Commentary

Wilson (1878–1937) had published his huge dissertation paper, “Progressive lenticular degeneration: A familial nervous disease associated with cirrhosis of the liver”[1] and then coined new pyramidal concept of the disease entity with his particularly talented brain. Therefore, it has been named as Wilson’s disease (WD) or hepatolenticular degeneration, representing a novel kind of extrapyramidal disorders. He is one of the world’s greatest neurologists of the first half of the 20th century and is one of the real founders of movement disorders. It is interesting that his father had moved to act as a professional Presbyterian clergyman for a long period in China from Scotland.

WD is an autosomal recessive abnormality in the hepatic excretion of copper caused by mutations in ATP7B gene that results in toxic accumulation of the metal in liver, brain, and almost all other organs (had been considered no
heart!). By clinical laboratory, WD is characterized mainly with significant lower ceruloplasmin (95%) and with possibly low total copper (but definitely high free copper ion) in serum, along with liver biopsy/pathogen and ATP7B gene diagnosis in some condition. The course stage of WD may be divided into presymptomatic (or asymptomatic), symptomatic, recovery, maintenance, and terminal phases.\(^{[3]}\) WD is a multi-system disorder that manifests mainly with hepatic (40%), neurological and psychiatric (40%), along with the others such as musculoskeletal, K-F ring and ophthalmic, endocrine-metabolic, sexual abnormal, hematological, immunological, renal, especially the last and rarest but fatal type, i.e., cardiac form. It is my great pleasure to read this interesting paper, “Cardiac arrhythmia in WD: An over sighted and overlooked”\(^{[3]}\) in this issue of J Neurosci Rural Pract, indicating that abnormal heart changes in WD patient. It is noted that Kuan may first use the term, “Cardiac WD” in 1987 for his academic contribution and described four types of cardiac manifestation: Cardiac arrhythmia, cardiomyopathy, cardiac death, and autonomic dysfunction.\(^{[4]}\) In one word, all physicians’ attention should be paid “provided it is suspected by heart.”

It is emphasized that the identification of abnormal copper deposition in heart of WD was pathogenically made by Bottier (1959). Azevedo et al.\(^{[5]}\) systematically showed the degree of myocardial damage and the copper deposition in the tissue form in the case of a 10-year-old boy with an abdominal WD. Wang et al. described a Chinese case of WD patient complicated with dextrocardia.\(^{[6]}\) Yang et al. (1997) found out definite three cases of cardiac type from a series of 494 Chinese WD inpatients with autopsy for two cases.\(^{[7]}\) Now, besides “functional” cardio-electrical changes of atrial fibrillation and abnormal response to the Valsalva maneuver and RR interval variation, other abnormally organic changes were also identified with microscopical examination of myocardial fragments by intracavitary puncture biopsy, pointing out the moderate myocardial damage and the presence of copper deposition (nearly 10 times more than the normal heart content).\(^{[8]}\) However, at present, no yet specific correlation with clinical severity and autonomic dysfunction could be established for WD patients.\(^{[8]}\)

How about the pathogenic mechanism for cardiac type of WD? It is possible that metabolic metal risks should be considered. Higher copper contents in the heart may be responsible for the cardiac symptoms of WD, particularly the toxic effects of free copper as well as the copper/iron-related free radical injury toward cardiac cells.\(^{[9]}\)

Generally, death can occur from the effects of copper toxicosis in the central nervous system (peripheral nervous system also be affected sometimes), but significant hepatic disorders may more often be fatal during the WD course. Of course, the patients should be tested for cardiac arrhythmia and cardiac function for these may have the therapeutic and outcome identification; otherwise, the literature of WD in Asia seems lower rate of heart disease.

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**References**