Case Presentation

Jared Routh, MD
Cardiology Fellow

20 year old female with pre-excitation

• CC: Pre-excitation on EKG
• HPI:
  • 20 year old female who initially presented to the ED after smoking marijuana she suspected was laced.
  • She left without being seen.
  • EKG was obtained and showed pre-excitation and T wave abnormalities.
20 year old female with pre-excitation

- HPI con’t:
  - In clinic, complained of rare palpitations.
  - Denies racing heart, lightheadedness/dizziness, syncope (ever).
  - Denies exertional symptoms (chest pain, dyspnea).
  - Denies orthopnea, paroxysmal nocturnal dyspnea, lower extremity edema.
- PMH, PSH – unremarkable.
- No medications.
- NKDA
- FH – paternal grandfather with stroke.
- Social history: Social alcohol use. Occasional marijuana use. Denies the use of other illicit drugs.

20 year old female with pre-excitation

- Physical examination:
  - Vital signs: HR 85, BP 115/75
  - Remainder of the examination unremarkable.
- EKG performed in clinic showed pre-excitation.
20 year old female with pre-excitation

- Plan:
  - 7 day Zio Patch
  - Treadmill exercise stress test to evaluate for resolution of delta wave at a higher heart rate
  - Transthoracic echocardiogram

Zio Patch

- 11 runs of NSVT
  - Longest 17 beats
  - Fastest 214 bpm
- 68 SVT episodes
  - Fastest 285 bpm
GXT

- Exercised for 9 min 16 sec and achieved 10.8 METS, peak HR 173 bpm
- Reason for stopping test: SOB
- Delta wave did not resolve at increased HR
- No exercise induced arrhythmias

Transthoracic Echocardiogram
Transthoracic Echocardiogram

Cardiac MRI
Cardiac MRI – LGE

Cardiac MRI – LGE
Invitae Genetic Testing

One Pathogenic variant identified in LAMP2. LAMP2 is associated with X-linked Danon disease.

<table>
<thead>
<tr>
<th>GENE</th>
<th>VARIANT</th>
<th>ZYGOSITY</th>
<th>VARIANT CLASSIFICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAMP2</td>
<td>c.1297T&gt;A (p.Tyr433*)</td>
<td>heterozygous</td>
<td>PATHOGENIC</td>
</tr>
<tr>
<td>GATA5</td>
<td>c.682C&gt;G (p.Arg228Cys)</td>
<td>heterozygous</td>
<td>Uncertain Significance</td>
</tr>
<tr>
<td>TTN</td>
<td>c.10699A&gt;C (p.Ile3563Asp)</td>
<td>heterozygous</td>
<td>Uncertain Significance</td>
</tr>
<tr>
<td>CAA</td>
<td>c.2653C&gt;A (p.Glu885Asp)</td>
<td>heterozygous</td>
<td>Benign (Pseudodeficiency allele)</td>
</tr>
</tbody>
</table>

About this test
This diagnostic test evaluates 100 gene(s) for variants (genetic changes) that are associated with genetic disorders. Diagnostic genetic testing, when combined with family history and other medical results, may provide information to clarify individual risk, support a clinical diagnosis, and assist with the development of a personalized treatment and management strategy.

Danon Disease

Lysosomal glycogen storage disease with normal acid maltase

Netta J. Danon, M.D., Sini J. Oh, M.D., Salvatore DiMauro, M.D., Jose R. Manaligod, M.D., Ph.D., Abe Eastroud, Ph.D., Satishchand Nande, M.D., and Louis H. Schillingfeld, Ph.D.

acid maltase (acid a-glucosidase) deficiency (AMG) occurs in infancy, childhood, and adults. In the infantile form (Pompe disease), glycogen accumulates in all tissues, especially heart, skeletal muscle, and central nervous system (CNS). Both the clinical course and the genetics of this type vary from the infantile to the adult form. However, the childhood form and adult form vary to clinical presentation, and both are primarily caused by a deficiency of acid maltase. Clinical manifestations of AMG share various similarities with glycogen storage and biochemical reaction with acid phosphatase in the vacuoles. Autophagic vacuoles increased amounts of intermembrane space of glycogen, and excessive muscle injury are some of the common findings in all three types.1-3 Biochemical analysis shows increased glycogen content and absence or deficiency of acid maltase activity in skin biopsies of these patients with pathologic changes in muscles that are typical of AMG. Although biochemical measurement of glycogen content, acid maltase activity was normal in muscle and urine.

