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CARDIOVASCULAR FLASHLIGHT

Intimal Lesions detected by Optical Coherence Tomography Herald Intraluminal Progression of Cardiac Allograft Vasculopathy Associated with Humoral Rejection

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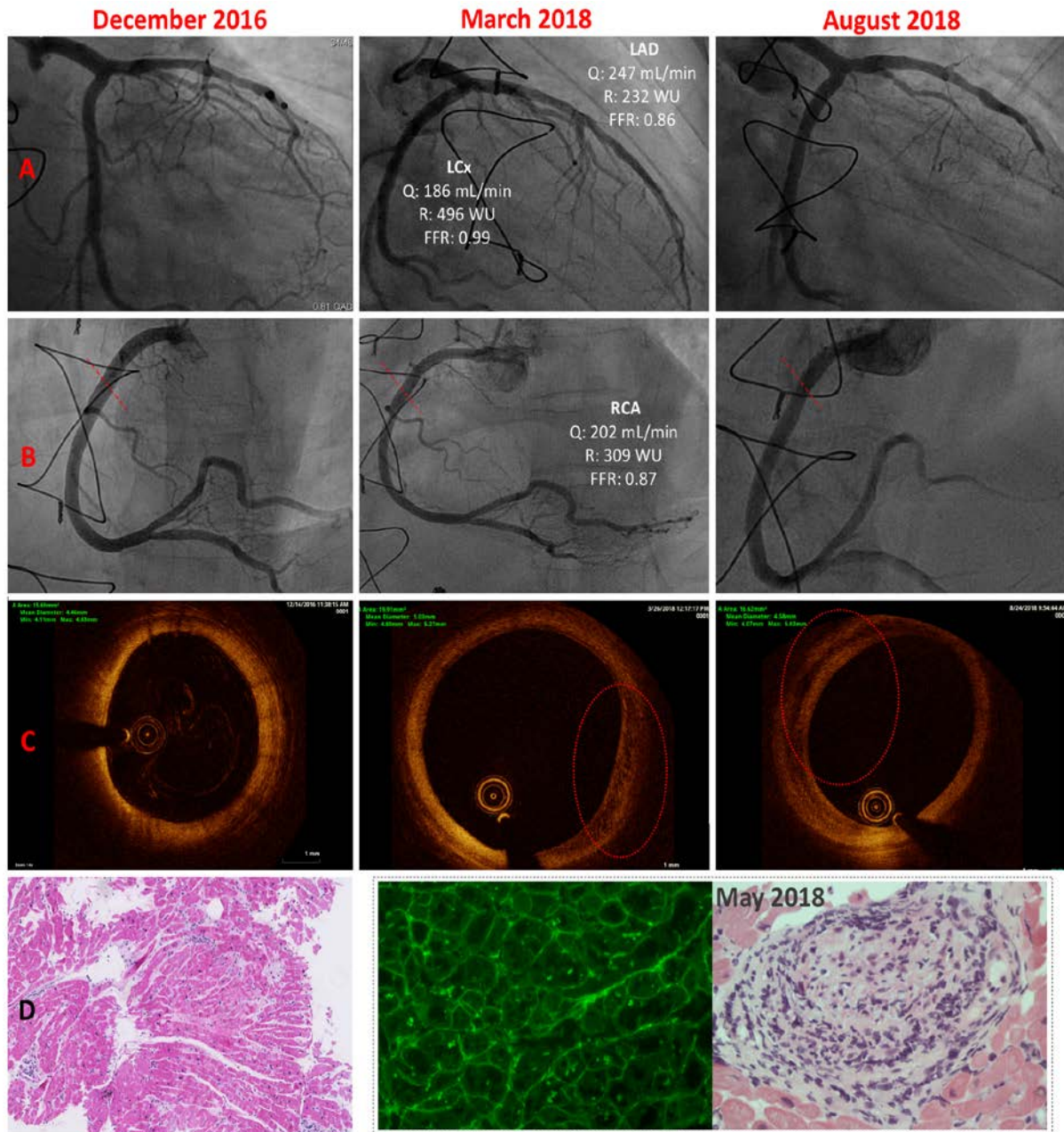


Figure Line A and B: Coronary angiogram of the right and left coronary artery (middle: maximal absolute coronary blood flow [Q], minimal absolute microvascular resistance [R] and fractional flow reserve [FFR] were measured by intracoronary thermodilution); the red line in the proximal RCA corresponds to the segment visualized by OCT; **Line C:** Optical coherence tomography in the right coronary artery (proximal segment: dashed line in B); **Line D:** Left: normal endomyocardial biopsy. Middle-right: histology of the antibody mediated rejection in 5/2018 (pAMR2), with pericapillary deposition of C4d (immunofluorescence staining in green) and mononuclear infiltrate filling a capillary vessel (cross-section).

This case illustrates humoral-rejection related cardiac graft vasculopathy (CAV) in a 44 years-old heart transplant recipient. In 3/2018 at 3 years posttransplant *de novo* anti-HLA class II donor-specific antibodies (DSA: DQ2 + DQ7 >25'000 MFI) were detected. The coronary angiogram (CA) in 2016 had been unsuspecting (line A,B; left) but optical coherence tomography (OCT) had noted a pathologic intima:media thickness ratio of 2:1 (line C, left). The CA in 3/2018, however showed mild type C CAV lesions in the distal LAD and RCA (line A,B; middle); moreover, OCT marked intimal “opacity” (line C, middle, 2-6 o'clock) compatible with “layered fibrotic plaques” described elsewhere¹. Absolute coronary flow and fractional flow reserve suggested a normal coronary microcirculation (line A,B; middle), therefore, only antiproliferative treatment was reinforced in view of the unsuspecting endomyocardial histology (line D, left) and absent signs of DSA mediated endothelitis (negative immunofluorescent C4d-staining). In 5/2018, a follow-up endomyocardial biopsy showed moderate antibody-mediated rejection² (pAMR2 H+/I+: line D middle-right), successfully treated with corticosteroids, eculizumab, intravenous immunoglobulins, and rituximab on top of tacrolimus and mycophenolate. However, in 8/2018, the patient developed severe LV dysfunction without persistent histological signs for AMR, while the CA noted type C CAV lesions with occlusion of the distal LAD, LCx and the left marginal artery; the OCT showed persisting intimal opacity (line C, right, 6-1 o'clock) compatible with sustained DSA-related toxicity. This case illustrates that intimal opacity detected by OCT heralded progression of intraluminal CAV in this recipient with positive DSA.

Literature:

¹Clemmensen TS, Koefoeld Nielsen P, Jensen LA, Poulsen SH, Holm NR, Logstrup BB, Christiansen EH, Dijkstra J, Valen KPB, Eiskjaer H. Donor-specific antibodies are associated with micro- and macrovascular coronary disease, restrictive myocardial damage, and poor outcome in heart-transplanted patients. *Clin Transplant* 2017;31 :e13033.

²Rotman S, Miller DV, Toquet C, Berry GJ. (2016) Pathology of Antibody-Mediated Rejection. In: Leone O, Angelini A, Bruneval P, Potena L (eds). *The Pathology of Cardiac Transplantation*. Springer, Cham.