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# Multiple Micro-Neo-Vessels Detected by Optical Coherence Tomography (OCT) May Predict a Progression of Cardiac Allograft Vasculopathy in Posttransplant Recipients

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A 34-year-old man at the status of over 10-years post heart transplantation (HTx) underwent serial coronary angiography together with optical coherence tomography (OCT). He was previously non-compliant with immunosuppressive medication and developed cellular and antibody-mediated rejection at the year X-1.5 (**Figure 1A**). The OCT at that time showed multiple micro-neovessels and bright spots without angiographically-apparent cardiac allograft vasculopathy (CAV) (**Figure 2**, left panel). After improving his medication adherence which enabled him to keep adequate everolimus trough levels, the rejection was resolved at the year X (**Figure 1B**). The previously-seen bright spots progressed to layered fibrotic plaque (LFP) with an increase in its thickness (**Figure 2A and C**, right panel, yellow arrow), whereas the micro-neovessels regressed (**Figure 2B**, right panel).

CAV is the leading cause of post-HTx death. Intravascular imaging modality including OCT helps to visualize angiographically undetectable CAV. The micro-neovessels are associated with the infiltration of inflammatory cells, causing coronary narrowing when lasting over a year. Bright spots are considered to be a sign of macrophage deposition, indicating chronic vascular rejection. The LFP is identified as a separate plaque component superficial to lipid or calcified plaque. An abundance of LFP suggests the presence of organized and repeated mural thrombosis. The micro-neovessels are more frequently and quantitatively seen in CAV than atherosclerotic coronary diseases.<sup>1,2)</sup> The OCT can not only detect the subclinical CAV but also identify its reversibility and ongoing process. These findings would help investigate the mechanism of CAV progression.

We obtained informed consent from the patient.

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**Conflict of Interest**

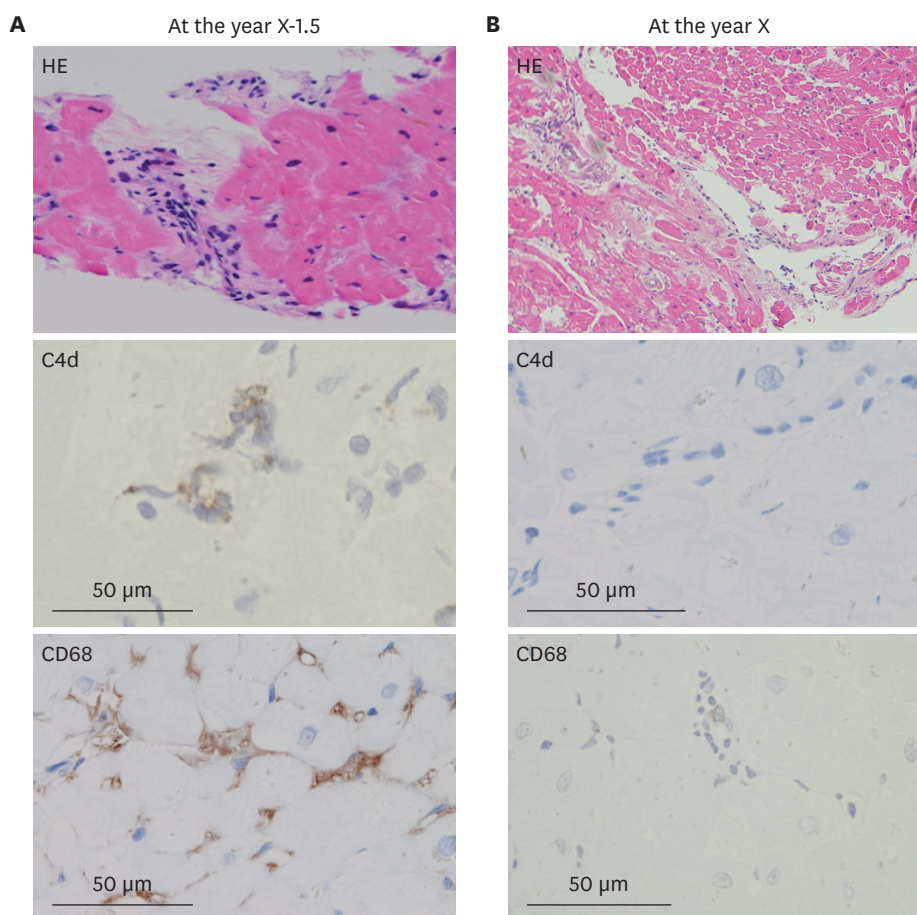
None of the authors has a financial relationship with a commercial entity that has an interest in the subject of the presented manuscript or other conflicts of interest to disclose.