One report suggests that X-linked adrenoleukodystrophy (XALD) was not detected in all affected patients, and that analysis of skin biopsy with acid maltase activity is required to rule out AMG

The following laboratory studies were normal: lipids, amino acids, plasma, and blood cell count. Alkaline phosphatase was 109 IU/L (normal, 30 to 115 IU/L). Serum glucose-6-phosphate dehydrogenase (G6PD) was 200 IU/L (normal, 0 to 140 IU/L). Serum adenosine deaminase (ADA) was 150 IU/L (normal, 0 to 115 IU/L), and serum
Danon Disease

- LAMP2 mutation
  - Lysosome associated membrane protein
  - Involved in autophagy and lysosomal protein degradation
  - Deposition of intracytoplasmic vacuoles
- X-linked dominant inheritance pattern
  - De novo mutations have been reported
  - Males are hemizygous for LAMP2

Clinical Manifestations

<table>
<thead>
<tr>
<th>Table 1 Reported clinical characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<tr>
<td><strong>Cardio</strong></td>
</tr>
<tr>
<td>Symptomatic heart disease 38.5 77.7</td>
</tr>
<tr>
<td>Chest pain                              41.6 37.5</td>
</tr>
<tr>
<td>Palpitations                            37.5 68.8</td>
</tr>
<tr>
<td>Hypertrophic cardiohypertrophy 88 33.3</td>
</tr>
<tr>
<td>Clinical cardiohypertrophy              12 27.7</td>
</tr>
<tr>
<td>Conduction abnormality                   46.4 80</td>
</tr>
<tr>
<td>Wolff-Parkinson-White                     64.2 26.7</td>
</tr>
<tr>
<td>Cardiac dilation                         55.3 30.8</td>
</tr>
<tr>
<td>Ocular/retinal abnormalities             44.2 31.3</td>
</tr>
<tr>
<td>Neurologic</td>
</tr>
<tr>
<td>Learning and cognitive problems          100 46.6</td>
</tr>
<tr>
<td>Visual and retinal abnormalities         69.2 64.2</td>
</tr>
<tr>
<td>Symptomatic muscle disease               66 30</td>
</tr>
<tr>
<td>Muscle cramping                          4.1 15.3</td>
</tr>
<tr>
<td>Nystagmus                                9.1 38.5</td>
</tr>
</tbody>
</table>

Cardiac manifestations


CMR in Danon Disease

Rigolli M et al. JACC CV Imaging 2021;14:514-516.
Strain imaging in Danon Disease

Changsheng M. Eur Heart J Case Rep 2021;12.

Clinical Outcome and Phenotypic Expression in LAMP2 Cardiomyopathy

Barry J. Maron, MD
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Paula Spirito, MD
Gregory B. Wright, MD
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Jonathan Neufman, PhD
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Massive myocardial storage diseases that mimic the clinical and phenotypic expression of hypertrophic cardiomyopathy (HCM) have recently been reported in young patients, including those diseases due to mutations in the X-linked lysosome-associated membrane protein gene (LAMP2, OMIM 308400). Danon disease.

The morphological expression and the clinical course experienced by patients with this newly identified cardiomyopathy are incompletely resolved. Therefore, it is informative to report our experience with an assessment of the natural history.

Conclusion:  
Mutations in X-linked lysosome-associated membrane protein gene (LAMP2) Danon disease produce a cardiomyopathy in young patients that clinically mimics severe hypertrophic cardiomyopathy (HCM) due to sarcomere protein mutations. However, the natural history and phenotypic expression of this newly recognized disease is incompletely resolved and its identification may have important clinical implications.

