Not contrast highlighting the vasculature, but calcifications: severe atherosclerosis in a modern patient and in mummies

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HARVARD MEDICAL SCHOOL YEAR III
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Agenda

- Our patient (Ms. K)’s history (atherosclerosis, transplant, and diabetes) and recent presentation
- Expected radiological findings of diabetes, focusing on atherosclerosis
- Mechanisms of atherosclerosis, focusing on diabetes
- Additional imaging findings for Ms. K
  - 2013 CT (C+)
  - 2011 coronal CT (C-)
  - 2012 carotid ultrasound
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- Imaging of atherosclerosis
- Horus Study of atherosclerosis in past populations (Lancet 2013)
- Take-home Points
Our patient: Ms. K

- 51 year old woman
- End-stage renal disease secondary to focal segmental glomerulosclerosis (FSGS)
  - DDRT in 2000 followed by a separate pancreas transplant that year
  - Currently listed at BIDMC for a third kidney transplant
- Congestive heart failure
  - 12/2012: ejection fraction of 25%
  - Status-post resynchronization with BiV ICD
- Coronary artery disease
  - 3/2011 status-post CABG x3
  - LIMA to LAD, rSVG to pLVCA, rSVG to PDA
- Left bundle branch block
- Mitral regurgitation, with a valve replacement also from 3/2011
- Myocardial infarction
  - 5/2003 – NSTEMI status-post PDA stenting
  - 6/2006 - DES x2 to RCA
Ms. K’s Recent Presentation

- Abdominal pain
- What are we worried about?
  - LOTS!
  - She has a prior history of pneumotosis intestinalis which resolved spontaneously…and she has heavily calcified mesenteric vessels
- She has a nearly 20 year history of Type I diabetes
Radiologically-manifest complications of diabetes mellitus

- **Cardiovascular**
  - Atherosclerosis
  - Coronary artery disease
  - Diabetic cardiomyopathy
  - Peripheral vascular disease with intermittent claudication

- **Gastrointestinal**
  - Emphysematous infections
  - Fatty infiltration of the liver
  - Mesenteric ischemia
  - Gastroparesis and motility disorders of the small bowel and esophagus
  - Cholelithiasis

- **Genitourinary**
  - Diabetic nephropathy, papillary necrosis
  - Emphysematous infections
  - Renal artery stenosis

- **Musculoskeletal**
  - Diabetic ulcers
  - Charcot foot
  - Osteomyelitis
  - Muscle infarction

- **Neurological**
  - Increased risk of stroke secondary to atherosclerosis
  - Rhinocerebral mucormycosis

Source: American Diabetes Association

Katie van Schaik, HMS III, July 2013
Gillian Lieberman, MD
What do many of these diabetic complications have in common?

Atherosclerosis
Mechanisms of Atherosclerosis

Figure 2. The metabolic abnormalities that characterize diabetes, particularly hyperglycemia, free fatty acids, and insulin resistance, provoke molecular mechanisms that alter the function and structure of blood vessels.
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Ms. K’s CT (C+) for abdominal pain, at the level of the gall bladder, 2013

Axial CT (C+); PACS, BIDMC

Calcified vessel

Aorta

Atrophic native kidneys with calcified vessels
Ms. K’s CT (C+), at the level of the proximal iliacs, 2013

Aorta splitting into iliac vessels
Calcified vessel

Axial CT (C+); PACS, BIDMC
Ms. K’s CT (C+), at the level of the femoral heads, 2013

Drain

Transplanted kidney from 1995

Calcified vessels

Axial CT (C+); PACS, BIDMC
Ms. K’s CTA was unremarkable for an acute process, her pain diminished without intervention, and she was referred to the pain clinic for follow-up.

