Myocardial Disease

Maintenance of Certification
Self-Assessment Module
2016

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None

No relevant financial relationship(s) with industry:
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References to off-label agents or instruments in their presentation:
None
Target Audience

General pathologists, surgical pathologists, autopsy pathologists, cardiovascular pathologists, forensic pathologists, molecular pathologists, pathology residents, and pathology fellows.

Overview

Cardiovascular specimens are commonly encountered in clinical practice, but formal training on how to handle them is lacking. Both the Society for Cardiovascular Pathologists (SCVP) and the Association for European Cardiovascular Pathology (AECP) have recognized the need for a uniform approach to the handling and reporting of cardiovascular specimens. Pathologists and clinicians alike need to be aware of the value and limitations of newer ancillary diagnostic techniques such as genetics and proteomics. This module aims to familiarize participants with the fundamentals of handling surgery and biopsy-derived myocardial specimens. Specifically, the course will address information that is relevant and actionable for clinicians. It also seeks to inform participants about the emerging technologies available to help inform diagnoses and clinical practice.

Learning Objectives

The participant will:

- Describe the fundamental approaches to handling cardiovascular specimens (both surgery- and biopsy-derived).
- Explain the impact of emerging ancillary tools such as molecular genetics (including molecular microscopes) and proteomics, and critically appraise specimen handling and result reporting.
- Synthesize clinically actionable information that is essential to convey to care providers and, ultimately, the patient and/or the patient’s family.
References

Overview

- Types of specimens
  - septal myectomies
  - endomyocardial biopsies
  - apical cores
  - atrial appendages

- Prototype disease
- Examination and processing of specimens
- Tips for reporting

Septal Myectomy Specimens
Hypertrophic Cardiomyopathy

- Definition
  Diastolic disorder, with hypertrophy, asymmetric septal thickening, myocyte disarray and LVOTO (in 30%)

- Clinical features
  Age: symptomatic at any age
  Sex: M:F = 1:5:1

- Genetics
  Mutations in sarcomere genes
  AD with variable penetrance
  Incidence = 1 / 500

- Mortality
  1-6% (SCD, CHF, other)
Septal Myectomy Specimens
Hypertrophic Cardiomyopathy - Proteins Involved

Sarcomeric Proteins

Septal Myectomy Specimens
Hypertrophic Cardiomyopathy - Pathologic Features

- **Gross findings**
  - Cardiomegaly (~2X normal weight)
  - LV hypertrophy, with/without dilatation
  - Prominent septal hypertrophy
  - Subaortic endocardial fibrosis

- **Microscopic findings**
  - Myocyte hypertrophy (diffuse)
  - Myocyte disarray (in septum)
  - Interstitial & endocardial fibrosis

Septal Myectomy Specimens
Hypertrophic Cardiomyopathy - Gross Features

Aut Spec (Ant View)  Aut Spec (4-chamber)
Septal Myectomy Specimens
Hypertrophic Cardiomyopathy - Gross Features

- **Level of LVOTO**
  - Sub-aortic
  - Mid-LV
- **Hemodynamics**
  - Mid-systolic obstruction
  - MV SAM
- **Pathology**
  - Sub-aortic fibrosis (contact lesion)
  - Mirror-image of ant MV leaflet

Septal Myectomy Specimens
Hypertrophic Cardiomyopathy - Surgical Intervention

Aut Specimens (Long- and Short-Axis)
Septal Myectomy Specimens
Examination & Processing of Specimens

Gross Examination
• Features to note
  • Endocardial thickening
  • Tissue amount (incl. weight)
• Sections to submit
  • Generally 1 cassette worth
• Stains to order
  • H&E
  • Congo Red / SAB (>65 yrs)

Histologic Examination
• Features to note
  • Myocyte hypertrophy
  • Interventricular fibrosis
  • Myocyte disarray
  • Endocardial fibrosis
  • Presence of amyloid
  • Presence of inflammation