Objectives:  
To determine the clinical consequences, outcome, and phenotypic expression of LAMP2 cardiomyopathy associated with diagnostic and management strategies.

Setting, Patients:  
Clinical course and outcome were assessed prospectively in 7 young patients (6 boys) with defined LAMP2 mutations from the time of diagnosis (age 7-17 years, median, 14 years) to October 2008. Phenotypic expression of this disease was assessed both clinically and at autopsy.

Results:  
Over a mean (SD) follow-up of 8.6 (2.6) years, and by age 14 to 24 years, the study patients developed left ventricular systolic dysfunction (LVD: systolic fraction, 25% (7%)); and cardiac enlargement, as well as particularly adverse clinical consequences, including progressive refractory heart failure and death (n = 4) sudden death (n = 1), aborted cardiac arrest (n = 1), or heart transplantation (n = 1). Left ventricular hypertrophy was particularly marked (maximum thickness, 29-40 mm; mean, 41 (27 mm), including 2 patients with massive ventricular septal thickness of 40 mm and 50 mm at ages 23 and 14 years, respectively. In 6 patients, a ventricular proarrhythmia pattern at study entry was associated with markedly increased voltages of R-waves or S-waves (15-145 mm, mean, 89 (39 mm), and deeply inverted T-waves. Autopsy findings included a combination of histopathologic features that were consistent with a heritable storage disease (incrustation of vacuolated myocytes but also typical of HCM due to sarcomere protein mutations [ie, myocyte disarray, small vessel disease, myocardial scarring]).

Conclusions:  
LAMP2 cardiomyopathy is a profound disease process characterized by progressive clinical deterioration leading rapidly to cardiac death in young patients (n = 20 years). These observations underscore the importance of clinical and early consideration of heart transplantation.
Table. Clinical, Demographic, and Pathologic Findings in 7 Patients With LAMPM Cardiomyopathy (continued)

<table>
<thead>
<tr>
<th>Patient (M)</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Status status (most recent)</td>
<td>Sudden death (found dead in bed)</td>
<td>Acute HF death</td>
<td>Failure (CIDP) with life support for VT [230 min]</td>
<td>Acute HF death</td>
<td>Sudden death</td>
<td>Progressive HF, liver, renal, systemic failure, pulmonary edema</td>
<td></td>
</tr>
<tr>
<td>Creatinine</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Cardiac enzymes elevated</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
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<tr>
<td>Genetic transmission</td>
<td>Sporadic</td>
<td>Sporadic</td>
<td>Sporadic</td>
<td>Sporadic</td>
<td>Sporadic</td>
<td>Sporadic</td>
<td>Sporadic</td>
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<tr>
<td>Mutation</td>
<td>Y150ter (homozygous at residue 109)</td>
<td>M218L (homozygous at codon 67)</td>
<td>M218L (homozygous at codon 67)</td>
<td>M218L (homozygous at codon 67)</td>
<td>M218L (homozygous at codon 67)</td>
<td>M218L (homozygous at codon 67)</td>
<td>M218L (homozygous at codon 67)</td>
</tr>
</tbody>
</table>

Take home points

- Danon disease is also mistaken for HCM (or other HCM mimics).
- Diagnosis requires clinical suspicion especially in young patients with LVH and WPW.
  - Avoid misdiagnosis and delays in care
- Genetic testing should be considered in patients with undifferentiated cardiomyopathy

![Table](https://example.com/table.png)

2020 ACC/AHA HCM Guidelines.
Clinical manifestations

Males
- Cardiomyopathy – nearly all
- Skeletal muscle weakness 80-90%
- Cognitive impairment 70-100%
- Conduction abn 86-100%
  - WPW 69%
- Myopathy 80-90%
- Retinal involvement 69%

Females
- Cardiomyopathy – nearly all
- Equal rates of dilated and hypertrophic
- Skeletal muscle weakness 33-50%
- Cognitive impairment 6-47%
- Conduction abn 80-100%
  - WPW 27%
- Myopathy – much less involvement
- Retinal involvement 64%
Cardiac MRI
# HCM Mimics

