Tuberous Sclerosis
A Neurologist’s Point of View

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Objectives

- Learn neurological manifestations of disease
- Educate how these patients present
- Inform audience of treatment options, medical and surgical
- Educate regarding widely variable prognosis
Introduction

- First fully described by Bourneville around 1880
- TSC 1 (Hamartin) vs TSC 2 (Tuberin)
- About 15% of patients with TS show no identifiable mutation and are milder forms of disease
- Accounts for 0.66% of mentally retarded patients and 0.32% of patients suffering from epilepsy
- Defects in tumor suppressor genes, resulting in numerous **benign** lesions

Manifestations of Disease

- Cognitive delay may or may not be present
- Cortical tubers
- Subependymal giant cell astrocytomas
- Cutaneous malformations
- Epilepsy
Cortical Tubers

- Neurons can become up to 3-4 times their normal size
- Surgically resected tubers show activation of a cell-size control pathway (mTOR)
- Possible foci of epileptogenicity

mTOR Pathway

Diagram showing the mTOR pathway, including nutrients/mitogens, PKD, PTEN, PIP3, PDCK, AKT/PKB, TSC1, TSC2, Rheb, Rapamycin, S6K1/2, 4E-BP1, and other components involved in the signaling pathway.
Subependymal Giant Cell Astrocytomas (SEGAs)

- Occur in 5-15% of TS patients
- Usually present in first or second decade of life
- Benign intraventricular mass
- Usually occur near the Foramen of Monroe
- Can result in obstructive hydrocephalus, but unpredictable what lesions should be removed vs. observed
- Image every 1-3 years, if patient develops symptoms, or for any change in clinical status

Cutaneous Manifestations

- Shagreen patch
- Hypomelanotic macules
- Adenoma sebaceum
- Ungular and subungual fibromas
- Dental enamel pits
- Gingival fibromas
Epilepsy

- Infantile spasms
- Partial seizures which may or may not secondarily generalize
- May require multiple antiepileptic medications

Patient 1

- 5mo female presented for evaluation of spells
- Spells lasted for seconds and occurred in clusters usually upon awakening
- Patient would become extremely fussy during the events
- Mom had previously been told episodes were due to reflux
- Normal development
- Exam revealed brisk reflexes

http://www.youtube.com/watch?v=l5x-Eh8w-tI&feature=related
Patient 2

- 14yo male with known history of global developmental delay and intractable epilepsy on multiple medications and VNS placement presented with respiratory distress, fever, and increased seizures.
- He was later diagnosed with pneumonia.
- On exam, he was nonverbal (baseline), didn’t follow commands (baseline), had a shagreen patch, multiple adenoma sebacea, subungual fibromas, hyperreflexia with clonus.

Imaging
Imaging

[Imaging image 1]

[Imaging image 2]
Medical Treatment

- ACTH
- Vigabatrin
- Oxcarbazepine
- Levetiracetam
- Topiramate
- Valproic Acid
- Lamotrigine
- Rufinamide
- Diastat
- Ketogenic diet
- Rapamycin

Surgical Treatment

- Vagal Nerve Stimulator
- Corpus callosotomy
- Tuber resection
Evaluation for Surgery

- Video EEG
- MRI
- Alpha-Methyltryptophan PET (AMT-PET)
- Ictal SPECT

Prognosis

- Widely variable
- TSC1 vs TSC2 mutation
- Age of seizure onset
- Presence or absence of Infantile spasms
- Tuber burden
- Controlled vs. Intractable Epilepsy