Septal Myectomy Specimens
Tips for Reporting

Template

Overview

• Types of specimens
  • septal myectomies
  • endomyocardial biopsies
  • apical cores
  • atrial appendages
• Prototype disease
• Examination and processing of specimens
• Tips for reporting
Endomyocardial Biopsy Specimens
Overview & Technique

Diagram of Procedure
Specimen Size

Endomyocardial Biopsy Specimens
Cardiac Amyloidosis - Gross Features

- **Texture**
  - Firm
  - Waxy

- **Atria**
  - Normal size or dilated
  - Subendocardial deposits

- **Ventricles**
  - Thick walls
  - VS: VFW ↑

Four-Chamber View

Endomyocardial Biopsy Specimens
Cardiac Amyloidosis - Gross Features

- **Texture**
  - Firm
  - Waxy

- **Atria**
  - Normal size or dilated
  - Subendocardial deposits

- **Ventricles**
  - Thick walls
  - VS: VFW ↑

Four-Chamber View
**Endomyocardial Biopsy Specimens**
Cardiac Amyloidosis - Gross Features

- **Texture**
  - Firm
  - Waxy
- **Atria**
  - Normal size or dilated
  - Subendocardial deposits
- **Ventricles**
  - Thick walls
  - VS: VFW 1

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**Endomyocardial Biopsy Specimens**
Cardiac Amyloidosis - Histologic Features

- [Congo Red Staining](#)
- [Pericellular](#)
- [Vascular](#)

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**Endomyocardial Biopsy Specimens**
Cardiac Amyloidosis - Histologic Features

- [Congo Red Staining](#)
- [Pericellular](#)
- [Vascular](#)
Endomyocardial Biopsy Specimens
Examination & Processing of Specimens

**Gross Examination**
- **Features to note**
  - Number of specimens
  - Size (range)
- **Sections to submit**
  - Embed all
  - EM study?
- **Stains to order**
  - H&E (X 2)
  - Restrictive hemodynamics
  - Iron stain
  - Congo red (10 μm) or SAB
  - Acute HF (myocarditis?)
  - H&E (3 - 8 additional levels)
  - Storage Dx. or Drug Tox.
  - Post-fix in glut for EM

**Histologic Examination**
- **Features to note**
  - Restrictive hemodynamics
  - Presence / absence of amyloid (extent, distribution, vasc./endocard involvement, sub-type)
  - Presence / absence of Fe
  - Hypertrophy (extent) and Fibrosis (extent & distribution)
  - Eosinophilic infiltrate, mural thrombus
  - Dilated features / Acute HF
  - Hypertrophy (extent) and Fibrosis (extent & distribution)
  - Myocarditis (lymphocytic / granulomatous)