<table>
<thead>
<tr>
<th>Clinical Features in Patients With &quot;HCM Phenocopies (Mimics)&quot;</th>
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<tbody>
<tr>
<td><strong>Typical Presentation Age</strong></td>
</tr>
<tr>
<td>Infants (0-12 mo.)</td>
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<td>Early childhood</td>
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<tr>
<td></td>
</tr>
<tr>
<td>School age and adolescence</td>
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<tr>
<td></td>
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<td></td>
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<tr>
<td></td>
</tr>
<tr>
<td>Adulthood</td>
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</table>

HCM mimics hypertrophic cardiomyopathy.

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**MHIF Cardiovascular Grand Rounds | February 14, 2022**

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(Not) Just another mitral stenosis case

2/14/2022

Iulia Tulai MD, Cardiology Fellow
Minneapolis Heart Institute
Case presentation

- 35 y.o. female – cardio-obstetric clinic

PMH:
- Symptomatic rheumatic mitral stenosis
  - Diagnosed 5 months ago
    - Stress echo mitral gradient 8 → 28 mmHg
  - Scheduled for balloon valvuloplasty
  - Cancelled – 6 weeks pregnant

Case presentation...

- History:
  - 35 y.o. female – cardio-obstetric clinic visit
  - Symptomatic rheumatic mitral stenosis
  - 17 weeks pregnant
    - SOB walking 100 feet
    - Intermittent palpitations
    - No syncope
    - BP 90s/60s, HR ~70s
    - Already on Toprolol 12.5 mg daily
What would you do?

Why the panic?
Hemodynamics of pregnancy

1. **↑ Blood volume** ~50% increase
   - Estrogen-mediated stimulation of RAAS
   - plasma >> RBC mass → “anemia”
   - 20-100% increase, average ~50% increase

2. **↑ CO {↑ SV, ↑ HR} ~30-50% above baseline**
   - ↑ preload (increased blood volume)
   - ↓ SVR (relaxin, elastase)
   - ↑ HR by ~10-15 BPM

3. **↓ BP and ↓ SVR**
   - DBP >> SBP → wider pulse pressure
   - Begins in 1st trimester
   - Nadir ~ 10 mmHg below baseline at the end of 2nd trimester

4. During labor & delivery → 75% ↑ CO (contractions)
   - ↑ SV: *autotransfusion* = 300-500 ml blood displaced into the maternal circ. / each uterine contr.
   - ↑ HR

5. **Postpartum** – rapid volume shift
   - blood loss: 300-500 ml (vaginal) / 500-800 ml (C-section)
   - temporary ↑ venous return:
     - autotransfusion
     - relief of caval compression
   - **↑ SV, ↑ CO** → brisk diuresis

6. Hypercoagulability
Mitral stenosis in pregnancy

- **Mild MS** – usually well tolerated

- **Severe MS:**
  - $\leq 1.5 \text{ cm}^2$ – 30% of patients will develop HF [2nd trimester]
  - $\leq 1.0 \text{ cm}^2$ – 50% of patients will develop HF [2nd trimester]

- **0-3% mortality** in developed countries

How can we help such patients?

1. **Prevention** = Preconception planning / visit
   - Risk stratification tools: CarPreg II, ZAHARA, mWHO

2. Medical treatment / optimization

3. Valve intervention
1. Prevention - Risk stratification tools

- CarPreg
- ZAHARA
- mWHO

Medical treatment / optimization

Valve intervention

How can we help such patients?

1. Prevention = Preconception planning / visit
   - Risk stratification tools: CarPreg, ZAHARA, mWHO

2. Medical treatment / optimization

3. Valve intervention
1. Decrease transmitral gradient - betablockers
   - Low BP; can’t uptitrate her betablocker
   - Ivabradine – not approved in pregnancy
     - animal studies: embryofetal toxicity, teratogenicity and increased post-implantation loss

2. Prevent CHF; maintain euvoledma
   - Check serial BNPs
     - Differentiate pregnancy Sx vs CHF Sx
     - Should remain normal throughout pregnancy

3. Identify tachyarrhythmia
   - If Atrial fibrillation:
     - needs anticoagulation
     - maintain sinus rhythm?
How can we help such patients?

