The multiple manifestations of TSC

Tuberous sclerosis complex (TSC) is a multisystem genetic disorder\textsuperscript{1,2}

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

- TSC1/TSC2, the hamartin/tuberin complex, is a protein complex produced by the genes TSC1 and TSC2\textsuperscript{1,3}
- In normal cells, the function of the TSC1/TSC2 complex is to inhibit mTOR, an important intracellular signaling molecule\textsuperscript{1}
- TSC1 or TSC2 genetic mutations lead to hyperactivation of mTOR signaling\textsuperscript{1}
An Overview of TSC Manifestations

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

**LUNGS**
- Lymphangioleiomyomatosis occurs in 80% of females aged 40 years or older.

**KIDNEYS**
- Angiomyolipomas
  - Second leading cause of premature death after severe intellectual disability.
  - Multiple renal cysts
An Overview of TSC Manifestations

**EYES**
- Multiple retinal hamartomas occur in 30% to 50% of patients
- Retinal achromic patch

**TEETH**
- Dental enamel pits

**HEART**
- Cardiac rhabdomyomas

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

**OTHER**
- Nonrenal hamartomas
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)

- **Hypomelanotic macules**
  - Occur in 90% of TSC patients, typically at birth or in infancy

- **Seizures**
  - More than 80% of patients with TSC have seizures in the first 3 years
  - 66% of patients with TSC have refractory seizures (vs 23% of patients with seizures in the general population)

- **Renal angiomyolipomas**
  - Occur in 80% of TSC patients, typically developing in late childhood and beyond

References:


