Neurocutaneous Disorders

Dr. jafar Nasiri
Associate professor of child neurology
Isfahan University of Medical Sciences

Definition

They are group of syndromes characterized by involvement of the brain & skin.

Types :

- neurofibromatosis type ١ & ٢
- tuberous sclerosis
- sturge webber syndrome
- von hipple lindau disease
- incontinentia pigmenti
- ataxia telangectasia
- Maffucci's Syndrome
- Epidermal Nevus Syndrome
- Parry–Romberg Syndrome
- Neurocutaneous Melanosis

Neurofibromatosis NF١&NF٢

- Incidence ١:٣٠٠٠ live birthes/prevalenc ١/٥٠٠٠٠
- A.D
- ١/٣ due to new mutation

Neurofibromatosis NF٢

- the central form, the hallmark of which is bilateral vestibular schwannomas, called NF٢.
- The distinction between the disorders was subsequently verified when the two genes were found to be distinct

NF 1

- **not only** the peripheral and central

nervous systems,

- **but also** many other systems, including:

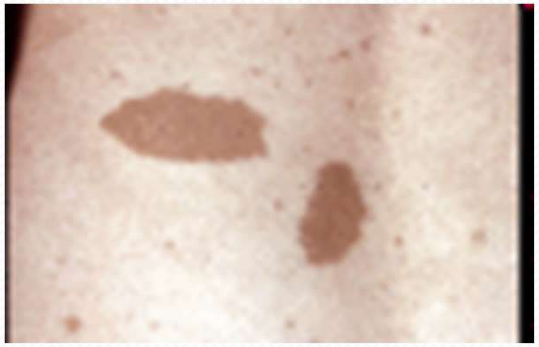
- skin
- bone
- endocrine
- gastrointestinal,
- vascular systems

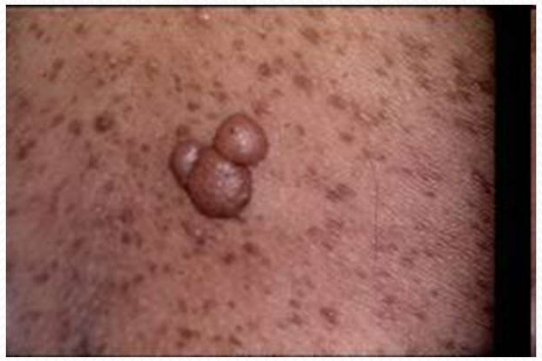
Neurofibromatosis ١,...

- Criteria for Diagnosis ,٢ or more of the following:
- ٦ or more café au lait macules
- Family histry in first degree relative
- ٢ or more neurofibromas OR ١ plexiform neurofibroma
- optic glioma
- lisch nodules
- osseous lesion

