35th Mihara Award Memorial Lecture

Clinical Significance of Molecular Biomarkers in Cerebrovascular Disease

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In many developed countries, stroke is the leading cause of disability among elderly individuals and is also a major preventable cause of dementia. With advanced aging of our population, a remarkable increase of stroke incidence is expected to continue in the near future. In order to overcome this stroke epidemic, we attempted to develop neuroprotective strategies to minimize brain damages in stroke patients through series of our researches on molecular pathophysiology of ischemic stroke. However, clinically effective neuroprotective agents with robust evidences for ischemic stroke have not yet been developed up to now and in the hyperacute and acute stages of ischemic stroke patients, intravenous thrombolytic therapy with tissue plasminogen activator (tPA) and clot removal by endovascular treatment have been proven to be effective for improving functional outcome of the patients.

In parallel with the continued efforts to increase the chance for acute ischemic stroke patients to receive these reperfusion treatment, promotion of primary and/or secondary prevention for stroke is the most important and effective way to decrease stroke victims. In our previous series of clinical studies such as OSACA study, CATHARSIS and J-STARS, by using several imaging modalities such as carotid ultrasonography and magnetic resonance imaging (MRI), we attempted to stratify the risk of the patients with established risk factors for stroke and reported the importance of the measurement of the carotid intima-media thickness (IMT) as surrogate marker of atherosclerosis and validation of brain examination with imaging systems have indicated that asymptomatic brain parenchymal lesions including asymptomatic brain infarction, deep white matter lesions and cerebral microbleeds, and intracranial and extracranial arterial stenotic lesions are predictors of future strokes and crucial risk factors of dementia.

Although there are no clinically validated molecular biomarkers of acute and chronic stages of stroke, evolving technologies have provided high throughput approaches to promote researches on the identification of novel blood-borne molecular biomarkers which are associated with basic pathophysiology of brain ischemia. Several candidate

molecular biomarkers such as chemokines, microRNAs, exosomes may be involved in the underlying mechanism of brain ischemia and may also be useful in the individualization of treatment decision, determining stroke etiology, providing prognostic information and developing new drugs. In our recent studies, we showed that telomere G-tail length can be a promising biomarker for stratifying the risk of stroke and dementia and in the present investigation, by adding several other candidate biomarkers such as microRNAs, we will further clarify the clinical importance of molecular biomarkers in the best management of cerebrovascular disease.