait disturbances, often alongside psychiatric symptoms such as depression, anxiety, and cognitive impairment.

Asterixis

Asterisk

Asterixis refers to a jerking tremor of the hand that is apparent when the wrist is extended, commonly called a flapping tremor. It can be a sign of hepatic encephalopathy and a feature of Wilsons disease.

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Kayser-Fleischer Rings

Kaiser Fish Ring

Almost all patients with neurologic involvement in Wilson disease develop characteristic eye lesions in the cornea called Kayser-Fleischer (KF) rings, which are brownish-green deposits of copper in Descemet's membrane. These rings are best visualized using slit-lamp examination and serve as a key diagnostic feature of Wilson disease. While commonly associated with neurological symptoms, KF rings may also appear in asymptomatic patients or those with hepatic involvement. Their presence strongly suggests copper accumulation and helps differentiate Wilson disease from other movement disorders

Slit Lamp Exam

Lamp

Kayser-Fleischer (KF) rings can be detected by slit-lamp examination, which consists of a high-intensity light source focused to shine a thin sheet of light into the eye, allowing detailed visualization of the corneal layers. These brownish-green copper deposits accumulate in Descemet's membrane and are most prominent at the superior and inferior corneal margins. Slit-lamp examination is crucial for diagnosing Wilson disease, especially in patients with neurological symptoms, as KF rings may be absent in early hepatic disease. Their presence strongly suggests copper accumulation and aids in distinguishing Wilson disease from other disorders.

Hemolytic Anemia

Hemolysing-RBCs from Anemone

The production of reactive oxygen species (ROS) due to excess free copper in the blood can lead to hemolytic anemia by causing oxidative damage to red blood cell (RBC) membranes. This results in increased RBC fragility, leading to their premature destruction (intravascular hemolysis). Hemolytic anemia in Wilson disease is typically Coombs-negative and may present as an acute episode, sometimes preceding hepatic or neurological symptoms. The release of free hemoglobin from lysed RBCs can further contribute to oxidative stress, exacerbating liver dysfunction and worsening copper toxicity.

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