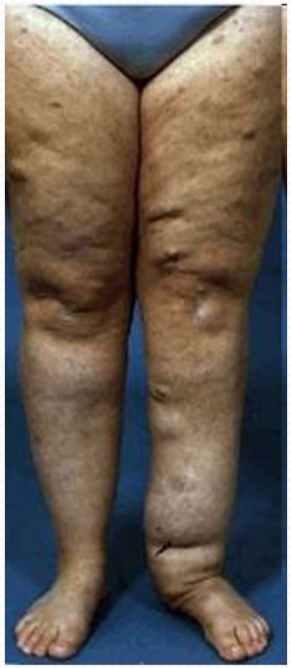
NF1

café au lait macules



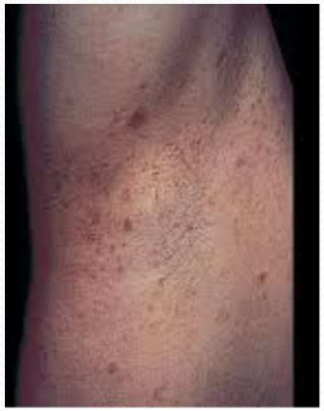


neurofibroma



plexiform neurofibromas

Cutaneous



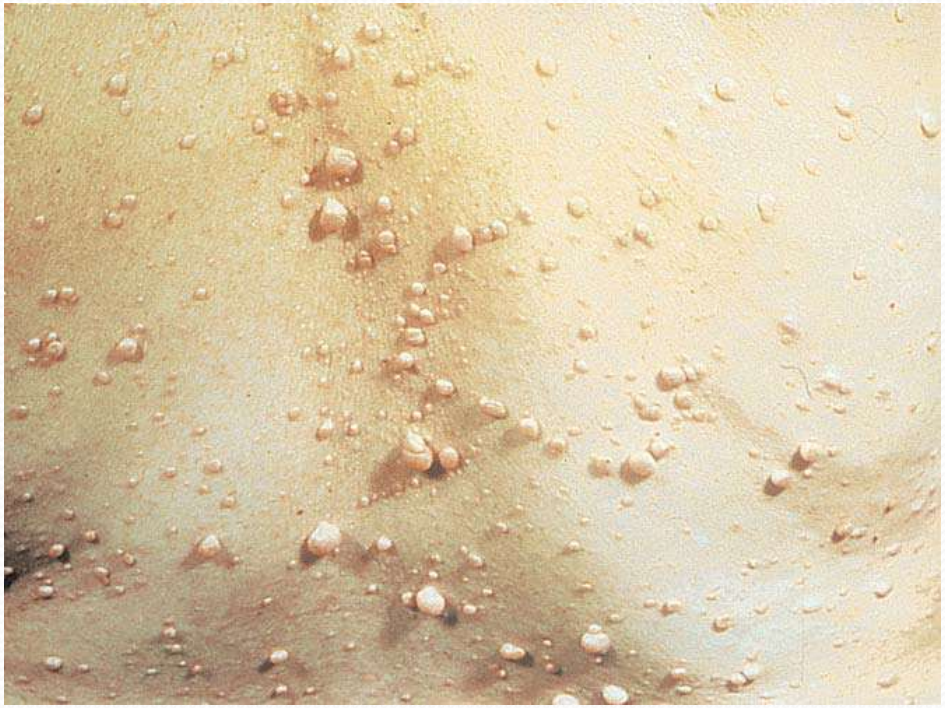
axillary freckling

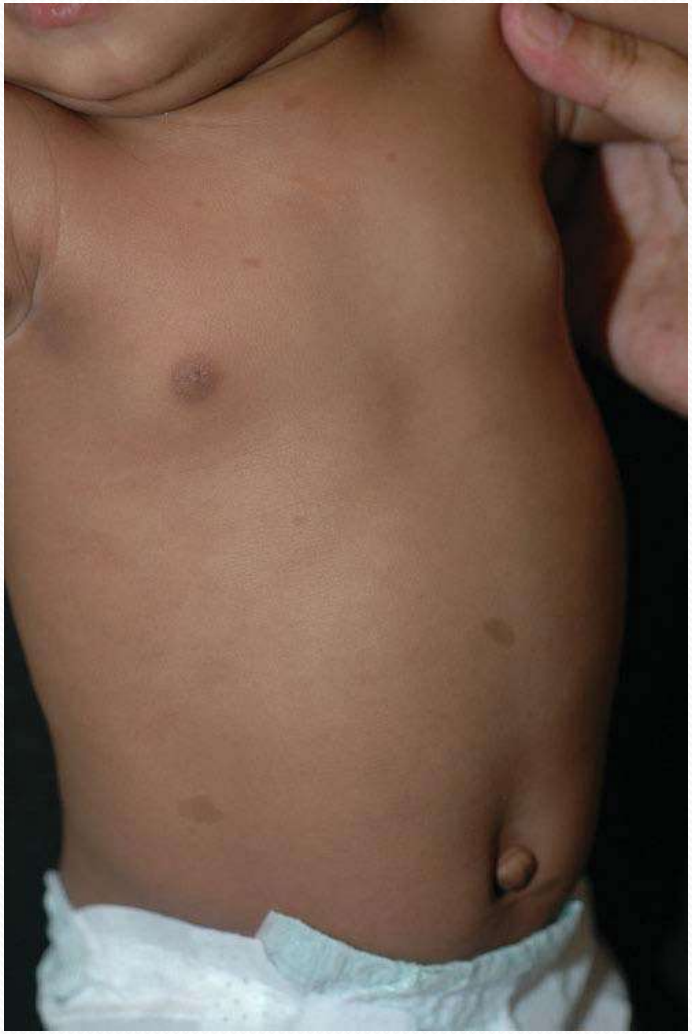
Other

- Ocular
  - optic gliomas
  - lisch nodules

- Skeletal
  - scoliosis
  - pseudoarthrosis
  - sphenoid dysplasia
- HTN, renovascular

