5.14.7. Systemic Conditions (VII): Inherited Disorders (II): Neurocutaneous Syndromes

Cerebrofacial (encephalofacial/facial) angiomatosis

- Sturge-Weber syndrome
  - sporadic
  - nevus flammeus (portwine stain)
    - angioma involving skin and subcutaneous tissues
    - follows the distribution of CN V
    - present from birth
    - usually unilateral
  - perieto-occipital leptomeningeal hemangioma
    - ipsilateral to the facial nevus flammeus
    - MRI will show leptomeningeal enhancement
    - CT scan is best for showing the calcification
    - calcification of the cortex underlying the hemangioma
    - seizures are a major problem
  - unilateral congenital open-angle glaucoma
    - 30%–70%
    - may occur at any time
    - usually associated with an angioma of upper eyelid
  - clinical manifestations
    - heterochromia iridis
    - choroidal hemangioma
      - yellow-orange, moderately elevated
      - "tomato ketchup" appearance
      - exudative retinal detachment
      - ≤50%

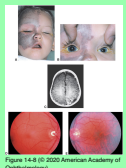

Figure 14-8 (© 2020 American Academy of Ophthalmology)

- Klippel-Trénaunay-Weber syndrome
  - variant of cerebrofacial angiomatosis
  - cutaneous nevus flammeus and hemangiomas
    - amenable to laser treatment
  - nonocular findings
    - intracranial angiomas
    - varicosities
    - hemihypertrophy of the limbs
  - ocular findings
    - conjunctival telangiectasia
    - congenital glaucoma
    - uncommon

"phakomatoses"

- General
  - hamartomas involving different organ systems
    - skin
    - eyes
    - CNS
    - viscera
  - phakoma
    - tumor formed from normal tissue elements
      - hamartoma
        - elements normally found at the involved site
        - not true neoplasms
        - lack the capability for limitless proliferation
      - choristoma
        - tumorlike growth composed of tissue not normally present at the site of growth
- entities
  - neurofibromatosis (NF)
  - tuberous sclerosis (Bourneville syndrome)
  - cerebrofacial angiomatosis (Sturge-Weber syndrome)
  - retinal angiomatosis (von Hippel disease)
  - ataxia-telangiectasia (Louis-Bar syndrome)
  - Wyburn-Mason syndrome
  - Klippel-Trénaunay-Weber syndrome

Neurofibromatosis

- von Recklinghausen neurofibromatosis (NF1)
  - more common
  - autosomal dominant
  - chromosome 17
  - clinical presentation
    - pigmented skin lesions
      - multiple cutaneous pigmented macules (café-au-lait spots)
    - iris (Lisch) nodules
      - pigmented iris hamartomas
      - 94–97% of patients with NF1 >6 years
      - do not become symptomatic
      - mild cases may show only iris nodules + café-au-lait spots
    - other ocular involvement
      - congenital glaucoma
      - retinal astrocytomas
      - osseous defects of the orbit
        - greater wing of the sphenoid
        - orbital encephalocele
    - osseous malformations
      - vertebral and long-bone defects
    - nervous system
      - tumors of the brain, spinal cord, and meninges
        - meningioma
      - tumors of the cranial, peripheral, and sympathetic nerves
        - neurofibromas
          - multiple
          - histologically benign
          - 2 types
            - fibroma molluscum
            - plexiform neurofibroma
          - may involve eyelid and face
      - optic nerve or chiasmal gliomas
        - children
        - proptosis
        - vision loss
    - pheochromocytoma

Figure 14-6 (© 2020 American Academy of Ophthalmology)

- bilateral acoustic neurofibromatosis (NF2)
  - less common
  - autosomal dominant
  - chromosome 22
  - café-au-lait spots or peripheral neurofibromas
    - 60%
  - Lisch nodules are not a feature of NF2
  - bilateral acoustic neuromas
    - present symptomatically in young adulthood
  - other CNS tumors may occur
    - not as frequently as in NF1
  - other ocular findings
    - combined retinal–retinal pigment epithelial hamartomas
    - posterior subcapsular cataracts

