Consensus nomenclature for inflammatory ascending aortic disease

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Talk Outline

• Case Vignette 3
• Working definitions for this talk
• Atherosclerosis
• Histologic patterns of aortitis and periaortitis
• Major causes of aortitis and periaortitis

Clinical History

• 60 year old Caucasian man with enlarged aortic root (68 mm) and enlarged ascending aorta (49 mm)
• Referred for non-emergent aortic root and ascending aorta replacement

Case Vignette 3

Clinical History

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Inflammatory Aortic Disease
Aortic Specimen

- Multiple fragments up to 4 cm across (thickness not noted grossly)
- Two (2) cassettes submitted, with three (3) pieces each
- Protocol H&E and Movat pentachrome cut and stained up front
- An additional five (5) blocks were subsequently submitted

Inflammatory Aortic Disease

- Mild atherosclerosis (raised plaques)
- Medial degeneration with patches of hemorrhage and healing injury
- Marked adventitial fibrosis
- Scant adventitial inflammation

Inflammatory Aortic Disease

- Moderate to severe atherosclerosis (raised plaques with medial damage)
- Medial degeneration with patches of hemorrhage and healing injury
- Marked adventitial fibrosis
- Scant adventitial inflammation

Inflammatory Aortic Disease

- Striking patches of elastic fiber loss
- Also highlighted the atherosclerosis, albeit not inflamed, and not uniformly distributed

Final Diagnosis

AORTA, ASCENDING, ANEURYSM REPAIR:
Most consistent with healed aortitis. Moderate atherosclerosis.
What is “healed aortitis”?
How should aortitis be classified?
How do you grade atherosclerosis?

**Working Definitions**
(these are mine, not consensus necessarily)

**Definitions (my own, for sake of this talk):**

**Aortitis** – presence of histologically proven inflammation (i.e. leukocytes) in the media of the aorta, a risk factor for aneurysm and dissection

**Periaortitis** – presence of histologically proven inflammation in the adventitia of the aorta

Consensus committee recommends these be reserved for non-atherosclerotic disease.

**Endaortitis** – presence of histologically proven inflammation in the intima of the aorta (I have never actually used this term)

**Healed aortitis/periaortitis** – findings best explained by prior inflammation in the absence of active inflammation (i.e. no leukocytes)
(analogize to “healed arteritis” in temporal artery biopsies)

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**Conensus statement on surgical pathology of the aorta**
from the Society for Cardiovascular Pathology and the Association for European Cardiovascular Pathology: I. Inflammatory diseases


Cardiovascular Pathology
Volume 24, Issue 5, Pages 267-278 (September 2015)
DOI: 10.1016/j.carpath.2015.05.001

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**Atherosclerosis**
Inflammatory Aortic Disease

Grading atherosclerosis in surgically resected segments of aorta

**Grading/Qualifier**: No significant atherosclerosis
**Gross Histology**: Normal or fatty streaks
**Histology**: Sudden intimal fibrous plaques

**Grading/Qualifier**: Mild atherosclerosis
**Gross Histology**: Raised plaques
**Histology**: Extracellular lipid deposition without fibrosis (AHA grade I/II)

**Grading/Qualifier**: Moderate atherosclerosis
**Gross Histology**: Raised or confluent plaques
**Histology**: Extracellular lipid deposition with fibrosis (AHA grade III and above)

**Grading/Qualifier**: Severe atherosclerosis
**Gross Histology**: Raised or confluent plaques
**Histology**: Extracellular lipid deposition with fibrosis (AHA grade IV and above)

**Atherosclerosis with plaque disruption and surface thrombus**: Ulcerated plaque with surface thrombus
**Histology**: Atherosclerotic plaque (AHA grade III and above) with surface disruption and surface thrombus

* Used in conjunction with the grade mild, moderate, or severe


Histologic Patterns of Aortitis and Periaortitis

Atherosclerosis

- Two specific inflammatory patterns also noted in consensus document:
  - Atherosclerosis with excessive neutrophils – exclude infection
  - Inflammatory atherosclerotic aneurysm (IAA) – exclude primary periaortitis

Granulomatous Aortitis

- Clusters of epithelioid macrophages
- With or without giant cells
- With or without well formed / compact granulomas

Consensus was to use “granulomatous” according to its broader definition.