NF ١





Complications of NF1

- seizure
- intracranial tumor
- nerve sheath, root tumor
- polyneuropathy
- vasculopathy
- macrocephaly
- learning disability
- UBOs

malignant transformation in NF ١

- Most tumors are benign, but overall increased risk of malignancy by ٥%
  - Plexiform neurofibromas occur in ٢٥% of NF patients, and undergo malignant transformation to neurofibrosarcoma in ١٠-١٥%
  - Malignant transformation signs include rapid tumor growth and pain
- Others:

A. Leukemia: myeloproliferative and myelodysplastic leukemias are associated with NF١

B. Lisch nodules: hamartomas in the iris stroma; benign

C. Optic glioma: ١٥% patients; before age ٦; benign

D. Pheochromocytoma: increased incidence, occurs in adulthood

Neurofibromatosis ٢,diagnostic criteria

- **Confirmed NF٢**
- Bilateral vestibular schwannomas
- or
- A first-degree relative with NF٢
- and either
- Unilateral vestibular schwannoma before age ٣٠ years
- or any two of
- Meningioma, schwannoma, ependymoma, juvenile lens opacity
- **Presumptive NF٢**
- Unilateral vestibular schwannoma before age ٣٠ years and at
- least one of: meningioma, schwannoma, ependymoma, juvenile
- lens opacity
- or
- Two or more meningiomas and unilateral vestibular schwannoma
- before age ٣٠ years or at least one of: meningioma,
- schwannoma, ependymoma, juvenile lens opacity

Tuberous Sclerosis

- autosomal-dominant inheritance that affects multiple organ systems
- The disorder results from a mutation in the *TSC۱* gene in chromosomal region ۹q۳۴ or the *TSC۲* gene in chromosomal region ۱۶p۱۳ and is inherited in an autosomal dominant fashion, although up to two thirds of cases result from spontaneous genetic mutation
- one of the most common single-gene disorders seen in children and adults, with an estimated incidence of ۱ in ۵۸۰۰ live births.

- both the brain and the skin have more than one major criterion for diagnosis
- therefore a diagnosis of definite tuberous sclerosis complex can be based on skin findings alone, or on neuroimaging findings alone
- The major neurologic manifestations of tuberous sclerosis complex are seizures, autism, developmental delays, including mental retardation, and behavioral and psychiatric disorders
- Epilepsy is the most common presenting and also is the most common medical disorder

Tuberous Sclerosis

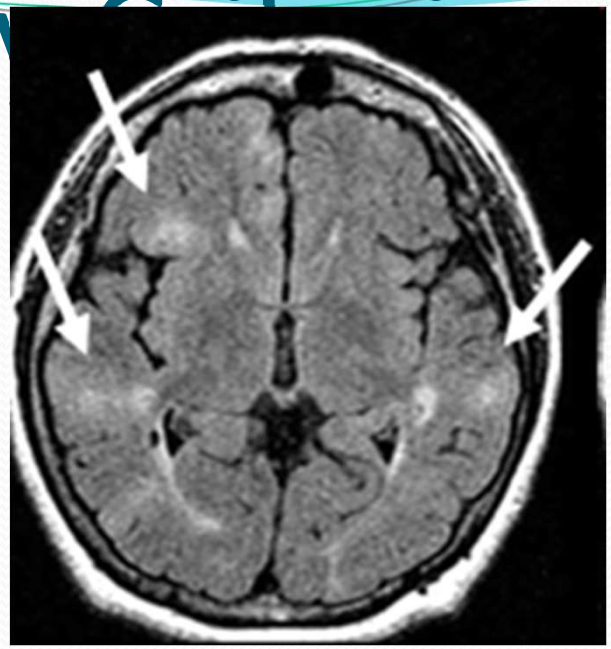
Major Features

- Facial angiofibromas or forehead plaque
- Nontraumatic ungual or periungual fibroma
- Hypopigmented macules (more than ٣)
- Shagreen patch (connective tissue nevus)
- Cortical tuber
- Subependymal nodule
- Subependymal giant cell astrocytoma
- Multiple retinal nodular hamartomas
- Cardiac rhabdomyoma, single or multiple
- Lymphangiomyomatosis
- Renal angiomyolipoma

