Tuberous Sclerosis

• Also referred to as Bourneville’s disease or tuberous sclerosis complex (TSC)
• Characterized by hamartomas in multiple organs
• Wide-range of clinical manifestations, predominantly affecting the skin, brain, kidney, heart, lung, eye and bone
• Autosomal dominant disorder, although spontaneous mutation in up to two-thirds of cases
• Associated with abnormalities of chromosomes 9 & 16
• Prevalence of 1/10,000 to 1/100,000
• Most common of dominantly inherited genetic disorders
Vogt’s Classic Triad (1908)

- Adenoma sebaceum (facial angiofibromas)
- Seizures
- Mental Retardation

However, only 30% of patients with tuberous sclerosis have all three features of the triad.

Facial angiofibromas

Dermatological Manifestations

- Facial angiofibromas
- Forehead fibrous plaques
- Periungual fibromas
- Shagreen patch
  - Connective tissue nevus usually on the dorsal surface
- Hypomelanocytic macules (Ash leaf spot)
  - Use Wood (UV) light


Neurological Manifestations

- Subependymal glial nodules
- Cortical tubers
- Subependymal giant cell astrocytomas
- Seizures, mental retardation, autism, ADHD
Patient A

- 48 year-old male patient at the Beth Israel Deaconess Medical Center with tuberous sclerosis
- Suffers from seizures and severe mental retardation
- Has hamartomas in the kidney, eye and brain
Patient A’s Head CT
Calcified subependymal glial nodules
Head MRI

- Superior for identifying cortical tubers
- Rarely, subependymal nodules transform into giant cell astrocytomas
  - When in the region of the foramen of Munro, cause hydrocephaly
  - Major cause of death in patients with tuberous sclerosis

MRI of a 6 year-old showing a giant cell astrocytoma resulting in hydrocephaly and enlargement of left ventricle

Renal Manifestations

- Renal angiomyolipomas (AMLS)
- Renal cysts
- Rarely, renal cell carcinoma
Patient A’s CT of the Abdomen

Multiple renal angiomyolipomas
Renal Angiomyolipomas on CT

Renal angiomyolipomas are hamartomas consisting of fat, smooth muscle, and blood vessels.
- Often multiple and bilateral
- Occur in up to 80% of patients with TS, incidence increases with age
- On CT, renal AMLs appear as well-marginated cortical masses of predominantly fat attenuation with scattered heterogeneous soft-tissue attenuation due to hemorrhage, fibrosis, or vascular and smooth muscle components.
Interesting finding
By the way, did you notice the interesting finding on patient A’s abdominal CT?

A beautiful example of INTUSSUSCEPTION in the distal duodenum

There is no evidence of an association between tuberous sclerosis and intussusception in the literature.
Renal Angiomyolipomas on MRI

On \( T_1 \) weighted images, AMLs appear as areas of high signal intensity.

On fat suppression sequences, AMLs would appear as areas of signal loss.

Renal Ultrasound

- On ultrasound, AMLs appear as heterogeneous masses which are predominantly hyperechoic with acoustic shadowing
- Difficult to distinguish AML from renal cell carcinoma on US
- Renal cysts would appear as echolucent lesions on US

Normal renal US of a 4 year-old boy with TS

Follow-up US 18 months later shows development of a new AML

Gross pathology of renal angiomyolipomas

Gross specimen showing the heterogeneous composition of AMLs

Complication of AMLs: hemorrhage

Role of Angiography

- Intrarenal, perirenal, retroperitoneal and intraperitoneal hemorrhage have been reported as complications of angiomyolipomas.
- Transcatheter embolization of the AMLs is a potential treatment, sparing the patient from undergoing a nephrectomy or partial nephrectomy.

Cardiac Manifestations

- **Cardiac rhabdomyomas**
  - Hamartomas within myocardium
  - Associated with arrhythmias, inflow and outflow obstruction, and heart failure
  - On echocardiography, appear as smooth, ovoid, hyperechoic lesions
  - 80% of individuals with cardiac rhabdomyomas have TS
  - Most regress spontaneously during childhood
Fetal Ultrasound

- Echocardiogram of a fetus at about 22 weeks gestation shows hyperechoic masses within the myocardium of both ventricles and atria
- Abnormal fetal heart rhythm
- Diagnosis of tuberous sclerosis confirmed at autopsy, which showed multiple cardiac rhabdomyomas and multifocal cortical tubers in the brain

Lung Manifestations

• Lymphangioleiomyomatosis (LAM)
• Micronodular pneumocyte hyperplasia
  – Hamartomatous proliferation of type 2 pneumocytes
Lymphangioleiomyomatosis

- Characterized by proliferation of smooth muscle cells of bronchi, alveoli, vessels, and lymphatics
- Interstitial infiltrates seen on plain film or CT progresses to honeycomb lung: multiple thin-walled cysts throughout lungs
- Found in about 1% of patient with tuberous sclerosis, almost exclusively female
- Complications: pneumothoraces, pneumomediastinum, chyloous pleural effusions, pulmonary hypertension and cor pulmonale

High-resolution chest CT shows numerous cysts

Skeletal Manifestations

- Sclerosis
  - Predilection for calvaria, spine, ribs, long bones, metacarpals, metatarsals and phalanges

Sclerosis of two pedicles in the lumbar spine of a patient with TS

Sclerosis in phalanges of index & middle finger and 2nd metacarpal in a 5 year-old boy with TS


http://www.ijri.org/archives/19990902/radquiz02.htm
Skeletal Manifestations (cont.)

- **Bone cysts**
  - Distal phalanges
- **Osteomatous-like protuberances**
  - Tubular bone of hands and feet

Other Non-Radiological Manifestations

• Retinal involvement:
  – Mulberry retinal astrocytomas
  – Plaque-like hamartomas
  – Achromic patches

• Dental issues:
  – Dental enamel pitting
  – Gingival hamartomas

• Intestinal hamartomatous polyps
Summary

• Tuberous sclerosis is a disease that affects multiple organ systems
• Many different imaging modalities can be used to diagnose and follow patients with TS
  – Cranial CT and MRI
  – Abdominal ultrasound, CT and MRI; Angiography (treatment)
  – Echocardiography
  – High-resolution chest CT
  – Skeletal radiographs
References

- BIDMC patient files.
Acknowledgements

• Chad Brecher, MD
• Larry Barbaras and Cara Lyn D’amour
• Pamela Lepkowski
• Gillian Lieberman, MD