**Data Sharing Statement**

The data generated in this study is available from the corresponding authors upon reasonable request.

**Author Contributions**

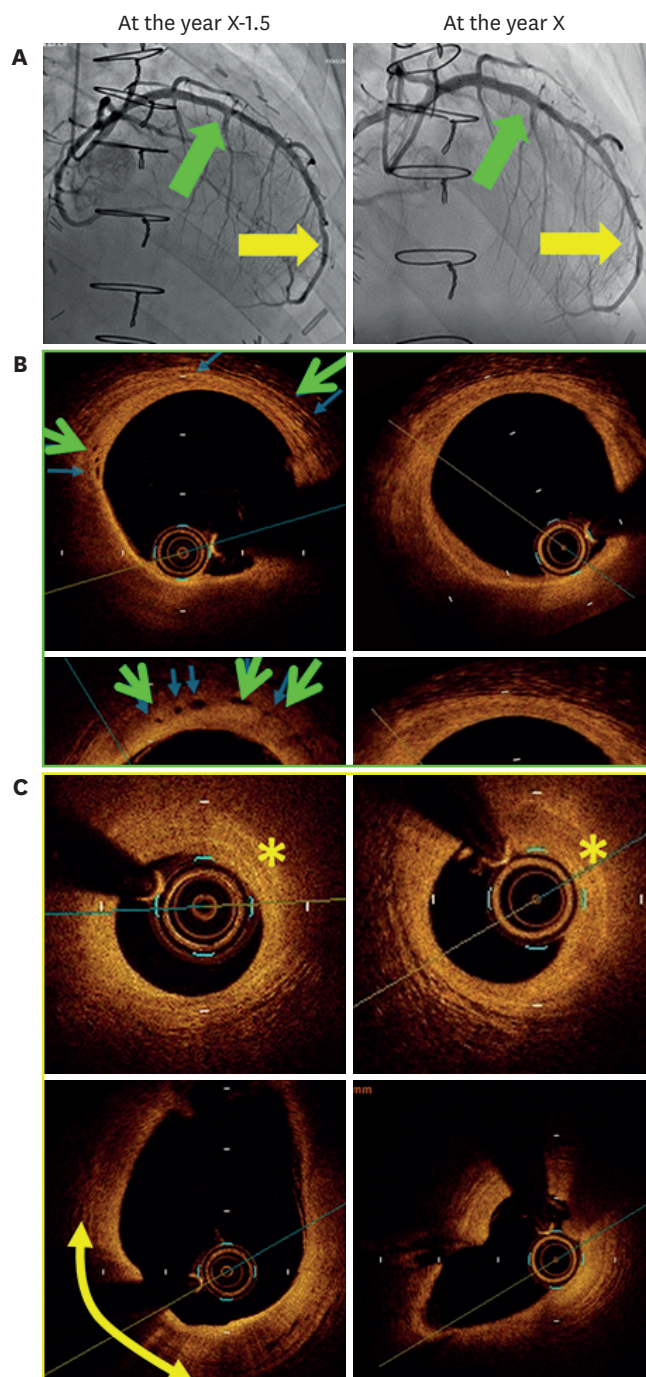
Conceptualization: Kato TS; Data curation: Suzuki T, Kato TS; Funding acquisition: Kato TS; Investigation: Suzuki T, Kato TS, Nishikura T, Shibata K, Tanno K, Wakabayashi K; Methodology: Kato TS, Nishikura T, Shibata K; Project administration: Kato TS; Supervision: Kato TS, Wakabayashi K; Visualization: Kato TS; Writing - original draft: Suzuki T, Kato TS; Writing - review & editing: Kato TS, Wakabayashi K.



**Figure 1.** Hematoxylin-Eosin staining and the immunostaining of C4d and CD68. The histology at the year X-1.5 showed mild cellular and antibody-mediated rejection (A, ISHLT grade 1R and pAMR 2), which were resolved in the specimen at the year X (B, ISHLT grade 0, pAMR 0). ISHLT = International Society for Heart and Lung Transplantation; pAMR = pathologic diagnosis of antibody-mediated rejection.

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**Figure 2.** The angiograms of left coronary artery (A), and the associated OCT findings at the proximal (green arrow) and distal (yellow arrow) segments of a left anterior descending artery (B and C, respectively) obtained at the year X-1.5 (left) and the year X (right). The multiple micro-neovessels in the proximal segment seen at the year X-1.5 (B, green arrows) regressed without coronary narrowing. The bright spot at the distal segment progressed to the layered fibrotic plaque and the localized fibrotic plaque increased in thickness (C, yellow arrow and star marks, respectively), reflecting the stability of the coronary plaque.