Minor Features

- Dental pits (more than ١٤), randomly distributed
- Hamartomatous rectal polyps
- Bone cysts
- Cerebral white matter radial migration lines
- Gingival fibromas
- Nonrenal hamartomas
- Retinal achromic patch
- “Confetti” skin lesions
- Multiple renal cysts

Diagnostic Certainty Criteria



- Definite TSC

- ٢ major features or

- ١ major feature + ٢ minor features

- Probable TSC

-١ major feature + ١ minor feature

- Possible TSC

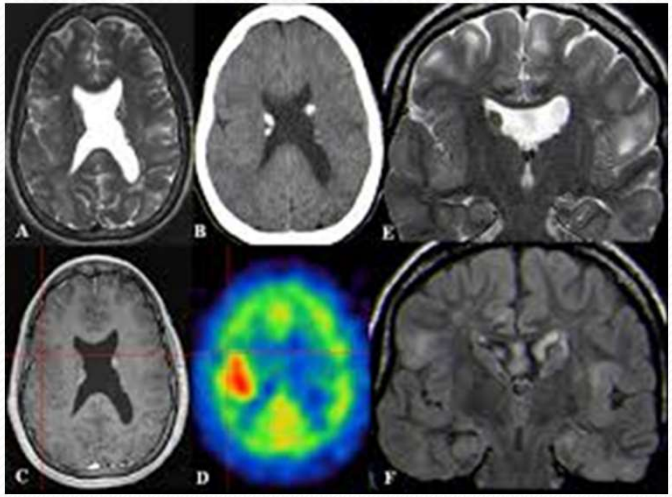
- ١ major feature or

- ٢ or more minor features

TS

Neuro

- cortical tubers
- subependymal nodules
- giant cell tumors
- white mater heterotopia
- Seizures (٩٠%)
  -infantile spasms (٥٠%)
- Mental retardation
- DD
- behavioral concerns

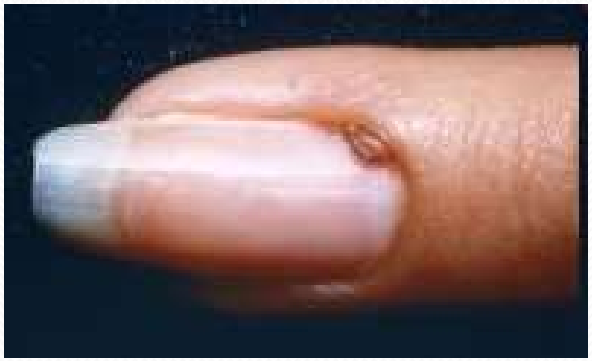


Other

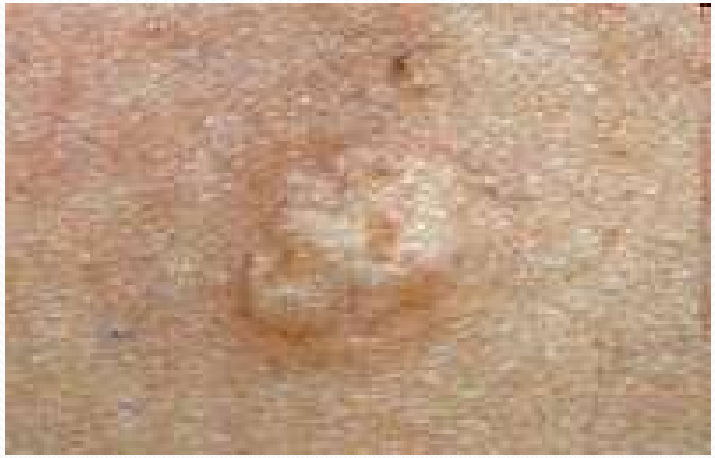
- Ocular
  - retinal hamartomas
  - achromic patches
- Cardiac
  - atrial rhabdomyoma
- Renal
  - angiomyolipomas
- Lung
  - lymphangioleiomyomatosis (LAM)
- skin

