Pulmonary Vein Stenosis, Congenital, Acquired or Congenitally Acquired?

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Pulmonary Vein Stenosis

- First reported by Reye in 1951, Medical J. of Australia
- Further described by Ferencz, in the late 50's, and then by J. Shone, K. Amplatz, J. Edwards in 1962

Diagnosis of Pulmonary Vein Stenosis

- MRI/CT (Dr. Yoo)
- Echocardiography
- Cardiac Catheterization
**Echocardiography of pulmonary veins**

- Pulse and continuous wave Doppler for evaluation of pulmonary venous blood flow:
  - systolic flow (S wave)
  - diastolic flow (D wave)
  - Atrial contraction (A wave)

- Normal pulmonary venous return exhibits varied flow velocities, with S and D waves

- Pulmonary vein stenosis has higher velocities with a more continuous wave

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**Echo diagnosis: PV stenosis**

- Normal pulmonary venous Doppler flow pattern

- Doppler signal with pulmonary Venous obstruction pattern

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**Echo evaluation of PV stenosis**

- S

- D
PV stenosis, monophasic Doppler flow

Echocardiography & PV Stenosis
- Echocardiography of pulmonary veins
  - May be limited by poor echo windows
    - More common when chronic lung disease is present
    - Sedation may be necessary to adequately image vessels in younger patients
  - Older/larger patients difficult to visualize the pulmonary veins

Normal pulmonary venous return

Pulmonary vein stenosis evaluation by cardiac catheterization
- Pulmonary Artery:
  - Selective pulmonary artery angiography, visualize pulmonary veins on levophase
Cardiac Catheterization for PV stenosis

- **Pulmonary Artery:**
  - Determination of PA pressure
  - PA wedge to LV end-diastolic pressure gradient
    - gradient across the pulmonary vein, assuming no mitral stenosis
PA wedge to LV gradient

Pulmonary Vein Catheterization

- Direct entry into individual PV’s
  - evaluation by angiography to look for stenosis
  - direct pressure measurements, with pull back from pulmonary vein to left atrium
  - Requires presence of atrial septal defect or trans-septal puncture for access to the left atrium.

Treatment of PV Stenosis

- Surgical Therapy (Dr. Azakie)
- Catheter Based Intervention
  - Balloon dilation
  - Stent placement
  - Cutting balloon
Catheter based therapy of PV stenosis

- Balloon dilation of PV's:
  - Some acute improvement in PV flow and pressure gradient
  - Very high recurrence rate, at 50-100% over time
  - May hasten PV stenosis due to vascular inflammatory response to dilation (?)

Catheter based therapy of PV stenosis

- Intravascular stent placement:
  - Excellent acute post cath results, lower gradients, improved systemic saturations
  - Stent placement is also fraught with high recurrence of obstruction, intraluminal stenosis within the stent
  - Potential improved therapy with steroid eluting stent into PV
    - (currently only coronary steroid eluting stents)
Catheter based therapy of PV stenosis
- Cutting balloon treatment of PV stenosis
- Disruption on endothelial lining may improve PV stenosis

Cutting balloon PV dilation
- Most experiences report continued high rate of re-stenosis
- Slightly higher risk procedure
- Frequent catheterization and cutting balloon may improve longer term results (?)
Successful Long Term Treatment of pulmonary vein stenosis

Histologic and pathologic evaluation

- Riedlinger studied path specimens from 7 patients with PV stenosis
  • Age at diagnosis was 3 weeks to 6 months

- Histologic appearance indicates that the PV stenotic lesions are myofibroblast-like in origin
  • Features of smooth muscle cell and fibroblasts

- Stenotic lesions were comprised of a loose extracellular matrix with myxoid tissue and smooth muscle cells

Riedlinger et al, Cardiovascular Physiology (15)2006;91-99

Histologic and pathologic evaluation

- A lack of mitotic figures in all samples

- Immunoreactivity for platelet derived growth factor receptors and Tyrosine kinase receptors

- Suggests an autocrine or paracrine role in pathogenesis of PV stenosis
  • Potential therapeutic targets may exist

Riedlinger et al, Cardiovascular Physiology (15)2006;91-99

Histologic and pathologic evaluation

- They propose that expanded intima, with myofibroblast and matrix deposition is causative lesion of PV stenosis

- Other diseases with myofibroblastic proliferation have been successfully treated by radiation, chemotherapy, and gamma interferon

