3) Genodermatosis - Dr. Darseem

1. Neurofibromatosis
2. Tuberous sclerosis
3. Xeroderma pigmentosum
4. Incontinentia pigmenti
5. Ehlers Danlos syndrome
6. Pseudoxanthoma elasticum

**Neurofibromatosis:**

Autosomal dominant condition, affect about 1 in 3000 people, manifested by developmental changes in the nervous system, bone and skin.

There are many types, the most important two are:

1. Von Recklinghousen's neurofibromatosis (NF1) which accounts for 85% of cases.
2. Bilateral acoustic neurofibromatosis (NF2).

**Clinical features:**

1. **Von Recklinghousen's neurofibromatosis (NF1):**
   - *Café au lait patches* (light brown oval macules), usually developing in the first year of life. Finding of 6 or more lesions 1.5cm or more in diameter in adults, 0.5cm in diameter in children, is diagnostic.
   - *Axillary freckling* in two-thirds of affected individuals may extend to neck, may involve the inguinal, genital and peineal areas.
   - Variable numbers of skin *neurofibromas*,
     - they are soft tumors some small and superficial, others larger and deeper.
     - ranging from flesh-coloured to pink, purple or brown.
     - some are firm, some soft and compressible which can be pushed down into the panniculus by light pressure with fingers (button-hole sign).
     - neurofibromas may not appear until puberty and become larger and more numerous with age.
     - subcutaneous plexiform neurofibroma are large nodules containing multiple neurofibromas, on palpation they feel like a bag of worms.
   - Small circular pigmented hamartomas of the iris (*Lisch nodules*).

*Other features:*

- Neurofibroma will occasionally change into neurofibrosarcoma,
- Mental deficiency,
- Epilepsy,
- Renal artery stenosis.
- CNS tumors, e.g. intracranial tumors.
- Bone lesions, e.g. macrocephaly, kyphoscoliosis, short stature.
- Pheochromocytoma → hypertension.
- Hypogonadism.
Criteria for diagnosis of NF-1

The presence of 2 or more of these criteria is diagnostic.

- Six or more café-au-lait macules of >5 mm in prepubertal & >15 mm in postpubertal.
- Two or more neurofibromas or one plexiform neurofibroma.
- Freckling in axilla or perineum.
- Optic glioma.
- Two or more Lisch nodules.
- Distinctive bony lesion.
- A 1st degree relative with NF-1 by these criteria.

2. Bilateral acoustic neurofibromatosis (NF2):

- Bilateral acoustic neuromas.
- Few, if any, cutaneous manifestations.
- No Lisch nodules.
- Other features; other tumours of the CNS specially meningiomas and gliomas.

Tuberous sclerosis:

- Autosomal dominant condition, affect about 1 in 12000 children under 10 years.
- It is characterized by a triad of epilepsy, mental retardation, skin lesions called adenoma sebaceum. (usually angi-fibromas of face).
- Also called epiloa (epilepsy, low intelligence, adenoma sebaceum).

Clinical features:

Skin changes:

- Small oval white patches (ash leaf macules) occur in 85% of cases, their number ranges from 1-100, important as they may be the only manifestation at birth.
- Adenoma sebaceum (angio-fibroma), present in 90% of cases older than 4 years of age, persist indefinitely, pink or yellowish, translucent, waxy, acne-like papules (1-3 mm) on the face, often around the nose, cheeks and forehead.
- Peri-ungual fibromas (koenen tumors) occur in 50% of cases, develop in adult life as pink sausage-like lesions emerging from nail fold. Nails may show longitudinal groves, long leukonychia & short red streaks.
- Connective tissue nevi (shagreen patches) are seen in 40% of cases. Cobblestone, 1-8 cm in diameter, yellow plaques often arise in the skin over the base of the spine, composed of collagen and develop in the first decade of life.

Other skin findings:

- Skin fibromas, café-au-lait spots, oral papillomatosis, gingival hyperplasia.

Systemic features:

- Epilepsy, Mental retardation.
- Ocular signs, including retinal phakomas and pigmentary abnormalities.
- Hyperplastic gums.
- Gliomas and calcification of the basal ganglia.
- Renal and heart tumours, Cystic lesions of lung.
Diagnosis:

- Any baby with unexplained epilepsy should be examined with wood’s light to look for ash leaf macules
- Skull X-ray and CT scan help to exclude involvement of the CNS and kidneys

Xeroderma pigmentosum:

- Autosomal recessive disorder, characterized by the defective repair of DNA after its damage by UV radiation, extreme sun sensitivity, freckling and skin cancer.
- The condition is rare affecting about 5 per million in Europe.

