LETTER TO THE EDITOR

Diagnosis of Wilson's disease

I read the paper of Kok *et al.*[1] in this journal with some surprise. The authors try to make the case that the patient they describe was difficult to diagnose with Wilson's disease and it was only molecular analysis of the ATP7B gene for mutations that saved the day. In fact, the patient should have been quite easy to diagnose if they had done quantitative copper assay on the liver biopsy instead of only a copper stain. The authors acknowledge that copper stains are unreliable for diagnosis, but for some reason never obtained a quantitative liver copper. They seem to justify not doing a quantitative copper assay by referring to a paper that tries to make the case that liver copper assays vary wildly in Wilson's disease,[2] but that is not the experience of most Wilson's disease workers.[3,4]

When this patient first appeared with a urine copper of 2.31 µmol/24 hours (150 µg/24h) and a mildly reduced ceruloplasmin, Wilson's disease was a highly likely diagnosis – normal urine copper is not <1.5 µmol/24 hours (97.5 µg/24 hours) as the authors state, but is about 0.8 µmol (52 µg/24 hours). Assaying copper on the liver biopsy would have confirmed the diagnosis, and the patient would not have had to suffer damage for an additional 15 years without treatment until molecular analysis was done.

Molecular analysis of the gene has its problems. Because of the large array of causative mutations, it is difficult to assess for all the mutations. And about 25% of the time, complete sequencing of the coding regions fails to reveal two causative mutations. Assay of copper in liver biopsies is still the 'gold standard.'

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