Histology of In-stent Stenosis

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Disclosures

- Boston Scientific, Medical Advisory Board
- WL Gore & Associates, Consultant
Why bother with biopsy?

Case: MTS with recurrence of PTS
• 41 year old woman referred after symptom recurrence 2 months after left iliac vein stenting for PTS
• 6/15/2018 venography, diffuse severe in-stent stenosis.
Left iliac vein in-stent stenosis
Fresh thrombus: ~15%
Organizing thrombus: 0%
Old Thrombus: 0%
Diffuse intimal thickening: ~85% with some vascularization plus hemosiderin

Diffuse intimal thickening with collagen and smooth muscle cells

Hemosiderin
Blood vessel
• Biopsy #1 grossly and histologically looked predominantly chronic; we judged that thrombolysis had little to offer, and stents were angioplastied and re-lined
After angioplasty and relining with Wallstents, 6/15/2018
• 10/3/2018 because of prominent in-stent stenosis, venography was repeated 4 months later.
10/3/2018, 3.75 months after re-lining
• Gross appearance of thrombus was red and re-black, suggesting recent thrombus despite anticoagulation and anti-platelet therapy.
Left iliac vein in-stent stenosis:
  Fresh thrombus: ~20%
  Organizing thrombus: ~75%
  Old thrombus: 0%
  Diffuse intimal thickening: ~5%
Left iliac vein in-stent stenosis:

Organizing thrombus
Medical compliance and outflow into IVC seemed acceptable, so ascending venography to define inflow and assess anatomical suitability for femoropopliteal recanalization.
Ascending venogram 11/1/2018

Post-thrombotic changes in popliteal vein

Femoral vein is occluded at adductor hiatus

GSV sequestered from deep veins
• Biopsy #1 with diffuse intimal thickening was used to forego thrombolysis and proceed with PTA and relining.

• Biopsy #2 with organizing thrombus was used to justify ascending venogram, since medical compliance and venous outlow into the IVC were not problematic.

• Biopsy is a useful tool in making practical decisions in venous stent patients. Dr David Gordon (UM pathology) has been classifying biopsy material to help us formulate more general strategies in stent management.
Clinical Decisions based on Biopsy

• Resume Coumadin
• Stop Coumadin altogether
• OK switch of anticoagulant from warfarin to DOAC or from standard to prophylactic dose
• Angioplasty and stent rather than thrombolysis
• Examine inflow with ascending venogram, with possible femoropopliteal recanalization and angioplasty
• Examine outflow with possible angioplasty and stenting of IVC stenosis
Pathologic Features Scored (at least 10% of biopsy material to be considered present):

- Fresh Thrombus (estimated pathological age 0-2 days)
- Organizing Thrombus (estimated pathological age >5 days)
- Old Thrombus (estimated pathological age >2 days)
- Diffuse Intimal thickening (estimated pathological age >5 days)
Fraction of stent biopsy samples containing at least some organizing thrombus vs. time after stent implantation.
Fraction of stent biopsy samples containing at least some diffuse intimal thickening vs. time after stent implantation.
Summary of Time Course of Human Vein in-stent Stenosis:

- **Fresh thrombus** appears to be most prevalent in the early times after stent implantation, although additional fresh thrombus can occur at any time. Note: here fresh in situ thrombus cannot be distinguished from procedural thrombus at the time of biopsy.

- **Organizing thrombus** can be seen at early time points sampled and throughout the development of in-stent stenosis.

- **Old thrombus** is less prevalent in in-stent stenosis over time; represents thrombus material which has either never been lysed and/or not yet organized.

- **Diffuse intimal thickening**: becomes more prevalent as the stent process ages, and likely represents either the end result of thrombus organizing or smooth muscle migration through the stent interstices without thrombus.

- **Calcification** is generally a late feature in the development of in-stent stenosis and can presumably represent calcification of diffuse intimal thickening (analogous to atherosclerosis) or thrombus material.