TS

Cutaneous

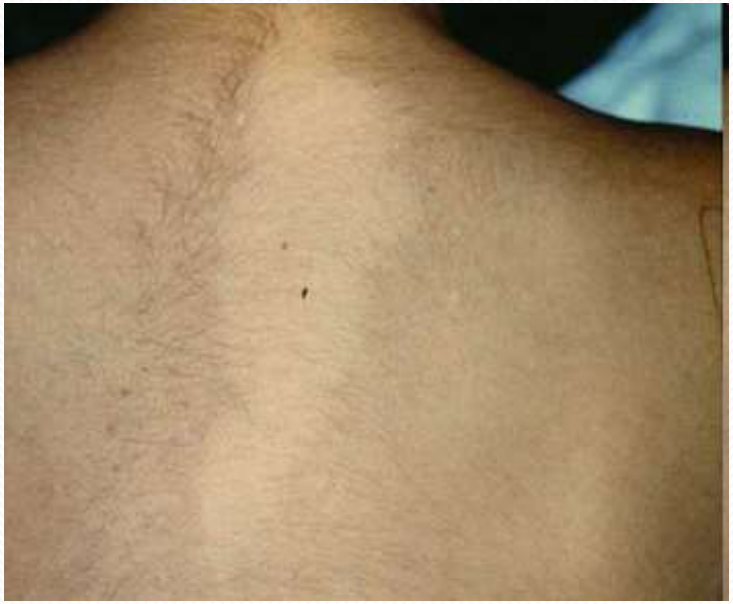


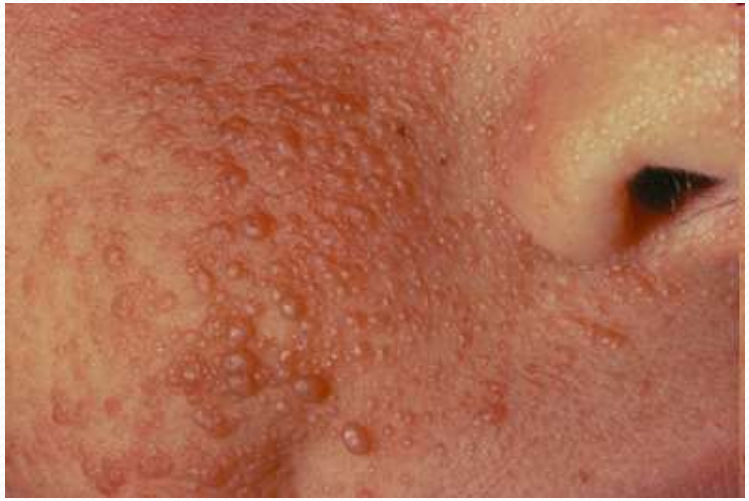
periungual fibroma



Shagreen patch

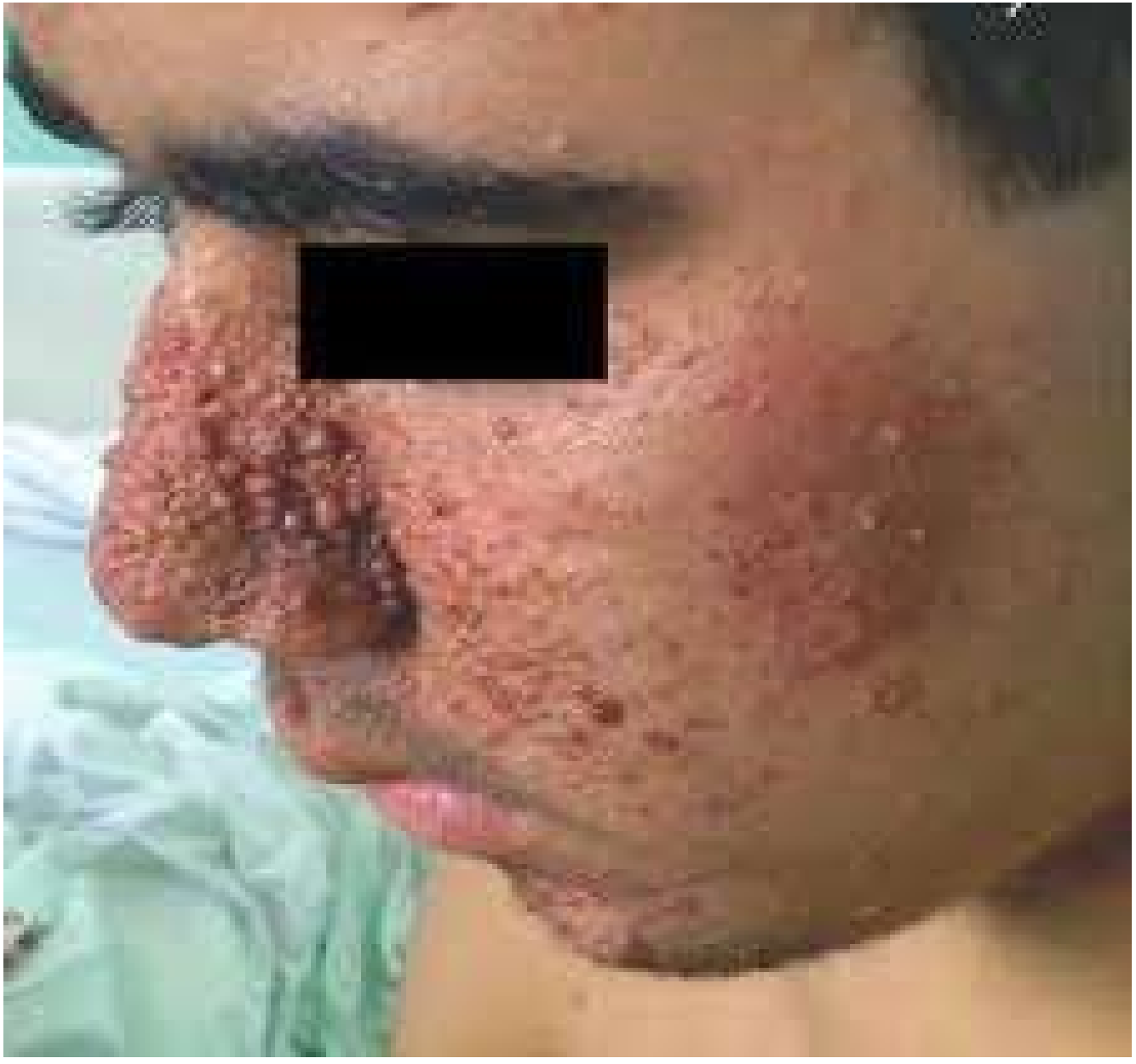
hypomelanotic macule





facial angiofibromas

Facial angiofibroma



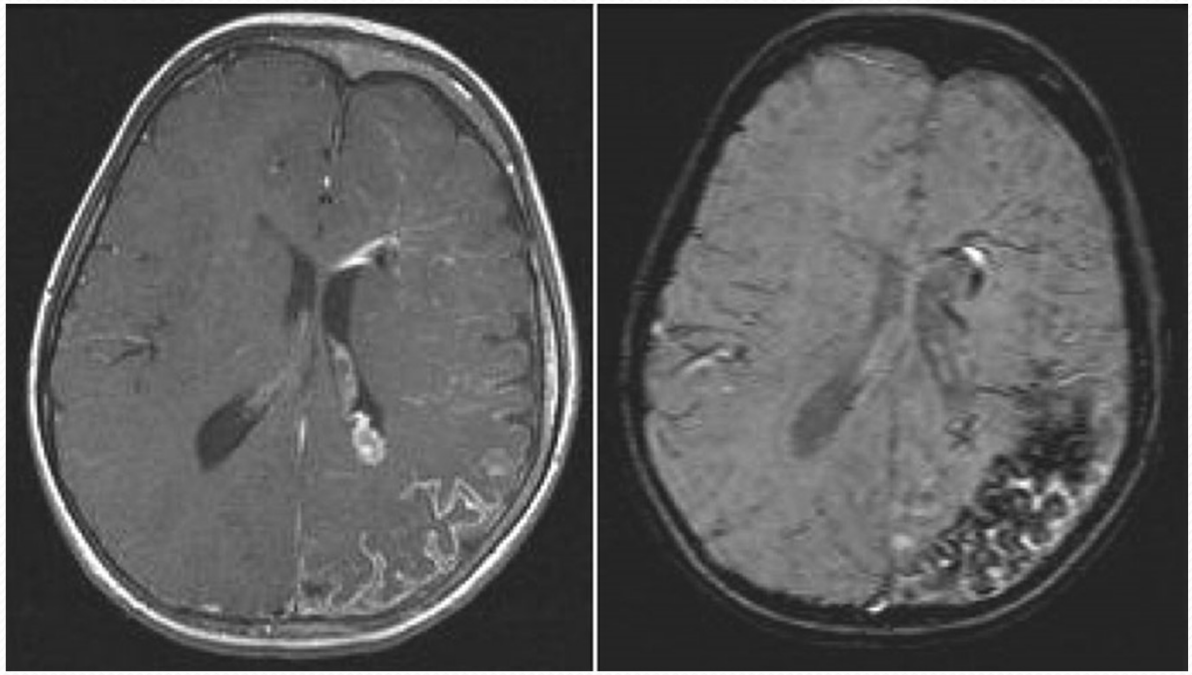
Sturge-Weber syndrome

- **also called encephalotrigeminal angiomatosis,**
