Complex Case Presentation

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Disclosures

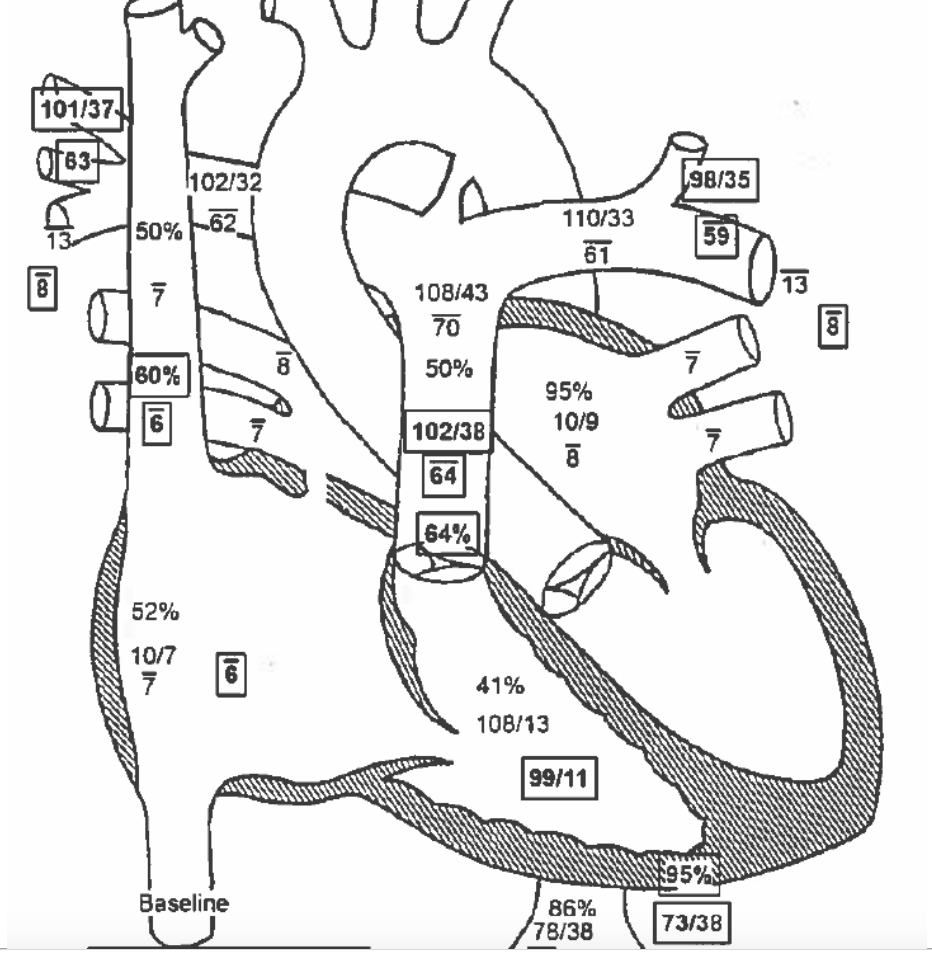
I have no financial interests to declare.

I have not conflicts on interest to declare.

I will discuss the off-label use of pulmonary vasodilators in an infant.

Complex Case Presentation

- Female infant, born at 37w4d female via NSVD to a 40 year old, Gravida 5, Para 302-3 mother; Apgar scores of 8 at 1 minute and 9 at 5 minutes: BW 3300 g
- Pregnancy complications: oligohydramnios/Perinatal complications: Post partum hemorrhage, uterine atony, required emergent hysterectomy
- Infant noted to have a “blistering rash” shortly after birth, Incontinentia pigmenti (IP) suspected
- Genetic testing revealed heterozygous mutation of IKBKG (NEMO), Incontinentia pigmenti diagnosis confirmed
- Age 5 months noted to have a murmur and was referred to cardiology; an echocardiogram showed suprasystemic right ventricular systolic pressures, small ASD, small PDA and no evidence of pulmonary vein stenosis
- Referred to Dr. Yung at Seattle Children’s on May 15, 2018; admitted to the hospital from clinic



Baseline

Qp = 0.77 L/min (2.27 L/min/m2)
Qs = 0.96 L/min (2.83 L/min/m2)
Rp = 74.00 units (25.16 units x m2)
Rs = 46.73 units (15.89 units x m2)
Qp/Qs = 0.80 : 1 | Rp/Rs = 1.58
Qep = 0.77 L/min (2.27 L/min/m2)

