Wilson Disease and Its Current Problems

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Wilson disease is an autosomal recessive disorder characterized by the progressive accumulation of copper in the body. The failure of hepatocytes to excrete copper into bile and the decreased copper incorporation into ceruloplasmin causes the metal to accumulate in the body (1-5). In 1993, Wilson disease gene, *ATP7B*, was identified by separate groups (6-8). *ATP7B* encodes a metal-transporting P-type adenosine triphosphatase (ATPase), which is expressed mainly in hepatocytes and functions in the excretion of copper into bile probably via the late endosome and lysosome (2, 5). Failure of this system results in copper accumulation in the body. Previously we did not have effective treatment for this progressively fatal disorder. However, now there are several treatments for this disorder. The clinical outcome of patients with Wilson disease has improved owing to the introduction of various drugs that reduce the copper accumulation in the body after the first description of D-penicillamine by Walshe (9). Therefore, Wilson disease is now one of the rare inherited disorders for which effective pharmacologic treatment is available (3, 4). There are several available therapies for Wilson disease, such as D-penicillamine, trientine, zinc salts and tetrathiomolybdate. Liver transplantation is an option for severe patients with Wilson disease and is curative (4). Furthermore, living-donor liver transplantation is also safe even using grafts from het-

erozygous donors (10).

However, there are still some problems regarding the management of patients with Wilson disease as suggested by Tatsumi et al (11) in this issue of *Internal Medicine*. The serious problems include non-compliance of the therapy and attempted suicide. Discontinuance of the treatment for Wilson disease often induces intractable hepatic failure even in previously stable patients (12-15). Although the mechanism has not been clearly demonstrated, restart with full dose of D-penicillamine may be associated with paradoxical worsening of symptoms (14). Most patients with this condition need liver transplantation (4). Because many patients are diagnosed at a young age, we should carefully educate these patients about this problem. Another problem is suicide as described Tatsumi et al (11). Suicide may be one of the psychiatric problems due to depression, decreased functional capacity, hopelessness or the need of long-term treatment (16). One report stated attempted suicide in as high as 7 of 45 patients with Wilson disease (17). In the management of patients with Wilson disease careful attention to prevent attempted suicide is important.

We should be aware of these problems and carefully educate patients with Wilson disease, because Wilson disease is one of the first fatal genetic diseases for which we now have several useful treatment strategies.

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