- **a neurocutaneous disorder with angiomas that involve the leptomeninges and the skin of the face**
- **typically in the ophthalmic (V١) and maxillary (V٢) distributions of the trigeminal nerve**
- **The hallmark of SWS is a facial cutaneous venous dilation, also referred to as a nevus flammeus or port-wine stain (PWS)**

Sturge-Weber Syndrome

Neuro

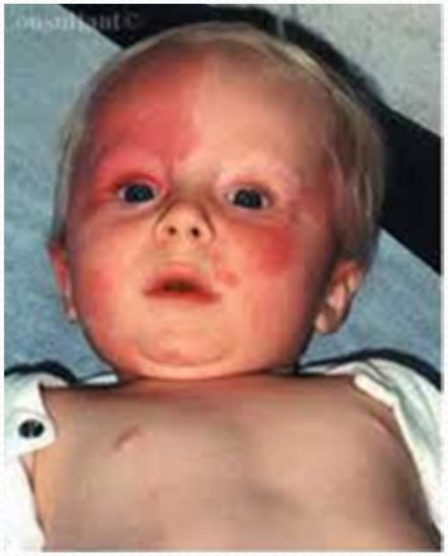
- Seizures
  - focal → generalized tonic clonic
- Hypoperfusion injury
- ID, DD
- Progressive



Sturge-Weber

Cutaneous

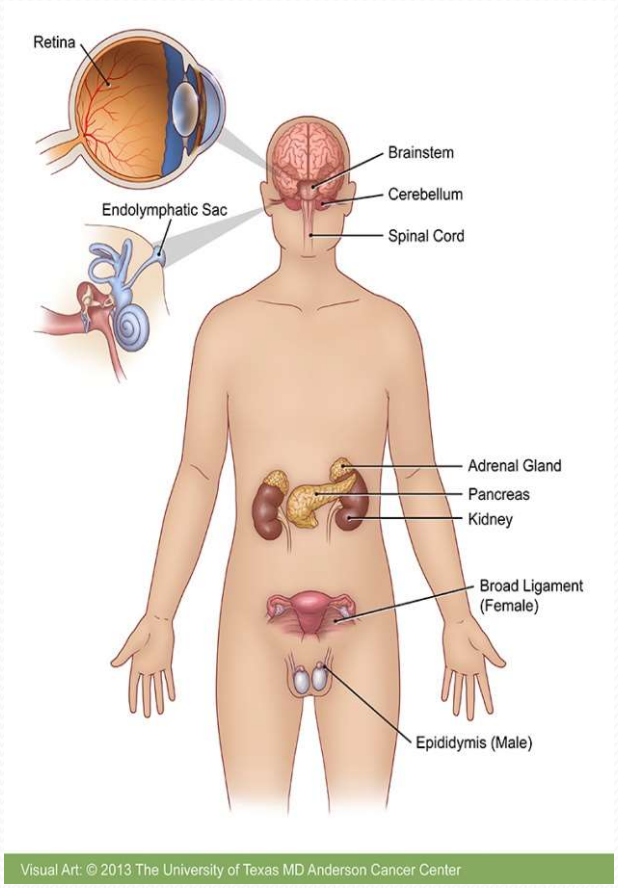
- Port Wine Stain
  - ١٠% incidence of SWS
  - Hemifacial hemangioma
  - CN٥
  - progressive



Other

- Ocular
  - visual field defects
  - glaucoma
  - other vascular anomalies
- GH deficiency
- central hypothyroidism

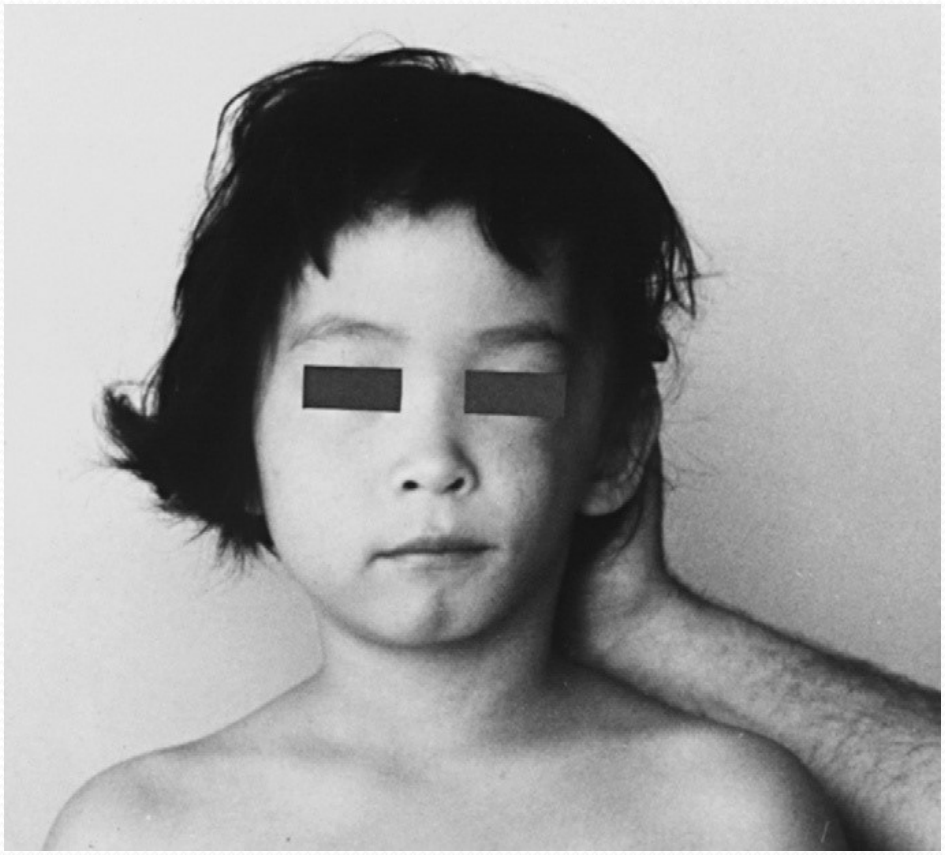
Von Hippel–Lindau Disease



- Autosomal dominant
- retinal, cerebellar, spinal **hemangioblastomas**,
- **cystic tumors** of the pancreas,kidney, and epididymis,
- renal cell carcinoma,
- endolymphatic sac tumors,
- pheochromocytoma

Parry–Romberg Syndrome (Facial Hemiatrophy)

- typically has onset between ٥ and ١٥ years of age
- progressive ipsilateral loss of facial soft tissue, cartilage, and bone
- Progression of this atrophic process generally lasts between ٢ and ١٠ years
- neurologic :recurrent headaches, trigeminal neuralgia, ipsilateral Horner's syndrome, contralateral partial seizures, and hemiparesis
- Cranial CT can be normal or document cerebral atrophy; contralateral intracerebral calcification



Klippel–Tre´naunay–Weber Syndrome

- *occurs sporadically*
- hypertrophy of the soft tissues and bone of a limb
- Limb hypertrophy usually is apparent at birth
- megalocornea, glaucoma,iridic heterochromia, syndactyly, polydactyly, macrodactyly, and clinodactyly
- Macrocephaly often is present