Neurocutaneous Syndrome

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Introduction

• A group of disorders characterized by frequent involvement of the skin and the CNS

• Also known as pharkomatoses

• Not all have skin involvement e.g. Von Hippel-Lindau syndrome and many include features outside of the CNS, and so the term NCS may be misleading

• Notable for their dysplastic nature and the tendency to form tumours in various organs
### Neurocutaneous disorders: Specific Cutaneous Abnormalities and associated disorders

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<th>Hyperpigmented Lesions</th>
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<td>• Neurofibromatosis</td>
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<td>• Epidermal nevus syndrome</td>
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<td>• Neurocutaneous melanosis</td>
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<td>• Incontinentia pigmenti</td>
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<th>Hypopigmented Lesions</th>
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<td>• Tuberous sclerosis complex</td>
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<td>• Sturge Weber syndrome</td>
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<td>• Osler-Weber-Rendu syndrome</td>
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<td>• Klippel-Trenaunay- Weber syndrome</td>
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<th>Retinal Involvement</th>
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Neurofibromatosis

- Consists of at least 3 distinct disorders – NF1, NF2 & Schwannomatosis
- Initial clinical & pathological account of the disease credited to von Recklinghausen in 1882
- NF1 is the most prevalent type of NF
NF1

- Autosomal dominant & notable for its great variability of expression
- Estimated prevalence of 1 in 4,000; half of which are new mutations
- NF1 gene located on 17q11.2. Exhibits a wide variability of expression and complete penetrance
- Disease is protean and virtually any system can be affected. It is also progressive as distinct features may be present for years but development of its complications may be delayed for years
Diagnostic criteria for NF1

✓ ≥ 6 café-au-lait macules >5mm in greatest diameter in prepubertal children & > 15mm in diameter in postpubertal

✓ 2 or more neurofibromas of any type or one plexiform neuroma

✓ Freckling in the axillary or inguinal regions

✓ Optic pathway glioma

✓ 2 or more Lisch nodules (iris harmatomas)

✓ A distinctive osseous lesion e.g. sphenoid dysplasia, kyphoscoliosis, cortical thinning in long bones ± pseudoarthrosis

✓ Diagnosis of NF1 in a first degree relative (parent, sibling or offspring)

❖ PRESENCE OF ANY 2 = NF1
Café-au-lait macules
Hallmark of NF1, present in nearly 100% cases. Present at birth, increases in size with a predilection for the trunk & extremities, sparing the face.

Neurofibromas & NF1 in a first degree relative
Lisch nodules are harmatomas on the iris, best identified with a slit lamp examination.

Axillary freckling

Optic glioma. Seen in about 15% of NF1. Most cases are asymptomatic. 20% have impaired vision or features of precocious puberty due to hypothalamic invasion.
Plexiform Neurofibromas

Usually evident at birth and result from diffuse thickening of the nerve trunks that are frequently located on the orbital or temporal region of the face. Overlying skin usually hyperpigmented and may result in overgrowth of an extremity & deformity of the corresponding bone.
Other complications of NF1

- Learning disability
- Speech defects
- ADHD
- Epilepsy – GTC, CPS
- Hydrocephalus due to aqueductal stenosis
- CVA & hemiparesis
- Brain tumours – optic gliomas, meningiomas, astrocytomomas. These account for significant morbidity & mortality
- Increased risk of other tumours – Wilm’s tumour, leukaemias, phaeochromocytomas, rhabdomyosarcoma
• Account for 10% of cases of NF

• Bilateral acoustic neuromas represent the most distinct feature of the disease

• Can also be diagnosed in the presence of a first degree relative with NF2 + either unilateral VIII N masses or any 2 of neurofibroma, meningioma, glioma, schwanoma or juvenile posterior subcapsular lenticular opacities

• Café au lait macules & skin neurofibromas are uncommon
Treatment of NF

• There is no specific treatment for NF & treatment is mainly symptomatic

• Genetic counselling

• Early detection of treatable conditions & complications

• Ophthalmic assessment, Hearing assessment-yearly even in the asymptomatic

• EEG
• Cranial CT scan/MRI
• Skeletal survey

• Yearly assessment of the asymptomatic
Tuberous sclerosis

- Autosomal dominant inheritance with a prevalence of 1 in 30,000, more recent studies – 1 in 5,800 live births
- TS gene is located on chromosome 9q34, but at least half are sporadic owing to new mutations
- TS is an extremely heterogeneous disease with a wide clinical spectrum and varies from severe mental retardation & incapacitating seizures to normal intelligence and a lack of seizures often within the same family
- As a rule, the younger the patient presents with symptoms and signs of TS, the greater will be the likelihood of mental retardation
- TSC affects many other organ systems other than the brain, including the heart, kidney, eyes, lung and bone
Clinical features of TSC

• Clinical presentation depends on the age of the patient, the organs involved and the severity of the disease

• Epilepsy is the most common presenting symptom in TSC and its also the most common medical disorder. Epilepsy occurs in 80-90% cases with seizures developing mostly in childhood. Infantile spasms occur in up to one-third of children with TSC

• Almost all seizure types can be seen in TSC but pure absence seizures have not been described
## Diagnostic criteria for TSC

### MAJOR FEATURES
- Facial angiofibromas / forehead plaque
- Periungual fibroma
- Hypopigmented macules
- Cortical tuber
- Sub-ependymal nodule
- Sub-ependymal giant cell astrocytoma
- Multiple retinal nodular hamatomas
- Cardiac rhabdomyoma
- Renal angiolipoma
- Lymphangiomyomatosis

### MINOR FEATURES
- Dental pits
- Harmatomatous rectal polyps
- Bone cysts
- Gingival fibromas
- Nonrenal hamatomas
- Confetti skin lesions
- Multiple renal cysts

**Definite TSC:** 2M or 1M + 2m

**Probable TSC:** 1M + 1m

**Possible TSC:** 1M or ≥ 2m
Subungal fibroma

Hypopigmented macules (Ash-leaf spot)

Shagreen patch - raised lesion with an orange peel consistency

Adenoma sebaceum

Subungal fibroma
Subependymal nodules and cortical tubers

Astrocytoma of the retina (Mulberry tumour)
TSC
Management

- EEG
- Cranial CT scan/MRI
- Renal USS
- Echocardiography

- Treatment involves
  - Seizure control
  - Identification & management of learning difficulties
  - Tumour resection
  - Relief of hydrocephalus & raised ICP