Clinical Study KPL-914-C001

- **CONDITION:** Recurrent idiopathic pericarditis
- **PI:** David Lin, MD
- **CONTACT INFO:** Christine Majeski, RN, CCRC, 612-863-3546, christine.majeski@allina.com
- **DESCRIPTION:** Open label phase 2 pilot study of KPL-914 in patients with symptomatic recurrent idiopathic pericarditis
- **CRITERIA LIST/QUALIFICATIONS:**
  - ≥ One recurrent episode of pericarditis
  - Symptomatic at time of enrollment
  - CRP >1mg/dl
  - On stable pericarditis medication prior to enrollment
- **SPONSOR:** Kiniksa Pharmaceuticals
Grand Rounds: Case Records from the Minneapolis Heart Institute

Ashenafi M Tamene MD
December 4th, 2017

“So, I’m the only one who sees a conflict of interest here?”
Case 1: A 46 y.o. male construction worker referred for an Echo

- Prior history of Type A aortic dissection (DeBakey Type II).
- Underwent repair with 32 mm Hemashield graft with resuspension of the aortic valve in 2004.
- History of hypertension, on Amlodipine and Benazepril.
- Intermittent upper chest tightness and lump in the chest for the past 3 months.
- No known family history of aortic syndromes or genetic disorders
Echo Conclusions

- Dilated aortic sinus with maximal diameter of 5.9 cm.
- Ascending aortic graft noted starting right above the sinotubular junction and appears normal.
- **Recommended CTA for further evaluation.**
- The aortic valve is trileaflet, no stenosis and moderate regurgitation.
- Normal LV/RV systolic function.
The patient was referred to cardiology clinic after a CT Angiogram
CTA Conclusions

• Proximal ascending aorta measuring 7.0 cm, increased in size compared to prior CTA in February 2010 (was 6.3 cm).
• Moderate amount of mixed attenuation fluid adjacent to the proximal and mid ascending aorta, mildly increased in size since February 2010.
• No definite evidence of active extravasation was noted (evaluation is limited due to lack of delayed phase imaging).

What would you do?

A. Urgent referral to CV surgery clinic.
B. Call Dr Harris STAT.
C. Hospital admission.
D. Tell the patient to take it easy.
Symptomatic Ascending Aortic Aneurysm

- Rarely symptomatic
- Pain
- Coughing
- Hoarseness
- Dyspnea
- Dysphagia
- Class IC indication for urgent repair.

Patient was admitted to ANW

- Seen by CV surgery and Cardiology consult service.
- Urgent aortic repair was recommended.
- “Upon entering the chest we found a large abscess cavity” ... “tube graft was completely surrounded by purulent fluid”
- Abscess was evacuated and irrigated
- Samples were sent for microbial studies
- Unable to get homograft in time to repair thus chest was closed with plan for definitive surgery in a few days
Clinical course ...

• Infectious disease were consulted
• Started on broad spectrum antibiotics (Vancomycin and Cefepime)
• Underwent Bentall procedure with 29 mm St. Jude HP mechanical valve conduit and reimplantation of coronary arteries
• Negative tissue and blood cultures
• Antibiotics discontinued on discharge

3 Months Post-op CTA
Anatomy of an Aortic Graft

- **Interposition graft**: Diseased native aorta is excised and biologic or synthetic graft placed. Graft is then re-anastomosed to the native anatomic structures.
- **Inclusion graft**: Native aorta is wrapped around the synthetic graft (not commonly performed currently).

Slightly hyperattenuating relative to aortic lumen on non-contrast CT

Hypoattenuating relative to Felt reinforcement and aortic lumen on contrast CT

*RadioGraphics 2013; 33:73–85*
What is Felt?

- Important to obtain non-enhanced images, may mimic pseudoaneurysm, can cause obstruction.

