The multiple manifestations of TSC

Tuberous sclerosis complex (TSC) is a multisystem genetic disorder[1,2]

Mammalian target of rapamycin (mTOR) overactivation is a core issue in organ abnormalities of the brain, kidneys, skin, heart, and lungs.[1]

- TSC1/TSC2, the hamartin/tuberin complex, is a protein complex produced by the genes *TSC1* and *TSC2*[1,3]
- In normal cells, the function of the TSC1/TSC2 complex is to inhibit mTOR, an important intracellular signaling molecule[1]
- *TSC1* or *TSC2* genetic mutations lead to hyperactivation of mTOR signaling[1]

An Overview of TSC Manifestations

BRAIN

- Seizures are the most common neurologic symptom of TSC[4]
  - TSC-related seizures are associated with significant disease morbidity and mortality[4]
  - Patients with TSC have a significantly increased risk of seizures throughout their lifetime[4]
    - >80% have seizures in the first 3 years[5]
    - >12% of adults who had no history of childhood seizures develop seizures[4]
    - Nearly 100% likelihood of recurrent seizures after a single seizure[4]
- Neurologic problems, including seizure, cause the greatest morbidity and mortality in TSC patients[2]
  - Subependymal giant cell astrocytoma (SEGA)[2]
  - Subependymal nodules[2]
  - Cortical dysplasias[2]

LUNGS

- Lymphangioleiomyomatosis occurs in 80% of females aged 40 years or older[2]

KIDNEYS

- Angiomyolipomas[2]
  - Second leading cause of premature death after severe intellectual disability[2]
- Multiple renal cysts[2]

An Overview of TSC Manifestations

EYES

- Multiple retinal hamartomas occur in 30% to 50% of patients[2]
- Retinal achromic patch[2]

TEETH

- Dental enamel pits[2]

HEART

- Cardiac rhabdomyomas[2]

SKIN

- Hypomelanotic macules[2]
- Angiofibromas occur in 75% of TSC patients, usually between 2 and 5 years of age[2]:
  - Fibrous cephalic plaque[2]
  - Ungual fibromas[2]
  - Shagreen patch[2]
  - "Confetti" skin lesions[2]
  - Intraoral fibromas[2]

OTHER

- Nonrenal hamartomas[2]

Most common TSC manifestations

There are several manifestations present in at least 80% of the TSC population

Dental enamel pits

- Occur in up to **100%** of patients with TSC (vs 7% of the general population)[2]

Hypomelanotic macules

- Occur in **90%** of TSC patients, typically at birth or in infancy[2]

Seizures

- More than **80%** of patients with TSC have seizures in the first 3 years[5]
- **66%** of patients with TSC have refractory seizures (vs 23% of patients with seizures in the general population)[4,6]

Renal angiomyolipomas

- Occur in **80%** of TSC patients,[2] typically developing in late childhood and beyond

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