62. THE DIAGNOSTIC CHALLENGES OF WILSON'S DISEASE RELATED TO COPPER FINDINGS

Author: Cumpata Veronica

Scientific adviser: Adela Turcanu, PhD, Associate Professor, Discipline of Gastroenterology, Department of Internal Medicine, *Nicolae Testemitanu* State University of Medicine and Pharmacy of the Republic of Moldova.

Introduction. Wilson's disease - a genetic disorder due to mutations of the ATP7B gene which causes disturbance of copper metabolism and its accumulation in various tissues, especially the liver and brain. Deviations in parameters of copper metabolism are not exclusively attributed to Wilson's disease. Complex biochemical processes are involved in copper homeostasis. Disruptions in these processes lead to separately described diseases contrary to the ATP7B defect.

Aim of study. To analyze the bibliographic data regarding the changes in copper homeostasis and the differential diagnosis of Wilson's disease related to its findings.

Methods and materials. An advanced search was performed in the PubMed, Medline, and ScienceDirect databases, taking into account relevant articles, published in the last 10 years. The search English terms used were: "human copper metabolism", "inherited disorders", "serum ceruloplasmin", "serum cooper", "serum" "free" "copper", "24-hour urinary copper", "hepatic cooper".

Results. A single biochemical test is not sufficient to establish a diagnosis of Wilson's disease. Typical findings include low serum ceruloplasmin and serum copper, high copper urinary excretion in 24-hour and high hepatic copper content. The decrease of serum ceruloplasmin is not 100% sensitive or specific, and it must be differentiated from over cases, as well malabsorption, autoimmune hepatitis, celiac disease, familial aceruloplasminemia, MEDNIK syndrome, Menkes disease, etc. Serum copper (which includes copper incorporated in ceruloplasmin) is usually decreased in proportion to the decreased serum ceruloplasmin. Hypocupremia can occur in insufficient oral intake, an increased zinc uptake, taking valproic acid, idiopathic cases. In some situations, it may be within normal range or markedly elevated, that's why the serum "free" copper was proposed as a diagnostic test for Wilson's disease. However, it is recommended to be used as a pharmacotherapy monitoring test rather than a diagnostic test. Interpreting 24-hour urinary copper excretion can be difficult due to the overlap with findings in other types of liver disease (e.g. autoimmune hepatitis, chronic active liver disease, or cholestasis), incorrect urine collection, and copper contamination of the collection device, while in case of impaired kidney function, the test is not applicable. Hepatic copper accumulation is the hallmark of Wilson's disease, but it can be misinterpreted due to inhomogeneous distribution of copper, long-standing cholestatic disorders, in idiopathic copper toxicosis syndromes such as Indian childhood cirrhosis.

Conclusion. Numerous conditions can influence copper homeostasis, including several genetic diseases. Not a single test is specific per se and, thus, a range of tests has to be applied. The diagnostic finding can only be interpreted plausibly in context with other findings (clinically and laboratory) to avoid false-positive or false-negative results.