Elevation of Heparanase in Vulnerable Plaque: Plasma and Pathological Analyses

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Background: It is generally accepted that the rupture of an atherosclerotic plaque, with ensuing clot formation, underlies most cases of myocardial infarction. The causes of coronary lesion progression from asymptomatic fibroatheromatous plaque to a lesion at high risk for rupture, vulnerable plaque (VP) are not fully understood. Heparanase (Hpa) is endoglycoside, associated with an inflammatory stimulus, platelet activation and formation of abnoramal blood vessels. The aim of our work is to examine the role of Hpa in the progression of stable atherosclerotic plaque to vulnerable plaque.

Methods: Hpa levels of patients with myocardial infarction (MI), stable angina (SA) and healthy subjects were determined using an ELISA anti-human heparanase immunoassay kit. Immunohistochemistry was used to detect the expression of heparanase, in coronary pathologic specimens obtained from post mortem analysis of patients with acute MI, SA and controls.

Results: Plasma Hpa level of 50 patients with MI (age 58 ± 14.7), 2-10 hours after clinical presentation was higher compared to 38 patients (age 65± 7.7) with SA (620± 189 pg/ml vs 237±101 pg/ml, p=0.04). Plasma Hpa level of 18 healthy subjects (age 46± 11) was 71± 17 pg/ml (MI vs SA vs healthy, p=0.0006). There was trend to reduction in Hpa, when second sample was taken 3-5 days after admission with non ST elevation MI (570± 158 pg/ml vs 147± 43.2 pg/ml, p= 0.08). High Hpa level (> 320 pg/ml) was associated with elevated white blood cell count (11.7± 3.4 vs 9.8± 3.7, p=0.03). Ten pathologic specimens obtained from VP stained for Hpa showed increase in the staining precent (3.7± 2.5%) as compared to 4 specimens of stable plaque (0.6± 0.4%, p=0.02) and 6 controls (1.2± 1.8%, p=0.04). Mean optical density (255- Pixel Gray level) was higher in VP compared to stable plaque (156± 15.5 vs 131± 18.8, p=0.02).

Conclusion: Hpa may have a role in development of VP and suggest a novel therapeutic target for prevention MI.