Wyburn-Mason syndrome

- sporadic
- AVM of the ipsilateral retina (racemose angioma)
  - increased in number, size, and tortuosity
  - vessels are usually fully developed
  - may involve any part of the posterior pole
  - spontaneous hemorrhage

Figure 14-11 (© 2020 American Academy of Ophthalmology)

- orbital AVMs
  - mild proptosis
  - conjunctival vascular dilation
  - bruit
- intracranial arteriovenous malformation (AVM)
  - midbrain
  - basofrontal region
  - posterior fossa
  - sites
  - spontaneous intracranial hemorrhage
  - convulsions
  - MRI scan of the brain should be obtained for patients with a retinal AVM
- AVMs of the maxilla, pterygoid fossa, or mandible
- direct communications between the arteries and the veins without an intervening capillary bed

Ataxia-telangiectasia

- Louis-Bar syndrome
- chromosome 11
- autosomal recessive
  - inactivation of a critical protein kinase that regulates response to DNA double-strand breaks
- progressive cerebellar ataxia
  - most common cause of progressive ataxia in early childhood
- oculocutaneous telangiectasia
  - almost always observed, especially as the child ages
  - conjunctival telangiectasia

Figure 14-10 (© 2020 American Academy of Ophthalmology)

- ocular motility deficits
  - head thrusting
  - abnormalities of the fast phase of OKN
    - inability to initiate saccades
  - impaired pursuit
  - total ophthalmoplegia
    - horizontal and vertical supranuclear gaze palsies
  - oculocephalic responses remain intact
- thymic hypoplasia
  - high incidence of malignancy
  - recurrent sinopulmonary infections
  - immunodeficiency
    - defective T-cell function
    - immunoglobulin deficiency

Tuberous sclerosis

- Bourneville syndrome
- autosomal dominant
  - 2 tuberous sclerosis genes
    - TSC1
      - chromosome 9q34
      - tuberin
    - TSC2
      - 16p13.3
      - hamartin
    - form a heterodimer that inhibits cell growth and proliferation
- hamartomatous angiofibromas
  - adenoma sebaceum
  - butterfly distribution over the nose and cheeks
- cognitive deficiency
  - many have normal mentation
- epilepsy
  - most patients have seizures
- other skin lesions
  - periungual fibromas
  - café-au-lait spots
  - shagreen patches
    - large, leatherlike, hyperpigmented, raised patches
    - located on the trunk
  - ash-leaf spot
    - leaf-shaped area of skin depigmentation
    - fluoresces under a Wood lamp
    - pathognomonic for tuberous sclerosis
- calcified astrocytic brain hamartomas
  - brain stones
  - evident on plain skull x-ray and CT scan
- cardiac rhabdomyomas
- kidney
  - renal cysts
  - angiomyolipomas
- astrocytic hamartomas of the retina or optic disc

Figure 14-7 (© 2020 American Academy of Ophthalmology)

Retinal angiomatosis

- von Hippel disease
- autosomal dominant
- genetics
- sporadic
- retinal capillary angioma
  - globular, smooth-surfaced, pink retinal tumor
  - fed by a single dilated, tortuous retinal artery and drained by a similar-appearing vein
  - often multiple
  - 50% bilateral
  - serous retinal detachment

Figure 14-9 (© 2020 American Academy of Ophthalmology)

- CNS hemangioblastomas
  - 25%
  - cerebellar hemangioblastomas
  - von Hippel–Lindau disease
  - may be associated with syrinxes
  - brainstem or spinal cord hemangioblastomas
- renal, pancreatic, hepatic, or epididymal cysts
- pheochromocytomas
- renal cell carcinoma
  - potentially lethal

Ophthalmology Mind Maps/Arman Mashayekhi, MD