Is Hyperhomocysteinemia Related to Widowers’ Stroke Syndrome?

Key words: homocysteine, widower, stroke

Recent evidence indicates that an elevated plasma level of homocysteine is a risk factor for ischemic cerebrovascular diseases. It is known that folic acid deficiency causes homocysteine elevation. It means this risk factor could be treatable by balanced food intake. The cerebrovascular effects of homocysteine is not fully elucidated.

Recently, Kossi and Zakhary (1) reported that hyperhomocysteinemia is a possible causal factor in free radical generation during the acute phase of thrombotic cerebrovascular stroke. Homocysteine could impair cerebrovascular function by metal-catalyzed production of activated oxygen species.

According to meta-analysis (2), among 14 clinical studies (1,769 stroke and 7,400 nonstroke cases), the pooled OR estimate of ischemic stroke associated with hyper-homocysteinemia was 1.79 (95% CI, 1.61–2.0; p<0.001). Among 19 included studies (2,788 stroke and 3,962 nonstroke cases), the OR associated with the MTHFR TT genotype was 1.23 (0.96–1.58). These data support an association between mild-to-moderate hyper-homocysteinemia and ischemic stroke. However, the MTHFR TT genotype may have a small influence in determining susceptibility to ischemic stroke.

We have also reported the apolipoprotein (a) [apo (a)] size polymorphism, and the T677C polymorphism of MTHFR gene by a case-control study. The small apo (a) was associated with both symptomatic subcortical infarction (SSI) and SBI. However, the MTHFR polymorphism was associated only with SBI (3).

The Rotterdam Scan Study also showed that total plasma homocysteine levels are associated with SBI and white matter lesions independent of each other and of other cardiovascular risk factors (5).

Matsui et al (6) reported that age (p<0.0001), male sex (p<0.0001), the habits of cigarette smoking (p<0.0001), and alcohol consumption (p=0.0002) were significantly associated with elevation of plasma homocysteine levels.

Gliksman et al (7) examined the relationship between marital status, living arrangements, widowhood and extent of social support, and risk factors for cardiovascular disease in men and women aged over 65 years. Unmarried men had the lowest mean HDL-C levels. Men living alone had the highest mean systolic blood pressures. This result suggests that living alone itself is a high-risk state for cerebrovascular diseases in men. It suggests poor nutrition balance in men living alone is a causal factor. A serum folate concentration less than 9.2 nmol/l associated with elevated levels of plasma homocysteine. The introduction of cereal grain folic acid fortification in 1998 has reduced homocysteine concentrations in the US population.

Kelly et al (8) reported that low vitamin B6 but not high homocysteine was strongly associated with cerebrovascular disease in this postfortification, folate-replete sample.

In this issue of the journal, Toyoda et al (9) describe two stroke cases with hyperhomocysteinemia.

A 53-year-old normotensive widower developed strokes 3 times during 5 months. He had history of smoking. His former two stroke types were lacunar stroke, and he was treated by antiplatelet drugs. His third stroke was thalamic hemorrhage. He showed a high level of plasma homocysteine and low vitamin B6 with MTHFR TT genotype. The second case was 59-year-old widower suffered from recurrent small-artery ischemic stroke showed high plasma homocysteine, low B6 and low folic acid with MTHFR TT genotype. He lived alone and his vegetable intake was not enough. Moreover, his alcohol consumption was 500ml of spirits per day and he was previous smoker. These patients are typical cases who proved that hyperhomocysteinemia could cause not only ischemic stroke but also hemorrhagic stroke due to nutrition imbalance. Heavy alcohol consumption and smoking may be the enhancer for the elevation of homocysteine in these cases. It is important that these two patients showed normalization of homocysteine level by multivitamin (B6, B12, folic acid) therapy. Hyperhomocysteinemia usually is related to ischemic stroke in adults. However, hemorrhagic stroke has been reported in infants (10).

Like widowers, in Japan there are many men living alone due to business (about 900,000 people). Therefore, we have to be keenly aware of nutritional balance and homocysteine in stroke patients. Because hyperhomocysteinemia could be improved with daily intake of balanced foods or multi-
vitamin supplements.

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References