Long-term Complications After Ascending Aorta Repair

- Progression of aortic disease/aneurysm
- Dissection and rupture
- Anastomotic pseudoaneurysm
- Endocarditis/graft infection
- Deterioration of bioprosthetic devices
- Aortic insufficiency
Guideline Recommendations for Imaging Follow up after Repair or Treatment

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Interval</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Dissection</td>
<td>Before Discharge, 1 month, 6 months, Yearly</td>
<td>CT or MR, plus TTE</td>
</tr>
<tr>
<td>Chronic Dissection</td>
<td>Before Discharge, 1 Year, 2 to 3 yearly</td>
<td>CT or MR, plus TTE</td>
</tr>
<tr>
<td>Aortic Root Repair</td>
<td>Before Discharge, yearly</td>
<td>TTE</td>
</tr>
<tr>
<td>AVR + Ascending</td>
<td>Before Discharge, yearly</td>
<td>TTE</td>
</tr>
</tbody>
</table>

*Circulation. 2010;121:e266-e369*

Duke Proximal Aortic Post-operative Surveillance Protocol

- **Aortic Dissection**
  - 3 Months
  - +/- 6 Months if any segment of Aorta >4.0 cm
  - 9-12 Months
  - Annually
    - Extend to q18-24 Months

- **Proximal Aneurysm**
  - 6-9 Months
  - 18 Months
  - q24 Months

*Ann Thorac Surg 2017; 103(3): 734–741*
Case 2: Urgent cardiology consultation for a 78 y.o. Somali male with chest pain

- Intermittent, sharp, pleuritic, left anterior chest pain for 3-4 days prior to admission
- Pain had no correlation with physical activity or movement
- Mildly elevated serum Troponin levels (peak 0.067)
- ECG and STAT Echo were obtained

Past Medical History

- History of subarachnoid hemorrhage and subdural hematoma due to mechanical fall, treated conservatively (2 months prior)
- History of GI bleeding
- Rheumatoid Arthritis
- Hypertension
- Iron deficiency anemia
- He presented with history of dark stools and ~4 gm Hemoglobin drop (from 11 to 7).
What would you do?

A. Start NSAIDs and Colchicine for treatment of acute pericarditis
B. Send the patient to the Cath lab for urgent pericardiocentesis
C. Reassure the internal medicine team that no further evaluation is required
D. Show me more images!
Echo Conclusions

• Moderate-to-large pericardial effusion with evidence of tamponade.
• Normal LV size, borderline wall thickness, normal global systolic function, calculated EF of 63%.
• Mildly enlarged left atrium.
• The aortic valve is trileaflet and sclerotic, no stenosis and mild regurgitation.

Next Step?

A. Start NSAIDs and Colchicine for treatment of acute pericarditis
B. Send the patient to the Cath lab for urgent pericardiocentesis
C. Reassure the internal medicine team that no further evaluation is required
D. Show me more images!
Echo Conclusions

- Small-to-moderate pericardial effusion that is largest anterior to the RA. On the subcostal views the effusion is small. No definite 2D evidence for tamponade.
- Unusual linear echodensities noted in the ascending aorta.
**Differential Diagnosis?**

**Echo Artifacts Mimicking Aortic Dissection**

<table>
<thead>
<tr>
<th>Properties</th>
<th>Dissection Flap</th>
<th>Artifact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random Mobility</td>
<td>Yes</td>
<td>Rigid and fixed relative to the aortic wall</td>
</tr>
<tr>
<td>Echo intensity</td>
<td>Constant along its course</td>
<td>Arise as side lobe and intensity progressively diminishes toward the aortic lumen</td>
</tr>
<tr>
<td>Color Flow</td>
<td>Margination of flow</td>
<td>No effect on the distribution of the color flow signal</td>
</tr>
</tbody>
</table>

*J Am Coll Cardiol Img 2014;7:406–24*
STAT Page from CT Reading Room
• Type A aortic dissection with anterior and posterior flaps terminating at the level of the brachiocephalic trunk.
• Fresh blood/contrast consistent with communication to the effusion.
Pericardial pathology is a frequent complication of acute Type A dissection?