1. Prevention = Preconception planning / visit
   - Risk stratification tools: CarPreg, ZAHARA, mWHO

2. Medical treatment / optimization

3. Valve intervention - When?

When to intervene in pregnancy?

- Delay Rx procedures at least 12 weeks from LMP
  - Organogenesis is complete

- Best time – after 4th month of 2nd trimester:
  - Organogenesis is complete
  - Fetal thyroid is inactive
  - Small uterine volume
Balloon valvuloplasty

- PBMV – 19 weeks gestation
- Guidance:
  - Fluoroscopic
  - Transthoracic
  - Intracardiac guidance
    - 491 mGy to the mother
    - Fetus – difficult to calculate, but... low
      - If fetus in the direction of the radiation beam, radiation ~ 0.15 x mother’s entrance skin dose
- Inoue 26 mm balloon used
- 3 total balloon inflations
- Post procedure MG ~ 5mmHg (from 8mmHg)
- Further dilatations not done (MR risk)

Now...

- 27 weeks gestation
- Medications:
  - Metoprolol XL 12.5 every evening
  - ASA 81 mg daily (gestational diabetes, risk of pre-eclampsia)
  - No anticoagulation (no Afib)
- Repeat TTE last week MVA ~ 1.8 cm2
- Cardiology visit last week: symptoms NYHA II-III
- She WILL need surgical MVR/R
Take home messages

1. Remember the hemodynamics of pregnancy
2. Remember to use mWHO for young women at any childbearing age – estimates mom’s risk
3. If a condition is in mWHO class IV
   - recommend against immediate pregnancy
4. Recommend contraception! {estrogen-free}
5. Safest window for ionizing radiation-therapies
   - At least 12 weeks after LMP
   - Safest – after 4th month of 2nd trimester
   - <10-20 cGy

Resources

Team-Based Care of Women With Cardiovascular Disease From Pre-Conception Through Pregnancy and Postpartum

2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy

The Task Force for the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC)
Heart disease complicates <1% of pregnancies

the normal hemodynamic changes of pregnancy can precipitate cardiac symptoms in previously stable women, or may exacerbate symptoms in those who had symptoms before pregnancy

Ideally, preconceptual planning includes:

1. advice to each woman about the risk of pregnancy for herself and the baby,
2. optimization of her cardiac condition, and
3. institution of careful monitoring and treatment starting before conception and continuing through pregnancy into the postpartum period.
Heart disease complicates < 1% of pregnancies

The normal hemodynamic changes of pregnancy can precipitate cardiac symptoms in previously stable women, or may exacerbate symptoms in those who had symptoms before pregnancy.

Ideally, preconceptual planning includes:
1. Advice to each woman about the risk of pregnancy for herself and the baby,
2. Optimization of her cardiac condition, and
3. Institution of careful monitoring and treatment starting before conception and continuing through pregnancy into the postpartum period.

Box 2 Cardiac findings in a normal pregnancy

- Normal history
  - Fatigue
  - Decreased exercise tolerance
  - Palpitations
  - Lower extremity oedema
  - Orthopnoea

- Normal examination
  - Midsystolic murmur at left base (pulmonic flow murmur)
  - Continuous murmur (mammary souffle)
  - Split S1
  - Distended neck veins with prominent a and v waves
  - Lower extremity oedema
Imaging considerations...

