Increased Plasma Lipoprotein(a) Level in Cardioembolic Stroke with Non-Valvular Atrial Fibrillation

Lipoprotein(a) [Lp(a)] is known to be homologous to plasminogen and thus competes with plasminogen for its binding site, inhibiting fibrinolysis (1, 2). Although some clinical data have shown the association of Lp(a) and coronary artery thrombosis (3), the relationship of Lp(a) and left atrial thrombus formation in patients with non-valvular atrial fibrillation is still unclear.

To determine the association of the Lp(a) level and left atrial thrombus formation in patients with non-valvular atrial fibrillation, 40 ischemic stroke patients with non-valvular atrial fibrillation were studied. The stroke patients were divided into two groups, cardiogenic (group 1: n=22) and non-cardiogenic stroke (group 2: n=18), according to the clinical course, computed tomography and transesophageal echocardiographic findings. Patients with atrial fibrillation, who had no history of cerebrovascular diseases, served as controls (control group: n=14).

Serum Lp(a) level was measured in all patients. Hematocrit and plasma fibrinogen levels, which were reported as markers of hypercoagulable status in non-valvular atrial fibrillation (4), were also measured. Left atrial diameter was measured by two-dimensional echocardiography. The data were expressed as mean $\pm$ SD. Differences among three groups were analyzed by one-way analysis of variance (ANOVA) or Kruskal-Wallis test. A value of $p<0.05$ was considered significant.

There were no differences in age (68.8 ± 8.4 vs 71.2 ± 8.9 vs 70.9 ± 9.0 years, NS) and left atrial diameter (4.1 ± 0.7 vs 4.1 ± 0.9 vs 4.0 ± 0.7 cm, NS) among the three groups. Hematocrit (41.9 ± 3.4 vs 40.0 ± 3.8 vs $40.1\pm 4.0\%$, NS) and plasma fibrinogen levels (356.2 ± 102.8 vs 330.7 ± 92.5 vs 329.2 ± 67.4 mg/dl,

NS) showed similar values in the three groups. Plasma Lp(a) level was significantly higher in group 1 compared with group 2 and control (17.8 ± 13.4 vs 8.2 ± 5.1 vs 6.9 ± 7.2 mg/dl, $p<0.05$) (Fig. 1).

Our results show that the serum Lp(a) level is higher in ischemic stroke patients associated with atrial fibrillation and left atrial thrombus formation. Lp(a) is composed of an low density lipoprotein (LDL)-like particle which contains apolipoprotein (a) [apo(a)]. The sequence of apo(a) shows a remarkable homology to the plasma zymogen plasminogen. Experimental studies suggest that Lp(a) competes with plasminogen for receptors on fibrin and thereby interferes with fibrinolysis (1, 2). Some clinical studies have demonstrated that Lp(a) may also inhibit fibrinolysis *in vivo*. Moliterno et al (3) found a higher plasma Lp(a) concentration in survivors of myocardial infarction in whom recanalization of the infarct artery failed than in those with a patent infarct artery. They concluded that Lp(a) may inhibit fibrinolysis of coronary artery thrombus. Although a high serum Lp(a) level is also reported as an independent risk factor for ischemic stroke with sinus rhythm (5), the association of Lp(a) and atrial fibrillation has not been well documented. In our study, the significantly high plasma Lp(a) level demonstrated in cardioembolic stroke patients with non-valvular atrial fibrillation suggests that plasminogen inhibitory action of Lp(a) may play an important role in left atrial thrombus formation.

Future prospective studies with larger numbers should be conducted to clarify the possible role of Lp(a) as an independent risk factor for left atrial thrombus formation and subsequent embolic stroke. Whether niacin, which has been shown to lower plasma Lp(a) level, can reduce the risk of cardiogenic embolism should also be studied.

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References

- 1) Miles LA, Fless GM, Levin EG, Scanu AM, Plow EF. A potential basis for the thrombotic risks associated with lipoprotein (a). *Nature* **339**: 301-303, 1989.
- 2) Hajjar KA, Gavish D, Breslow JL, Nachman RL. Lipoprotein (a) modulation of endothelial cell surface fibrinolysis and its potential role in atherosclerosis. *Nature* **339**: 303-305, 1989.
- 3) Moliterno DJ, Lange RA, Meidell RS, et al. Relation of plasma lipoprotein (a) to infarct artery patency in survivors of myocardial infarction. *Circulation* **88**: 935-940, 1993.
- 4) Black IW, Chesterman CN, Hopkins AP, Lee LCL, Chong BH, Walsh WF. Hematologic correlates of left atrial spontaneous echo contrast and thromboembolism in nonvalvular atrial fibrillation. *J Am Coll Cardiol* **21**: 451-457, 1993.
- 5) Shintani S, Kikuchi S, Hamaguchi H, Shiigai T. High serum lipoprotein (a) levels are an independent risk factor for cerebral infarction. *Stroke* **24**: 965-969, 1993.

Figure 1. Comparison of plasma lipoprotein (a) level in the three groups.