A. True       B. False

Aortic Dissection and Pericardial Effusion  
*Circulation. 2010;121:e266-e369*

- Frequent complication of acute Type A aortic dissection
  - Pericardial pathology upto 1/3 patients
  - Cardiac tamponade in 8-10%
- Two distinct mechanism:
  - Transudation of fluid across the thin wall of an adjacent false lumen (hemodynamically insignificant pericardial effusion)
  - Ruptured dissected aorta into the pericardium
To tap or no to tap?

Cardiac Tamponade in Aortic Dissection

<table>
<thead>
<tr>
<th>Source</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Circulation. 1994;90(5):2375-8</td>
<td>10 Patients, 5 had pericardiocentesis, 3 died and 2 survived</td>
</tr>
<tr>
<td>Circulation. 2012 11;126(11 Suppl 1):S97-S101</td>
<td>18 patients with tamponade, pericardiocentesis successfully performed while waiting for aortic surgery</td>
</tr>
<tr>
<td>Am J Cardiol. 2014;15;113(4):724-30</td>
<td>8 patients underwent pericardiocentesis, 7 survived</td>
</tr>
<tr>
<td>Eur Heart J Acute Cardiovasc Care. 2015;4(2):124-8</td>
<td>6 patients underwent pericardiocentesis, 5 survived</td>
</tr>
</tbody>
</table>

Class IIa, LOE C: In the setting of aortic dissection with hemopericardium, controlled pericardial drainage of very small amounts of the hemopericardium should be considered to temporarily stabilize the patient in order to maintain blood pressure at about 90 mmHg.

_Eur Heart J Acute Cardiovasc Care. 2015 Apr;4(2):124-8_
Controlled Pericardial Drainage for Tamponade from Type A Dissection

The amount of aspirated blood should be small enough to stabilize circulation of critical cardiac tamponade, as a bridge to urgent repair


- Initially 5-10 mL of hemopericardium aspirated
- Changes in BP were closely monitored (to prevent the excessive elevation of BP)
- Intermittent aspiration using 10-mL syringe and 5-10 mL aspiration each time
- Goal SBP ~ 80 to 90 mm Hg

Circulation. 2012;126:S97-S101
**Intra-operative Findings**

- “Upon opening the sternum and pericardium, we discovered a "severe bread and butter pericarditis". There was no evidence of hemorrhagic pericardial effusion" ... “extensive atheromatous ulceration in the ascending aorta”.
- Status post repair with 28 mm Terumo Gelweave graft.

**Case 3:** A 51 year old relatively healthy female, with first degree family history of SCD, presented with multiple episodes of palpitations and presyncopal spells for 3 months prior to admission

- At OSH ED she was found to have frequent unifocal PVCs and runs of non-sustained VT
- PMH unremarkable except for hypothyroidism, on replacement therapy with normal TSH
- Her father died suddenly at age 40 with no structural heart abnormality by autopsy (reported as arrhythmic death)
What would you do?

1. Exercise Echo
2. Exercise ECG
3. Nuclear stress test
4. Coronary CT angiogram
5. Invasive angiogram
6. Cardiac MRI
7. EP study and ablation
She was scheduled to have exercise SPECT and this happened 6 minutes and 30 seconds into exercise.
MRI Conclusions:
- LVEF 56%, normal LV wall thickness and size
- RVEF 60%, normal RV size and function, No delayed Enhancement

Coronary CTA:
- Normal Coronary arteries, Ca score of 0
**Next Step?**

A. Increase BB dose and discharge home
B. EP study and catheter ablation
RVOT VT

- Commonest form of idiopathic VT
- PVCs with LBBB morphology and inferior axis
- Presumed mechanism is triggered activity than re-entry
- Termination by adenosine and degree of suppressibility by beta-blockade
- Catheter ablation for symptomatic patients
- The major differential diagnosis is reentrant VT secondary to ARVC
Thank you!