- Consideration for this type of therapy with PV stenosis

Riedlinger et al, Cardiovascular Physiology (15)2006;91-99
Epidemiology of PV stenosis

Pulmonary Vein Stenosis

- **Congenital (Primary) PV stenosis:**
  - Present at birth, not necessarily diagnosed at birth
  - Abnormal development of the pulmonary venous system

- **Acquired PV stenosis**
  - Patients are born with unobstructed PV return, and later develop PV stenosis
  - Extrinsic process that leads to development of PV stenosis
    - Tumor, infection, RFA (adults)

Pulmonary Vein Stenosis

- **Congenitally Acquired:**
  - Patients are born with unobstructed PV return, and later develop stenosis
  - Abnormal substrate predisposing PV stenosis?
  - Endogenous or exogenous factors contributing to PV stenosis?

Congenital PV Stenosis

- Abnormal incorporation of the common pulmonary vein into the left atrium.
- Symptomatic in first months of life
- Associated with septal defects 30-80%.
**Congenital PV Stenosis**

- Number of pulmonary veins involved:
  - Variability is common
  - Single lung or both lungs may be involved
  - Stenosis from 1-4 veins

- Presentation and severity depends on number of veins involved and extent of stenosis
  - Respiratory symptoms, recurrent pneumonia, right heart failure, edema, hemoptysis
  - *Typically a progressive disease*, frequently leading to PV atresia of affected vessels.

**Congenital PV Stenosis**

- Characteristic of PV obstruction:
  - Discrete medial hypertrophy or intimal proliferation at PV - left atrial junction
  - Atresia of the PV at the PV - left atrial junction
  - Diffuse hypoplasia of PV from hilum of the lung to the left atrium

- PV stenosis may extend into the lung parenchyma
  - Most primary PV cases reported in the literature demonstrate medial hypertrophy of the pulmonary arterioles as part of the disease
  - May help explain significant pulmonary arterial hypertension when evaluation identifies only a single stenotic pulmonary vein
PV stenosis

- Pediatric Cardiac Care Consortium database was searched for PV stenosis or atresia
  - (Excluded TAPVR, ASO, cor triatriatum, prior lung transplantation)
- Catheterization/surgical database with 98,000 pts, over a 20 year period, 1982-2002, ~ 30 programs
- PV stenosis was identified in 31 pts, with completed follow up questionnaires in 26/31
  - PV stenosis incidence: 0.03 % of the database
  - Male: female 16:15

Holt DB et al, Am J Cardiol 2007;99:568-72

PV stenosis

- Increased risk of lung death (death or lung transplant) was associated with:
  - Younger age at diagnosis
    - <18 months at dx: 76% lung death
    - >18 months at dx: 30% lung death
  - Initial mean PA pressure
    - > 33mmHg, 88% lung death
    - < 33 mmHg, 0 % lung death

Holt DB et al, Am J Cardiol 2007;99:568-72

PV stenosis

- Bilateral lung involvement: 17/19 lung death
- Unilateral lung involvement: 0/9 lung death
- Bilateral lung transplant in 7/31 patients
  - All less than 18 months at transplant
    - 3/7 pts alive at 2, 5,11 years post tx.
  - Unilateral pneumonectomy in 5 patients

Holt DB et al, Am J Cardiol 2007;99:568-72

Acquired pulmonary vein stenosis

- Following repair of anomalous pulmonary venous drainage (surgical site stenosis)
- Extrinsic process: neoplasm, sarcoidosis, fibrosing mediastinitis.
- Following radiofrequency ablation at the level of the pulmonary veins for atrial flutter (adult disease)
- “Spontaneous” PV stenosis that may occur into adulthood.
  - ? Mild form of congenital PV stenosis
Acquired pulmonary vein stenosis

- Reduced morbidity and mortality as compared to congenital PV stenosis
- Responsive to interventional/surgical therapy with reasonable mid term results, however re-stenosis remains problematic

Congenitally Acquired PV Stenosis (?)

- Congenitally Acquired:
  - Patients are born with unobstructed PV return, and later develop PV stenosis
  - Abnormal substrate predisposing PV stenosis?
  - Endogenous or exogenous factors contributing to PV stenosis?