But Ms. K had and continues to have significant vascular disease elsewhere...
Ms. K’s coronal CT (C-), 2011

- Transplanted kidney from 2000
- Aorta with calcifications
- Transplanted kidney from 1995
- Femoral arteries
Ms. K’s coronal CT (C-), 2011, SMA view

Calcified SMA and branches

Transplanted kidney from 1995

Coronal CT (C-); PACS, BIDMC
Ms. K’s CT (C-), 2011

Splenic artery

Calcified, atrophic native kidneys

Renal arteries (native kidneys)

Iliacs and branches

Aorta

Coronal CT (C-); PACS, BIDMC
Ms. K’s carotid ultrasound, 2012

Calcifications

Carotid ultrasound, PACS, BIDMC
Ms. K’s carotid ultrasound with luminal calcification (2012)
Ms. K’s Abdominal radiograph, 2011

Mesenteric vasculature calcifications

Drain

Iliac calcifications

Abdominal radiograph; PACS, BIDMC
Ms. K’s Chest radiograph, 2011

- Prosthetic mitral valve with calcifications
- Coronary artery calcifications
- Sternotomy wires

Chest radiograph; PACS, BIDMC
Ms. K’s Chest CT (C-), 2011

- Aortic calcifications
- Calcifications of LMA
- Pleural effusion

Axial CT (C-); PACS, BIDMC
Ms. K’s Chest CT (C-), 2011, prosthetic mitral valve

- Prosthetic mitral valve with calcifications
- Pleural effusion
- Coronary artery calcifications
- Bypass graft surgical sutures
- Prosthetic mitral valve with calcifications

Axial CT (C-); PACS, BIDMC
Ms. K’s Chest CT (C-), 2011, RCA view

- Calcified right circumflex artery
- Pleural effusion

Axial CT (C-); PACS, BIDMC
Ms. K’s Chest CT (C-), 2011, with calcified splenic artery
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Imaging of atherosclerosis

- Depends upon the body system one wishes to image
- Plain radiographs (chest and abdomen)
  - Can show calcifications (i.e., Charcot foot) though imaging is not optimized in this modality
- CT
  - With contrast preferred, allows visualization of perfusion, provides a big-picture view which can rule out potential other causes of chest or abdominal pain if ischemia is a concern
  - Preferred for mesenteric ischemia; CTA coronary arteries with contrast is useful in the evaluation of chronic chest pain with a high probability of coronary artery disease
  - Without contrast will allow better visualization of calcifications
- Arteriography (chest and abdomen)
  - Allows diagnosis and treatment in a single procedure

Source: American College of Radiology ACR Appropriateness Criteria
Imaging of atherosclerosis

- **Ultrasound**
  - US abdomen has a high sensitivity and specificity for venous occlusion and can assess for other causes of abdominal pain.
  - US of the carotids can provide a general picture of degree of occlusion and flow through an occluded vessel, used especially if stroke is a concern.
  - US echocardiography has a similar sensitivity to stress SPECT MPI but without radiation; limited by patient’s body habitus and physician’s experience.
  - US also done to assess venous occlusion in peripheral veins.

- **MRI**
  - MRI heart with stress and without contrast has an accuracy equivalent or superior to stress SPECT MPI, diagnoses hemodynamically significant CAD in patients with intermediate to high likelihood of having significant stenosis.
  - MRA abdomen with and without contrast not so good; takes longer, limited in distal thrombosis/embolism or nonocclusive mesenteric ischemia.

Source: American College of Radiology ACR Appropriateness Criteria
Imaging of atherosclerosis

- Nukes (of more utility in cardiac imaging)
  - SPECT MPI rest and stress is the fundamental test for reversible and/or irreversible ischemic disease
    - Can segregate out those who need coronary artery angiography
    - Fused SPECT/CCTA can measure plaque burden and identify hemodynamic functional significance of coronary stenosis
  - Rb-82 PET heart stress
    - Higher spatial and temporal resolution than PET
    - Can fuse PET/CCTA exams similarly to SPECT

Source: American College of Radiology ACR Appropriateness Criteria
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Atherosclerosis in today’s population: modern malady?