- Compression of the IVC decreases CO by up to 30% when supine (3rd trimester) → imaging and flows can be affected

- TEE: >18 weeks pregnant woman’s fasting status = “full stomach”
  - High progesterone
    - → decreased gastric motility
    - → increased relaxation of the lower esophageal sphincter
    - + increased intra-abdom pressure
      - → high risk of emesis and aspiration
      - → endotracheal intubation is frequently recommended with TEE >1st trimester

Treatment considerations

- Knowledge of safety and efficacy

  - 1) Safety: FDA (A,B,C, D and X) → summaries w risks and benefits
    - LacMed – for lactating women

  - 2) Efficacy:
    - Increased hepatic clearance
    - Increased renal clearance
    - Decreased albumin and plasma binding proteins

  - → pharmacokinetics are altered in pregnant state
  - → effective dose of a drug may be HIGHER or LOWER than in nonpregnant state
  - → effective dose may change throughout pregnancy
Anticoagulation Strategies in Pregnant Women with MHV

- **Vitamin K antagonist (VKA):**
  - % average risk
  - 5: 0%, 10: 2%, 15: 4%, 20: 6%, 30: 8%, 40: 10%

- **Low-dose warfarin:**
  - % average risk
  - 5: 0%, 10: 2%, 15: 4%, 20: 6%, 30: 8%, 40: 10%

- **Low-molecular-weight heparin (LMWH):**
  - % average risk
  - 5: 0%, 10: 2%, 15: 4%, 20: 6%, 30: 8%, 40: 10%

- **LMWH + VKA:**
  - % average risk
  - 5: 0%, 10: 2%, 15: 4%, 20: 6%, 30: 8%, 40: 10%

- **Unfractionated heparin + VKA:**
  - % average risk
  - 5: 0%, 10: 2%, 15: 4%, 20: 6%, 30: 8%, 40: 10%

**Data From:** Steinberg Z et al. JACC, 2017

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**Woman With Mechanical Heart Valve**

- Pregnant women with a mechanical prosthesis should receive therapeutic anticoagulation with frequent monitoring during pregnancy (Y).
- Can women maintain therapeutic anticoagulation with frequent monitoring? (N)
- Counsel against pregnancy (Y)
- Patient counseled that there is no anticoagulation strategy that is safe for mother and fetus. Shared decision-making (Y)
- Warfarin dose >5 mg/d?
- Dose-Adjusted LMWH with monitoring of Xa levels available?
- 1st, 2nd, 3rd trimesters
- Continue warfarin for all trimesters (Y)
- Discontinue warfarin, switch to continuous LMWH or dose-adjusted LMWH (N)
- Stop heparin (Y)
- Discontinue LMWH for all 3 trimesters (N)
- Stop LMWH (Y)
- Discontinue warfarin for the 3rd trimester followed by warfarin for the 1st and 2nd trimesters (N)
- Discontinue warfarin for the 1st trimester followed by warfarin for the 2nd and 3rd trimesters (N)
- Stop LMWH (Y)
- Discontinue LMWH for the 1st trimester followed by warfarin for the 2nd and 3rd trimesters (N)

*Colors correspond to Table 2: Dose-adjusted LMWH should be given at least 2 hours before or after warfarin. For LMWH, target anti-Xa levels of 0.3 to 1.1 U/mL, 4 to 6 hours after dose. Additional LMWH should be given in the 1st trimester for 1 to 2 times normal. At least 30 minutes before delivery, LMWH should be continued.*
Why the panic?

• What would you do?

Mitral stenosis in pregnancy

- Pre-Conception Imaging
- Exercise Testing if Asymptomatic

- Proceed With Pregnancy With Expert Multidisciplinary Team

- Clinical and Echocardiography Assessment at Least Once / Trimester (Q4: 8 Weeks for > Mild MS or Symptomatic Patients)

- Nodal Blockade-goal HR < 80 beats/ min Diuretics as needed Anticoagulation Exercise restriction Valvuloplasty if failure of medical management

- Vaginal Delivery for Most Consider Assisted Second Stage for Moderate Disease Cesarean Delivery for Acute Decompensated Heart Failure or Very Severe Stenosis

- Postpartum Monitoring for Volume Overload and Diuresis

Valve Intervention

Asymptomatic
MVA > 2.5 cm²

Symptomatic
MVA < 1.5 cm²

69

70
Preconception visit:

1. Establish the level of *maternal and fetal risk*
   - risk stratification tools: CarPreg, ZAHARA, mWHO

2. **Optimization** of mom’s cardiac condition
   - Optimize CV condition & optimize medications

