Metals in brain : Copper

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Copper is an essential element for cellular function, but free copper is extremely toxic and can produce irreversible cellular damage. Therefore, both excessive copper and copper deficiency could be fatal for human life. Additionally, copper metabolism is also reported to be associated with various neurodegenerative diseases.

Wilson disease (WD) is a rare autosomal recessive disorder of copper accumulation and copper toxicity. The mutations of *ATP7B* gene lead to a failure of copper excretion in the bile transport that results in accumulation of copper primarily in the liver, the brain and the cornea. In terms of neurological symptoms, patients could show various clinical features including tremor, dysarthria, cognitive decline, dystonia, swallowing difficulty, gait disturbance, drooling, chorea, seizure. None of the laboratory parameters alone allows a definite diagnosis of WD even though typical findings are low serum ceruloplasmin, high 24 hour urine copper, high hepatic copper content and Kayser-Fleischer rings. Direct DNA sequencing did confirm WD in 98% of the Korean patients (Two mutations were detected in 70% and one mutation in 28% of the patients with characteristic biochemical and clinical findings). The treatment option for the first choice of WD is still a matter of debate. Because of frequent side effects and initial neurologic deterioration of penicillamine therapy, less toxic trientine or zinc has gradually replaced penicillamine over the past few years.

Menkes disease (MD) is a lethal multi-systemic disorder of copper metabolism related to *ATP7A* gene mutation. ATP7A is an energy dependent transmembrane protein, which is involved in the delivery of copper to the secreted copper enzymes, thus *ATP7A* gene mutations result in progressive neurodegeneration and connective tissue disturbances from copper deficiency. Clinical features range from mild occipital horn syndrome to intermediate and severe forms of classical Menkes disease which involves multiple organ systems such as brain, lung, gastrointestinal tract, urinary tract, connective tissue, and skin. A cure for the disease does not exist, but very early copper-histidine treatment may correct some of the neurological symptoms.

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