- Life expectancy doubled between 1800 and 2000
- Atherosclerotic vascular disease has replaced infectious disease as the leading cause of death in the developed world
- Whole body CT scanning has revealed atherosclerosis in a cross-sectional study of 650 asymptomatic people
  - Atherosclerosis was present in all men by age 60 and in all women by 70 years, as defined by the presence of calcification in at least one of five arterial beds examined in the study
  - Included carotid, coronary, proximal aorta, distal aorta, and iliac vessels
  - By age 50 years, atherosclerosis was present in all five arterial beds in 82% of men and 68% of women

Or ancient affliction?
The Horus Study (The Lancet, 2013)

- Identified atherosclerosis across 4000 years of human history in four geographically distinct ancient populations
- Whole body CT scans were obtained of 137 mummies
  - 76 ancient Egyptians (3100 BCE to 364 CE, 13 excavation sites)
  - 51 ancient Peruvians (200 to 1500 CE, 5 excavation sites)
  - 5 Ancestral Puebloans (1500 BCE to 1500 CE, 5 excavation sites)
  - 5 Unangan (Aleutian Islands) hunter gatherers (1756-1930 CE, one excavation site)
- Atherosclerosis was regarded as
  - **Definite** if a calcified plaque was seen in the wall of an artery
  - **Probable** if calcifications were seen along the expected course of an artery
- Vascular beds examined: carotid, coronary, aortic, iliac or femoral, and popliteal or tibial.

Source: Thompson (2013)
The Horus Study: Results I

- Probable (22) or definite (25) atherosclerosis was seen in 47 (34%) of 137 mummies.
- Those with atherosclerosis were older at time of death (43 [SD 10] years vs 32 [15] years, p<0.0001).
- Atherosclerosis was present in all four populations:
  - 38% of ancient Egyptians
  - 25% of ancient Peruvians
  - 40% of Ancestral Puebloans
  - 60% of Unangans
- Mean age at death:
  - 36.8 years (SD 13) for ancient Egyptians
  - 37.1 years (SD 17) for ancient Peruvians
  - 28.1 years (SD 12) for Ancestral Puebloans
  - 28.6 years (SD 18) for Unangans

Source: Thompson (2013)
The Horus Study: Results II

- Among mummies for which sex could be identified, atherosclerosis was present in:
  - 39% of women (17/44 identifiable women)
  - 39% of men (30/77 identifiable men)

- Probable or definite atherosclerosis was present in:
  - Aorta (20%)
  - Popliteal or tibial (18%)
  - Carotids (12%)
  - Coronary arteries (4%)

- Age was associated with increased odds of atherosclerosis severity, with the odds of increasing atherosclerosis severity increasing by about 69% per decade of life.

- Even after adjusting for mummy location (Egypt vs Americas), age continued to be significant, with sex, time period, and location being non-significant.

Source: Thompson (2013)
The Horus Study: Results (abdomen)

(A) Unangan woman (mummy 133) aged 47–51 years, late 19th century CE
(B) Egyptian woman aged 45–50 years, of unknown era from ancient Egypt
(C) Ancestral Puebloan woman aged 46–51 years, 1500 BCE to 500 CE
(D) Woman from ancient Peru, aged 41–44 years, 200–900 CE

Source: Thompson (2013)
(A) Unangan woman, aged 25–29 years, who lived in the late 19th century CE
(B) Hatiay, a male Egyptian scribe aged 40–50 years, 1570–1293 BCE

Source: Thompson (2013)
The Horus Study: Results (aorta and coronaries)

Sagittal three-dimensional (3D) volume rendered (A) and sagittal oblique 3D volume rendered (B) CT reconstruction of two mummies with coronary calcifications. (A) Coronary calcifications in the mummy of a Unangan woman aged 47–51 years who lived in the late 19th century CE. (B) Coronary artery calcifications in the mummy of Ahmose-Meritamun, an Egyptian princess aged 40–45 years who lived about 1580–1550 BCE.

Source: Thompson (2013)
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Take-home Points

Atherosclerosis is a complex, inflammatory process.

Diabetes, infection, and other diseases which increase inflammatory reactions in the body can hasten and worsen atherosclerosis.

Imaging of atherosclerosis depends upon the clinical presentation of the outcome of atherosclerosis and decreased circulation (acute vs chronic) and upon the body system involved.

The idea of atherosclerosis as an inflammatory process more strongly linked to inflammatory assaults and to aging (as opposed to climate or diet) is supported by paleopathological research.
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Bibliography