Management of Vascular Anomalies in Genetic and Syndromic Disorders

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Mosaic vs. Germline Mutations
– TIE2 mutations: 2 forms

• Germline:
  – AD: Multiple Cutaneous Mucosal Venous Malformation (VMCM)
  – Somatic: Blue Rubber Bleb Nevus Syndrome (BRBNS, Bean)

• Somatic:
  – Solitary Venous Malformation (VM)

SYNDROME MUTATION
Klippel-Trenaunay Syndrome PIK3CA
Parkes Weber Syndrome RASA1
Lymphatic Malformations (LM)
– Components: M-CM, Facial infiltrating Lipomatosis, Macrodactyly, etc.

PIK3CA-Related Disorders
– Klippel-Trenaunay syndrome (KTS)
– CLOVES syndrome
– Fibro-Adipose Vascular Anomaly (FAVA)

PTEN-Related Disorders
– Bannayan-Riley-Ruvalcaba syndrome
– Cowden syndrome
– Lhermitte-Duclos syndrome

RASopathies
– CM-AVM (RASA1)
– Parkes Weber syndrome (RASA1)
– NF1, Noonan, Noonan-like

TIE2-Related Disorders
– Multiple cutaneous and mucosal (VMCM) Germline
  – Sporadic causes: multiple cutaneous
  – Solitary cutaneous: Bean syndrome (BRBNS, Mosaic)

Vascular Anomalies Syndromes

<table>
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<th>Gene</th>
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Klippel-Trenaunay Syndrome (KTS)
– Slow-flow malformations
– Capillary, Lymphatic, and Venous: CLVM
– Fat: Bulk of overgrowth
– Inappropriate, delayed or lack of treatment
Klippel-Trenaunay Syndrome (KTS)

Venous Anatomy in KTS
- Marginal (calf)
- Marginal (thigh)-Superior Gluteal- Internal Iliac
- Sciatic-Inferior Gluteal- Internal Iliac
- Short Saphenous-Popliteal
- Deep Femoral
- Deep Veins

Treatment of KTS Venous Anomalies

- General rules:
  - Early treatment:
  - Hematologic evaluation
  - Start with the most proximal outflow (internal iliac)
  - Close entire length of veins
  - Avoid thermal therapy (laser, RFA) in:
    - Intrafascial veins: Sciatic vein (nerve)
    - Popliteal fossa: Top of short saphenous vein (Sciatic/tibial nerves)
    - Marginal vein around upper fibula (peroneal nerve)

- Permanent agents for large veins
  - Internal iliac, sciatic, gluteal

- Combination of techniques and tools:
  - Embolization, Sclerotherapy, Venous laser, Phlebectomy
  - Additional tools:
    - IVC filters: Bird’s nest
    - Core-removed wires
Femoral

Sciatic Aneurysm

Popliteal

Short saphenous

AT

Sciatic Inferior Glenal Internal Iliac: Coils

Marginal Laser

Removing core of a regular wire

Gianturco-Roehm Bird's Nest filter into Internal Iliac Vein
**Klippel-Trenaunay syndrome (KTS)**

**Treatment**
- Lymphatic:
  - Macrocystic: Sclerotherapy
  - Cutaneous: CO2 laser, Bleomycin
  - Sirolimus (Rapamycin)
- Capillary: Pulsed dye laser
- Fat: Surgical debulking

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**CLOVES Syndrome**

- Congenital Lipomatous Overgrowth
- Vascular anomalies
- Epidermal nevus
- Skeletal, Scoliosis, Spinal, Seizures

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**CLOVES Syndrome:**

- Vascular Malformations

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**CLOVES Syndrome:**

- Extensive management guidelines
  - Early treatment
  - Risk of thromboembolism
  - Skin leak, bleeding and infection
- Consider Sirolimus!
CLOVES Syndrome
Death by PE

CLOVES Syndrome

• Role of IR
  – Embolization & Sclerotherapy
  – CO2 laser photovaporization
  – Phlebectomy
  – Closure of markedly enlarged veins
    – Axillary-Subclavian
    – Truncal marginal vein
    – Lower limb as in KTS

Thromboembolic risk

Recurrent PE. Large IVC aneurysm

Spina-paraspinal AVM. Neurologic Risk
Glomuvenous Malformations (GVM)

- Role of IR
  - Sclerotherapy
  - CO2 laser photovaporization
  - Mini-phlebectomy

NOT a complication!

Parkes Weber syndrome
Capillary M-AVM syndrome (CM-AVM)

- RASA1 mutation
- Limb capillary malformation: light
- Limb overgrowth: length and girth
- “Multiple micro-AVF’s”
  - No gross shunts
  - Hypervascularity
  - Heart failure

Parkes Weber Syndrome

- Role of IR
  - No large definite shunt
  - Unclear

PTEN Hamartoma Tumor Syndrome (PHTS)

- Bannayan-Riley-Ruvalcaba syndrome (BRRS)
  - Macrocephaly
  - Fatty (+/- vascular) overgrowth
  - Penile freckling
  - Developmental delay
Bannayan-Riley-Ruvalcaba Syndrome (BRRS)

- 30 YOM with PTEN hamartoma syndrome
- Large left leg AVM

Post-embolization

• Consider PTEN:
  – Child with big head and penile freckles
  – Rapidly progressive high flow lesion
  – Overgrowth

Role of IR in Overgrowth Syndromes

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Overgrowth Syndromes

- Clinical:
  - New syndromes, tumors and malformations
  - Novel treatment
  - Characterization and classification
- Research:
  - Vascular biology, genetics, treatment outcome, etc