Lymphoplasmacytic Aortitis

- Lymphocytes and plasma cells
- No granulomas (i.e. no well formed collections of epithelioid histiocytes)

**Mixed Pattern Aortitis**

- Most or all inflammatory cell types present (histiocytes, lymphocytes, neutrophils, eosinophils, plasma cells, mast cells)
- No granulomas

**Suppurative Aortitis**

- Neutrophilic abscesses
- Necrosis and/or cell debris

**Major Causes of Aortitis and Periaortitis**

**Inflammatory Atherosclerotic Aneurysm**

- Defined in the literature by intraoperative findings
- In the context of significant atherosclerosis (usually abdominal):
  - Aortic wall thickening
  - Periaortic fibrosis with adhesions to surrounding organs
- Likely a mix of secondary disease from atherosclerosis, reactive changes to interventions (e.g. endovascular stent), and primary rheumatologic disease incidental to the atherosclerosis

**Giant Cell Aortitis**

- Aortic involvement by giant cell arteritis (GCA)
- Granulomatous pattern, occasional giant cells, rare granulomas
- Inflammation biased towards inner half of media
- Frequent laminar medial necrosis
- Often adventitial lymphoplasmacytic infiltrate
- Often prominent vasa vasorum and intimal hyperplasia
- Medial scarring common, less dense adventitial fibrosis

**Takayasu Aortitis**

- Typically patients under 50, often female; affects aorta and branch vessels
- Ranges from asymptomatic to pulseless disease and stroke
- Granulomatous medial inflammation, frequent giant cells, later stages with compact granulomas
- Biased towards the outer third of the media
- Medial scarring, prominent adventitial fibrosis, and fibrous intimal hyperplasia all common
- Wall thickness typically greater than in GCA
Inflammatory Aortic Disease

- Part of the IgG4 related disease spectrum
- Lymphoplasmacytic infiltrate, obliterative adventitial phlebitis, adventitial fibrosis (sometimes storiform), and/or tissue eosinophilia, sometimes lymphoid follicles
- Increased IgG4-positive plasma cells ratio and number
- No granulomatous or suppurative inflammation
- Exclude infectious etiology, overlaps with IAA

IgG4 Aortitis and Periaortitis

- Mycotic aneurysms characterized by suppurative inflammation and typically positive microbiological stains
- Mycobacterial aortitis (very rare) is typically granulomatous
- Syphilitic (leutic) aortitis (very rare):
  - Lymphoplasmacytic inflammation, “microgummas”, adventitial obliterative phlebitis, obliterative endarteritis, ischemic medial damage
  - Syphilis stains almost useless, but serology can be helpful

Infectious Aortitis


Other Causes

- Granulomatosis with polyangiitis (GPA, formerly Wegener’s granulomatosis)
- Churg-Strauss Syndrome (eosinophilic granulomatosis with polyangiitis, EGPA)
- Sarcoidosis
- Rheumatoid arthritis
- Systemic lupus erythematosus (SLE)
- Clinically isolated aortitis (i.e. idiopathic)

Closing Thoughts

- I often don’t know the right answer, but I can provide a shortened differential diagnosis, which clinicians seem to appreciate
- The clinicians don’t read our consensus documents usually, so you have to educate them on the terminology, or somehow adapt (e.g. “granulomatous”)
- Disease definitions continue to evolve (e.g. periaortitis)
- Some definitions don’t yet exist (e.g. healed aortitis vs. burnt out atherosclerosis)

Resource

Summation

• Consensus terminology for atherosclerosis is provided
• Consensus terminology of the major patterns of aortitis and periaortitis are given
• Descriptions of the common findings in many causes of aortitis and periaortitis are laid out to aid in clinical correlation
• Practical implementation of these guidelines may require further discussion

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No claims can be processed after that date!

After September 30, 2017 you will NOT be able to obtain any CME or SAMs credits for attending this meeting.

My post-meeting document may not reflect this version of my case.

Case Vignette 3, continued
Adventitial lymphoplasmacytic inflammation:
• End stage of something?
• Minimally active IgG4?

There is, arguably, phlebitis, albeit really mild and subtle, and not obliterator.

IgG4 count in three (3) densest fields averaged over 60 per HPF (>80, >80, and ~30)
• The fraction in those fields (against CD138) was approximately 65%

Lymphoplasmacytic infiltrate, focally dense?
• Fibrosis for sure, not storiform
• Phlebitis maybe, not obliterator to my eye
• IgG4 number and fraction met, but for aorta and retroperitoneum, not thoracic periaorta (undefined)


Multidisciplinary Conference
• Thoracic aortitis consistent with surgical findings, radiology
• Possible mesenteric issues (radiology, no symptoms)
• Bilateral salivary gland swelling that responded to rituximab