Patterns of Calcification in BTK Arteries

Jihad A. Mustapha, MD, FACC, FSCAI
CEO, Advanced Cardiac & Vascular Centers for Amputation Prevention
Grand Rapids, MI
Clinical Associate Professor of Medicine
Michigan State University College of Human Medicine
East Lansing, MI
First-in-man experience with the MOTIV Bioresorbable scaffold in below-the-knee arteries

Michel J. Bosiers, MD

Consultant Vascular and Endovascular Surgery
St. Franziskus-Hospital Münster
Director: Prof. G. Torsello
Disclosure

Speaker name: Jihad A. Mustapha

I have the following potential conflicts of interest to report:

- Bard Peripheral Vascular: Consultant
- Boston Scientific: Consultant, Research
- CardioFlow: Board of Directors, Stock, Research
- Cardiovascular Systems, Inc: Consultant
- Medtronic: Consultant
- Micromedical Solutions: Chief Medical Officer
- Philips: Consultant
- PQ Bypass: Research
- Terumo: Consultant
Histopathology of Medial Calcification

• Calcium deposits were identified by purple irregular deposits in the cytoplasm of the vascular smooth muscle cells (VSMC) or in the extracellular matrix along the VSMCs of the media on H&E stain.
Histopathology of Medial Calcification

We found multiple patterns of TM calcification & a combination is usually found in the same section. The most common patterns found were:

A. Diffuse, non-confluent calcification, “dusty” micro calcifications
   A. “Dusty” calcifications along the Internal Elastic Lamina (IEL) only, early stage (Figure B)
   B. “dusty” calcification within the thickness of the media (Figure D)
   C. Combination of the above (Figure A)

B. Confluent, solid, sheet-like or “lumpy” calcification
   A. “Lumpy” calcification along the IEL only (Figure C)
   B. Sheet-like or “lumpy” calcification (Figure E)
   C. Sheet-like concentric calcification (Figures G and H)

C. Combinations of A and B

D. Calcifications accompanied by ossification and / or cartilaginous metaplastic (Fig F)
“Dust” like calcification on both sides and along IEL

TM=Tunica Medial (medial calcification)
IEL=Internal Elastic Lamina
Ca+=Calcification
TI=Tunica Intima
• Medial calcification along IEL (arrows).
• Note: IE becomes a "boundary" to calcification which is localized only in medial calcification.

TM=Tunica Medial (medial calcification)
IE=Internal Elastic Lamina
TI=Tunica Intima
• Calcification along IEL on both TI and TM sides. Note: microscopic area of cartilaginous metaplasia (yellow arrows) even in this minor TM calcification.

TM=Tunica Medial (medial calcification)
EEL=External Elastic Lamina
IE=Internal Elastic Lamina
TI=Tunica Intima
• More confluent calcification, loss of VSMCs orientation in this area.

• Note: IEL is a “boundary” to calcification which is localized only in TM.

TM=Tunica Medial (medial calcification)
IE=Internal Elastic Lamina
TI=Tunica Intima
VSMC=Vascular Smooth Muscle Cells
Complete loss of VSMCs outlines and loss of nuclei
Area resembles “sheets” of amorphous mineralized matrix, occupying entire thickness on medial calcification
In the areas of severe calcium depositions, the VSMCs lose their nuclei and their cell boundaries, and become indistinguishable from the surrounding fibrous tissue. Eventually, larger areas of medial calcification become acellular and calcified in a sheet-like fashion.
• Confluent and medial calcification with microscopic bone (red arrow) and cartilage metaplasia
• Cartilage tissue contains chondrocytes in the lacunae (yellow arrows)
• In the vicinity of the calcium deposits, even in the earlier “dusty” patterns, the VSMCs demonstrate a haphazard arrangement; lose their elongated shape, transitioning into oval-shaped cells. These cells resemble osteoblasts, and/or chondrocytes and become embedded in medial calcification.

TI = Tunica Intima
VSMC = vascular smooth muscle cells
• Circumferential medial calcification, minimal neointimal hyperplasia, no tunica media calcification.
• G and H are serial sections.
- Circumferential medial calcification (TM), minimal neointimal hyperplasia, no tunica intima calcification.
- G and H are serial sections.
• In the areas of mild medial calcification IEL shows either no visible changes or different Internal Elastic Laminal (IEL) alterations, the most common being multiplications and disruptions.

• These changes are most often seen on the medial calcification side and rarely on the Tunica Intima (TI) side. In more severe medical calcification, not only the IEL but External Elastic Lamina (EEL) also shows attenuation and disruption (Figure B).

• Unlike calcification in the TI there was no evidence of lipid deposition or inflammatory cellular response to it in the areas of medical calcification. Even in severe ones.
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