Clinical features:

- The skin is normal at birth.
- Multiple freckles, roughness & keratosis on exposed skin appear between ages of 6 months and 2 years.
- Photosensitivity increases thereafter.
- The atrophic facial skin shows telangiectases and small angiommas.
- Many tumours develop on light-damaged skin; these include BCC, SCC, keratoacanthoma and malignant melanoma. Skin cancers often appear before age of 10. Many patients die before the age of 20 years. Most of the cancers appear on head and neck.
- Eye problems occur in 40% of cases and include photophobia, conjunctivitis, corneal opacities, neoplasm and ectropion.
- The condition may be associated with microcephaly, mental deficiency, dwarfism, deafness and ataxia.

Treatment:

- Skin cancers can be prevented by strict avoidance of sunlight.
- Early and complete removal of all tumors is essential.
- Retinoids can prevent the appearance of new cancers but, side effects are significant, and rebound in the number of cancers occur when the drug is stopped.
- Radiotherapy should be avoided.

Incontinentia pigmenti:

X-linked dominant disorder, usually lethal before birth in males. Characterized by spattered pigmentation on the trunk preceded by vesicular and verrucous changes.

Clinical features:

There are three stages in the evolution of the skin signs:

1. *Vesicular*; linear groups of blisters occur more on the limbs than trunk, most are evident by the time the infant is 4-6 weeks old, occur in 87% of cases.
2. *Warty*; after a few weeks or months the blisters dry up and the predominant lesions are papules with a verrucous hyperkeratotic surface, in two-thirds of cases, these usually resolve by one year of age.
3. *Pigmented*; after one year of age, a whorled, streaks or splashed macular pigmentation, following the lines of blaschko, ranging from slate-grey to brown color, replaces the warty lesions. Its bizarre patterning is a strong diagnostic pointer. This stage may last for many years and fade away, leaving no sequelae.

A fourth stage may be seen in some adult women manifesting faint hypochromic or atrophic linear lesions mostly on the extremeties.

Other skin manifestations:

- Patchy alopecia, onychodystrophy, subungual tumors and palmoplanter hyperhidrosis.
CNS defects: mental retardation, epilepsy or microcephaly, skull and palatal abnormalities may also be found.

Dental defects: delayed dentition, total absence of teeth, the incisors may be cone-or peg-shaped.

Occular defects: strabismus, cataract and optic atrophy.

Treatment:
- This is symptomatic & includes measures to combat bacterial & candidal infection during vesicular phase.

Ehlers-Danlos syndrome:
Caused by the abnormalities in the formation or modification of collagen and the extracellular matrix.

Clinical features:
- Hyperelasticity of the skin.
- Hyperextensibility of the joints.
- Fragility of skin and blood vessels.
- Easy bruising.
- Cigarette paper scars.

Complications:
Subluxation of joints, varicose veins, increased liability to develop hernias, kyphoscoliosis, aortic aneurysm and raptured large arteries, and intraocular hemorrhage.

Pseudoxanthoma elasticum:
This is a disorder of elastic tissue most obviously in the skin, blood vessels and eyes, either autosomal dominant or recessive.

Pathology:
- The elastic fibers in the mid-dermis become swollen and fragmented; their calcification is probably a secondary feature.
- The elastic tissue of blood vessels and of the retina may also be affected.

Clinical features:
The skin of the neck and axillae, and occasionally of other body folds or oral mucosa, is loose and wrinkled. Groups of small yellow papules give these areas a 'plucked chicken' appearance.

Other skin changes:
- Lax redundant folds of skin, nuchal comedones, exaggerated nasolabial folds, mental creases.
- Breaks in the retina show as angioid streaks, which are mostly appear before skin changes.
- Arterial involvement may lead to peripheral, coronary or cerebral arterial insufficiency.

Complications:
- The most important are:
  - Hypertention,
  - Recurrent gut hemorrhages,
  - Ischemic heart disease, mitral valve prolapse
  - Epistaxis,
  - Cerebral hemorrhage
- There is no effective treatment.