On Oxygen

Qp = 0.91 L/min (2.67 L/min/m2)
Qs = 0.97 L/min (2.85 L/min/m2)
Rp = 61.69 units (20.97 units x m2)
Rs = 47.54 units (16.16 units x m2)
Qp/Qs = 0.94 : 1 | Rp/Rs = 1.30
Qep = 0.82 L/min (2.42 L/min/m2)

Nitric Oxide

Qp = 0.80 L/min (2.34 L/min/m2)
Qs = 0.94 L/min (2.76 L/min/m2)
Rp = 64.67 units (21.99 units x m2)
Rs = 47.94 units (16.30 units x m2)
Qp/Qs = 0.85 : 1 | Rp/Rs = 1.35
Qep = 0.80 L/min (2.34 L/min/m2)

Complex Case Presentation

- Chest CT angiogram with contrast: Nonspecific haziness, likely low lung volumes. No pulmonary embolism. Enlarged right heart and pulmonary arteries.
- Sleep Study: Normal
- Abdominal ultrasound: Normal doppler evaluation of portal and hepatic venous systems.
- BNP 303
- Extensive laboratory work-up negative, except for elevated B2 glycoprotein and low C3/C4 (normal ANA)
- Infant was started on SQ Remodulin, Sildenafil and Bosentan
- Family relocated to Northern California in July 2018

Complex Case Presentation

Two months after starting therapy…

- Sildenafil 1 mg/kg PO TID, Bosentan 16 mg PO BID, SQ Remodulin at 40 ng/kg/min
- BNP 82
- Panama FC II/ WHO FC II
- Echo with systemic right ventricular pressure based on TR jet, PDA gradient and systolic septal position, mild RV dilation and hypertrophy, small PDA with bidirectional shunting, PFO with bidirectional flow across the atrial septum, normal biventricular function

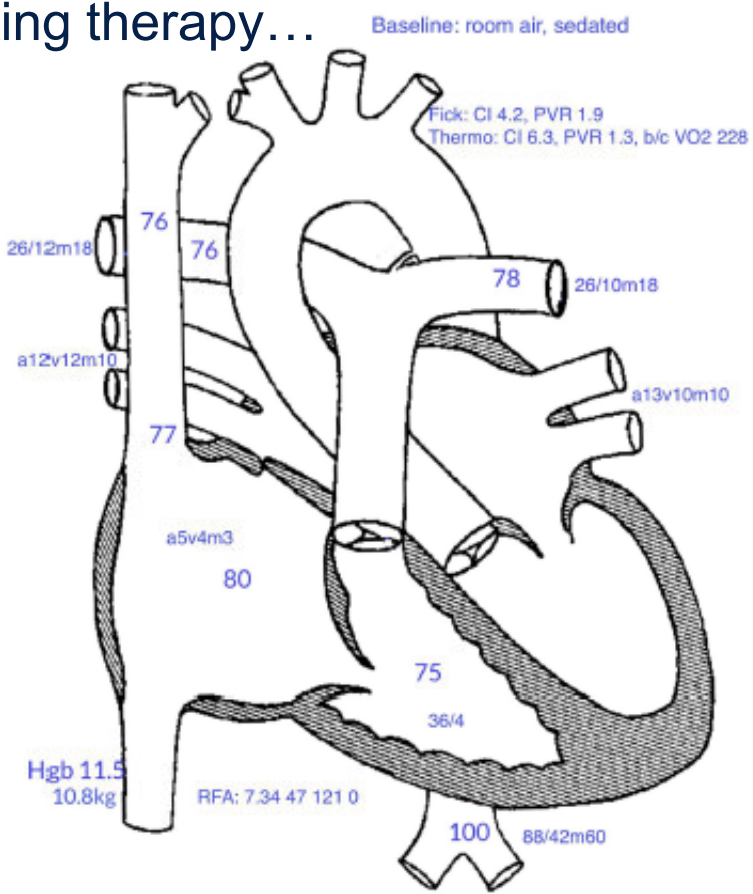
Complex Case Presentation

Five months after starting therapy…

- Sildenafil 1 mg/kg TID, Bosentan 32 mg BID, SQ Remodulin at 70 ng/kg/min
- Panama FC I/ WHO FC I
- Echo with marked improvement in the right ventricular size and hypertrophy to almost normal. The TR jet is estimating an RV pressure of about 50mmhg above RA pressure. IVC is not dilated. The PDA flow is all left to right with about 45mmhg gradient. These findings are consistent with an RV pressure of about 50% systemic. This is a significant improvement from her RV pressure at diagnosis which was suprasystemic.
- Hospital admission from 2/3 – 2/11/19 for E. Coli pyelonephritis and dehydration