Pulmonary Vein Stenosis
A Single center experience

- A retrospective review of the cardiac database at Children’s Healthcare of Atlanta, 1997-2007
- PV stenosis was defined by echo criteria as continuous, turbulent flow in the PV’s, with a mean echo gradient of > 5 mm Hg
- There were 26 infants diagnosed with PV stenosis during this 10 year time period, with 25 having catheterization confirmation of the PV stenosis
- Median age at diagnosis was 7.4 months, range 1day-35 months

Drossner, Pediatrics 2008;122(3):656-661

Pulmonary Vein Stenosis
A Single center experience

- Method of PV diagnosis:
  - 18/26 (69%) diagnosed by echocardiography
  - 8/26 (31%) diagnosed at cardiac catheterization, referred for evaluation of PH
  - Of the 18 patients diagnosed by echocardiography:
    - Nearly all had a prior echo with normal PV’s
    - 17/26 (65%) had 3 or more echocardiograms that did not identify the PV stenosis

Drossner, Pediatrics 2008;122(3):656-661
Pulmonary Vein Stenosis
A Single center experience

- Median gestational age 32 weeks, (24-41 wks)
- 16/26 (61%) were born premature
- Median birth weight 1,925 gms, (460-4445 gm)
- SGA present in 5 subjects

- Preterm birth strongly associated with development of PV stenosis
- Odds Ratio of 10.2 (95% ci 4.7-22, p < 0.001)

Drossner, Pediatrics 2008;122 (3)e656-661

Pulmonary Vein Stenosis
A Single center experience

- Bronchopulmonary dysplasia present in 11/26 (42%) infants with PV stenosis
- Recognized genetic defects were present in 8 (30%), with 5/8 being Trisomy 21

- Associated cardiac defects were present in 23/26 (88%):
  - PDA 12 (46%)
  - ASD 10 (38%)
  - VSD 8 (31%)
  - AVSD 4 (15%)

Drossner, Pediatrics 2008;122 (3)e656-661

Pulmonary Vein Stenosis
A Single center experience

- Median # of stenotic veins was 2, range 1-4
- Average systolic PA pressure at catheterization 60 mm Hg, avg. mean pressure of 42 mmHg
- Left lower pulmonary vein was most likely to be stenosed, with 17/26 (65%)
- Left upper PV next most common: 13 of 26 (50%)
- Surgical interventions occurred in 14 of 26 patients prior to diagnosis of PV stenosis

Drossner, Pediatrics 2008;122 (3)e656-661

Pulmonary Vein Stenosis
A Single center experience

- Incidence of PV stenosis:
  - 1.44 million infants were born in Georgia in the 10 yr time period reviewed
  - 82% of all pediatric heart disease in GA is treated at CHOA
  - Annual incidence of PV stenosis is 1.7 cases per 100,000 children < 2 years of age.

Drossner, Pediatrics 2008;122 (3)e656-661
Pulmonary Vein Stenosis
A Single center experience

- Based on the Metropolitan Atlanta Congenital Defects Program (CDC), we estimate:
  - Less than 1 in 100 preterm infants with a intracardiac shunt lesion is likely to develop stenosis of the pulmonary veins

Drossner, Pediatrics 2008;122 (3):e656-661

PV Stenosis Summary

- PV stenosis is a rare disorder, affecting approximately 1-2 per 100,000 children under 2 years
- A Progressive disease that typically starts with unobstructed pulmonary venous return
- Risk factors for pulmonary vein stenosis include prematurity, especially when associated with septal or other volume overload heart defects

PV Stenosis Summary

- Risk factors for poor outcome
  - Initial diagnosis less than 18 months
  - Initial mean PA pressure of > 33 mmHg at diagnosis of PV stenosis

PV Stenosis Summary

- Prior evaluation including catheterization and echocardiography does not rule out later diagnosis of PV stenosis
- Follow up echocardiography for PH requires careful assessment of pulmonary venous blood flow
PV Stenosis Summary

- PV stenosis is associated with high morbidity and mortality, 45% 2-year survival following diagnosis.
- Treatment: surgical and interventional catheterization is difficult at best, with poor long-term outcomes.
- Experimental studies of chemotherapeutics are ongoing.

Increasing frequency of PV stenosis?

- Improvement in diagnostic imaging.
- Increased awareness of PV stenosis by practitioners.
- Greater numbers of premature infants are surviving beyond infancy.

Pulmonary vein stenosis

- Congenital, Acquired or Congenitally Acquired?
- The answer is “C”, all of the above…

Thank You