**Endomyocardial Biopsy Specimens**
Tips for Reporting

**Template**

```
Diagnosis: Right ventricle, endomyocardial biopsy: Amyloidosis, no features, 3 sections

Comment: Sections include endomyocardial biopsy specimens, of which 1 is embedded by amyloid deposition (positive Congo red staining, fibrillar material, amyloidosis). Sections 2-3 show no amyloid deposition. Sections reveal no evidence of myocarditis.

(Histologic features):
- Endomyocardial biopsies:
  - Amyloidosis: Positive Congo red staining
  - Myocarditis: Negative

As expected, no myocarditis is negative.
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Overview

- Types of specimens
  - septal myectomies
  - endomyocardial biopsies
  - apical cores
  - atrial appendages

Apical Core Specimens
Technique and Specimen Overview

LV Assist Device  Apical Core Specimen
Apical Core Specimens
Ischemic Heart Disease - General Features

- **Definition**
  Systolic disorder, usually secondary to CAD

- **Clinical features**
  - Age: usually > 60 yo
  - Sex: M>F
  - **Incidence**
    1% after age 60
  - **Mortality**
    #1 cause of death in the U.S.

External View (with grafts)

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Apical Core Specimens
Ischemic Heart Disease - Pathologic Features

- **Short-Axis View**

- **Photomicrograph**
  Replacement-type fibrosis

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Apical Core Specimens
Ischemic Heart Disease - Pathologic Features

- **Short-Axis View**

- **Photomicrograph**
  Replacement-type fibrosis
Apical Core Specimens
Examination & Processing of Specimens

Gross Examination
- **Features to note**
  - Scars
  - Wall thinning
  - Mural thrombus
- **Sections to submit**
  - 1-2 perpendicular sections
    (endocardium to epicardium)
- **Stains to order**
  - H&E
  - Fe / Congo Red (depending on ha)

Histologic Examination
- **Features to note**
  - Myocyte hypertrophy
  - Interstitial fibrosis
  - +/- amyloid
  - +/- iron
  - Myocarditis

Apical Core Specimens
Tips for Reporting

Template

Diagnosis (AFP)

Apical Core (AFPC)

Received in formalin 10% for 24 hours.

A transmural myocardial specimen measuring 0.5 x 0.5 x 0.5 cm and weighing 0.01 g, with fibrous scar and with mural thrombus. Photomicrography of representative sections submitted for microscopic review.

Heart, left ventricle, apical non-infarcted. NIDM. Moderate fibrous hypertrophy and mild endocardial fibrosis. No acute myocardial fibrosis. No acute endocardial fibrosis. No acute amyloid deposition (evaluated with Oil Red O stain). Removed during explantation of left ventricular assist device.

Overview

- **Types of specimens**
  - septal myectomies
  - endomyocardial biopsies
  - apical cores
  - atrial appendages

- **Prototype disease**
- **Examination and processing of specimens**
- **Tips for reporting**
Atrial Appendage Specimens
Atrial Fibrillation - General Features

- **Definition**
  Most common sustained cardiac arrhythmia

- **Clinical features**
  Dyspnea, fatigue, syncope
  Thromboembolism

- **Prevalence**
  1% - 2% in North America
  9% in those > 80 yo

- **Mortality**
  1.5-1.9 -fold 1 mortality risk

Atrial Appendage Specimens
Specimen Overview

Atrial Appendage Specimens
Specimen Overview

Windsock
Atrial Appendage Specimens
Atrial Fibrillation - Histopathologic Features

- myocyte hypertrophy
- interstitial fibrosis
- interstitial fatty infiltration
- myocyte vacuolization
- endocardial fibroelastosis
- myocardial inflammation
- amyloidosis

[Image of Myocyte Hypertrophy]


Atrial Appendage Specimens
Atrial Fibrillation - Histopathologic Features

- myocyte hypertrophy
- interstitial fibrosis
- interstitial fatty infiltration
- myocyte vacuolization
- endocardial fibroelastosis
- myocardial inflammation
- amyloidosis

[Image of Interstitial Fibrosis]


Atrial Appendage Specimens
Examination & Processing of Specimens

**Gross Examination**
- Features to note
  - Size
  - Mural thrombus
- Sections to submit
  - 1-2 perpendicular sections

**Stains to order**
- H&E
- Congo Red / SAB (depending on hx)

**Histologic Examination**
- Features to note
  - Myocyte hypertrophy
  - Interstitial fibrosis
  - Mural thrombus
  - Myocarditis

[Diagram of examination and processing]
Atrial Appendage Specimens
Tips for Reporting

Template

Mass Procedure
Description: Received in formula labeled "__________" as an atrial appendage measuring __________ cm, with/without mural thrombus. Photographed, sections, representative sections submitted for microscopy as cassette A1/B1/_____.

Diagnosis: Right, right / left atrial appendage, excision: Mild / Moderate / Severe myxoid hyperplasia, with/without mural thrombus without intratumoral fibrosis, with/without mural thrombus, removed during the main procedure.

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• Types of specimens
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