3. Institute careful *monitoring and treatment plan*

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**Rheumatic MS - timeline of diagnosis**

➢ **TTE** (5 months prior):
  - MG 8 mmHg @ 89 BPM
  - PHT ~148-150 msec, MVA ~ 1.5 cm²
  - Ø PASP

➢ **Stress echo with bicycle ergometry** (5 months prior – on metoprolol):
  - Rest (HR=86, BP 96/70 mmHg):
    - MG 8 mmHg
    - PASP ~ 30 mmHg
  - Stress (HR=133 [73% APMHR], BP 122/74, 5.8 METS):
    - MG 28 mmHg
    - Ø PASP

➢ **TEE** (4 months prior):
  - Favorable mitral valve anatomy / Wilkins score for balloon valvuloplasty

➢ **Recommended balloon valvuloplasty**
  - Cancelled – 6 weeks pregnant
1. 1) Risk stratification tools

Preconception planning

It is recommended to perform risk assessment in all women with cardiac diseases of childbearing age before and after conception, using the WHO classification of maternal risk.

Heart in Flames: A Case of the Not-so-Sweethearts
Case

- 47 M with no significant PMH
  - 7/2020 -> developed worsening cough and fever, hospitalized with multifocal pneumonia
    - Started on treatment for CAP and clinically improved over 3 days
    - Slow progress at home
    - Started having intermittent pleuritic chest pain and developed LLE pain (behind left knee, travels down calf into ankle/foot)
  - 8/2020 -> ANW
    - LE u/s: normal
    - CXR: stable/slight improvement of b/l upper lobe opacities
    - EKG: no current of injury
    - CTPE negative for PE
      - RUL consolidation with evolution of central cavitation - Necrotizing PNA vs granulomatous infection
    - Troponin 5.7
      - Cardiology consulted
Coronary CTA

Presumed acute myopericarditis in setting of multifocal PNA vs pulmonary vasculitis
- ID, Pulmonology following
- ANA, ANCA testing pending; HIV and COVID negative
- Bronchoscopy planned

- TTE with LVEF 55%, abnl mid anterior septum and septum
  → CMR
Two discrete myocardial infarctions with evidence of MVO and edema in different coronary distributions
  - Consistent with multivessel embolism vs possible coronary vasculitis
  - Consider invasive angiography, if needed for diagnostic purposes (pending pulmonary evaluation)

Markedly inflamed pericardium on CMR c/w acute pericarditis
  - Continued on colchicine
Laboratory Evaluation

Normal Creatinine, + microscopic hematuria

ANCA-Associated Vasculitis

- Diagnosed with granulomatosis with polyangiitis (Wegner’s)
  - Supported by +ANCA and anti-proteinase 3 titers
  - Pulmonary disease, neuropathy, coronary arteritis
  - Lung bx for confirmation → no granulomas
    - Rheumatology thought GPA most likely dx and started on prednisone
New Chest Pain

- Acute onset of substernal chest pressure (not pleuritic)

Invasive Coronary Angiogram
SUMMARY OF FINDINGS:

1. Angiography confirming MRI findings of a discrete myocardial infarction in 2 territories consistent with a cardioembolic occurrence.
2. Occluded intermediate and occluded LAD diagonal, both relatively terminal.
3. Vasculitic changes noted in the distal first obtuse marginal branch with eating of the small vessel consistent with vasculitis.