12 months after starting therapy…

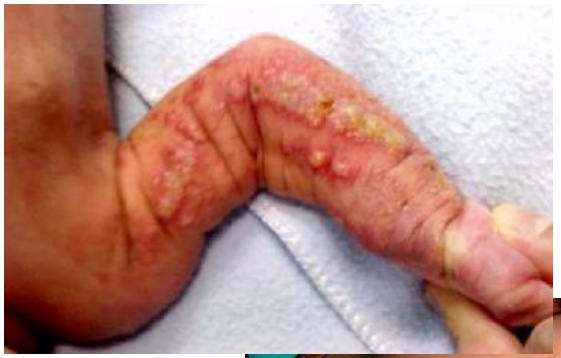
BNP 14

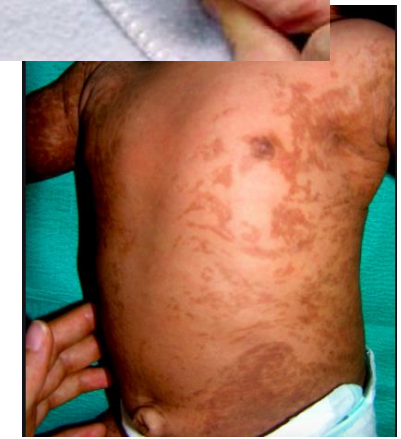


What next?

Incontinentia pigmenti

- Bloch-Sulzberger syndrome
- X-linked dominant trait
- Mutation of the IKBKG or NEMO gene
- IKBKG gene, encodes the NEMO protein, which serves to protect cells against TNF-alpha induced apoptosis
- Pathobiology IP of PAH remains unknown
- Primarily affects females, fatal in most males in fetal life
- Broad spectrum of clinical features affecting several organ systems – eyes, skeletal system, skin, hair, dental, and central nervous system
- Newborns with IP who develop seizures and early neurological involvement may have a worse prognosis





What next?

Incontinentia pigmenti

- Until 2018, all case reports of IP and PAH (without congenital heart disease) were fatal (only treated with Sildenafil)
- Case report by Dr. Bonnet and colleagues in 2018 reported a reversible case of PAH and IP with use of triple PAH therapy (epoprostenol, bosentan, and sildenafil) plus steroids (methylprednisolone) in 4 month-old female infant
- After 6 months of triple PAH therapy and steroids, infant had normal PAP and CO on RHC, weaned off therapy
- Infant continued to have normal PAP (on echo) and normal NT-proBNP at 6 months follow-up

Atallah et al. (2018). A case of reversible pulmonary arterial hypertension associated with incontinentia pigmenti. *Pulmonary Circulation*; 8 (4) 1-3.

Complex Case Presentation

Two months after cardiac cath…

- Weaned off SQ Remodulin
- Sildenafil 1 mg/kg TID, Bosentan 32 mg BID
- Panama FC I/ WHO FC I
- Follow-up echocardiogram with tricuspid regurgitant gradient of 31 mm Hg plus the RA pressure, minimal systolic septal flattening, tiny and restrictive patent ductus arteriosus with continuous left to right shunt, and normal biventricular size and function.
- Family decided to move back to Washington state!

Complex Case Study

Four months after discontinuation of SQ Remodulin…

- Transitioned to Tadalafil 10 mg PO daily, Bosentan 32 mg PO BID
- Panama FC I/ WHO FC I
- BNP 18
- Echo with borderline RVH, normal RV size and function. Tiny PDA left to right shunt, unchanged from prior (Kaiser/UCSF echo)
- New symptom of dragging right leg (since discontinuation of Remodulin?) and possibly more fatigue in afternoons (?)
- Referred to pediatric neurology; normal EEG, awaiting brain MRI/MRA

References

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