Serial evaluation of cardiac allograft vasculopathy after heart transplantation by dual-modality intravascular ultrasound and optical coherence tomography

T. Shiraki[1], T. Ohtani[1], H. Kioka[1], I. Mizote[1], Y. Tsukamoto[1], D. Nakamura[1], K. Yokoi[1], S. Ide[1], K. Nakamoto[1], Y. Takeda[1], S. Hikoso[1], Y. Sawa[2], Y. Sakata[1]

[1]Osaka University Graduate School of Medicine, Cardiovascular Medicine, Suita, Japan; [2]Osaka University Graduate School of Medicine, Cardiovascular Surgery, Suita, Japan

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Background: Cardiac allograft vasculopathy is a combination of the development of de novo plaque and the progression of donor-transmitted plaque.

Purpose: This study aimed to evaluate the development of de novo plaque and the progression of donor-transmitted plaque within 12-month after heart transplantation (HTx) using serial intravascular ultrasound (IVUS) and optical coherence tomography (OCT). The association between inflammatory cytokines and plaque progression was also examined.

Methods: We prospectively enrolled 40 recipients to conduct serial three-vessel IVUS and OCT analysis at 8-week and 12-month after HTx. De novo plaque was defined as having maximum intimal thickness (MIT) $\geq$0.5 mm at 12-month in the absence of donor-transmitted plaques (MIT $\geq$0.5 mm at 8-week). Serum cytokines were screened with a bead-based multiplex assay.

Results: A total of 13 de novo plaques (fibrous, n=10; fibroatheroma, n=3) were detected in eight recipients. Serum interleukin (IL)-31 at 8-week was associated with the development of de novo plaques (p=0.009). A total of 31 donor-transmitted plaques (fibrous, n=12; fibroatheroma, n=11; fibrocalcific, n=8) were detected in 17 recipients. Multiple regression analysis revealed that fibrous (p=0.026) and fibroatheroma (p=0.012) observed at 8-week were significantly associated with subsequent plaque progression within 12-month after HTx. $\triangle$Plaque burden was significant higher in de novo plaque than donor-transmitted plaque (38.8% [29.6–41.2] versus 8.7% [1.3–13.6], p$<$0.001). The prevalence of macrophage accumulation was lower in de novo plaque than in donor-transmitted plaque (8% versus 52%, p=0.006). Serum IL-31 at 8-week was correlated with the progression of donor-transmitted plaque as well as de novo plaque (r=0.663, p=0.029) although other cytokines like IL-1β, IL-6, IL-17, and tissue necrotic factor alpha were not.

Conclusions: In de novo plaques, fibrous plaque was the most common and macrophage accumulation was rarely observed. In donor-transmitted plaque, fibrous and fibroatheroma were independent predictor for the subsequent plaque progression. Serum interleukin-31 surge at subacute phase may play pathogenic role in cardiac allograft vasculopathy.