Case Follow-up

- Medically managed infarct of the intermediate artery
  - Hemodynamically stable and ?benefit of revascularization in setting of vasculitis

- Continued on high dose prednisone and started on IV rituximab

- Following with outpatient rheumatology and cardiology
  - Resolution of chest symptoms
  - Leg/foot pain persist, though slowly improving
  - ANCA negative as of 3/2021 (recurrence less likely)
Coronary Artery Vasculitis

- Cardiac manifestations in systemic vasculitis are variable
  - Myocarditis, pericarditis, valvular disease > coronary artery vasculitis
  - Generally rare, portend poor prognosis
  - CAV most commonly described in PAN, KD, TA, and GCA
- High index of suspicion for CAV in setting of unexplained ACS
  - Especially in young pts with known vasculitis
- RR of CHD-related mortality in pts with AAV 2-4x higher than controls
  - Accelerated CAD vs active inflammation

Cardiac Involvement in GPA

- Heterogeneous clinical presentation of GPA
  - Upper/lower RT and kidney involvement are typical
  - Cardiac involvement is rare (and variable)
    - European Vasculitis Study group: 5.7% of pts with newly dx ANCA-associated vasculitis had cardiac involvement of any type
      - Independent risk factor for relapse
- No difference in demographics / clinical features in patients with or without cardiac involvement in GPA
Multimodality Imaging

- Invasive angiography
  - Characteristic features of CAV, though limited ability to differentiate
  - Benefit of IVUS
- CTA or MRA
  - Recommended to evaluate for other vascular involvement
  - Additional benefit with MRI for evaluation of myocarditis/pericarditis
- PET
  - Helpful in evaluating hypermetabolism of aorta and first order branches
  - Poor sensitivity for medium and small-vessel vasculitis (incl. coronaries)
- Perfusion studies
  - Helpful for determining viability, though cannot differentiate vasculitic from atherosclerotic processes


Revascularization

- Limited data, regardless of etiology (case reports, retrospective cohort studies)
  - No prospective RCT on optimal timing or method of revascularization
  - Observational data suggest surgery should be avoided during active stage of inflammation
  - Regardless of revascularization strategy, management of underlying vasculitis is essential
- Meta-analysis comparing outcomes of endovascular vs open surgical intervention in TA pts
  - 770 patients - 389 endovascular, 420 surgical
  - Subgroup analysis based on lesion location
  - Coronary restenosis occurs more often with PCI than with CABG

Coronary Artery Vasculitis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Size Artery Involved</th>
<th>Estimated Arterial Incidence</th>
<th>Common Clinical Characteristics</th>
<th>Common Laboratory Abnormalities</th>
<th>Frequency Coronary Involvement</th>
<th>Suggestive Coronary Angiographic Features</th>
<th>Suggestive Extra-Coronary Angiographic Features</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Takayasu's arteritis</td>
<td>Large (v)</td>
<td>1-2 per million</td>
<td>Oesot &lt; 40 yrs</td>
<td>Limb claudication</td>
<td>Arterial stenoses</td>
<td>Asymmetric pulse/FP</td>
<td>Thickening or narrowing/inclusion of large arteries (aorta or primary branches)</td>
<td>GC, MTX, TNF-inhibitor</td>
</tr>
<tr>
<td>Giant cell arteritis</td>
<td>Large (&gt; v)</td>
<td>10-30 / 100,000*</td>
<td>Oesot &gt; 50 yrs</td>
<td>Cardiac symptoms (headache, jaw claudication, double vision, vision loss)</td>
<td>ESR, CRP</td>
<td>Rare</td>
<td>Tapered smooth narrowing</td>
<td>GC, CTZ</td>
</tr>
<tr>
<td>Polyarteritis nodosa</td>
<td>Medium (= v)</td>
<td>4-10 per million</td>
<td>Skin nodules, livedo</td>
<td>Abdominal pain</td>
<td>Testicular pain (men), Mononeuritis multiplex</td>
<td>Hepatitis serology (e.g. ANCA)</td>
<td>10-50%</td>
<td>Non-specific</td>
</tr>
<tr>
<td>ANCA vasculitis</td>
<td>Medium (&gt; v)</td>
<td>1:9 / 10,000</td>
<td>Recurrent abcessus</td>
<td>Pulmonary nodules</td>
<td>Migranes/strokes</td>
<td>(e.g. p-ANCA/AAPA or -ANCA/PBS)</td>
<td>Alternating aneurysms/narrowing (beaded pattern)</td>
<td>Non-specific</td>
</tr>
</tbody>
</table>


Takayasu Arteritis
