Genodermatosis: Inherited Skin Diseases

28

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Key points

- Genodermatoses are genetic skin conditions which can be classified into these three categories: chromosomal defect, a single gene defect or polygenetic. The condition may be inherited or due to a new mutation.
- Some genodermatoses are obvious at birth (congenital) while others may only become apparent in childhood or adult life (e.g. tuberous sclerosis).
- In albinism, lack of pigment can results in severe visual problems and makes the patient particularly sensitive to UVL damage and skin cancer.

What to tell the patient

- **Most cases of neurofibrosis** 1 are mild but neurological manifestations can occur in up to 40% of patients especially intracranial tumours, spinal cord tumours, peripheral nerve tumours and epilepsy.
- 60–70% of patients with tuberous sclerosis will have epilepsy or learning disabilities which may be present from birth or develop in adolescence or early adult life.

28.1 Introduction

Genodermatosis are skin disorders that are inherited as a result a genetic (chromosomal) defect. Some may run in families (inherited skin disorders) while others may occur as a result of a new mutation. Some are obvious at birth (congenital) while others may only become apparent in childhood or adult life (e.g. tuberous sclerosis). Patients and families may need genetic counselling to assess the risk of having more children with a certain chromosomal disorder.

28.2 Down Syndrome (Trisomy 21)

Most children with Down's syndrome are diagnosed at birth or shortly after. They usually have normal skin at birth but can develop various skin problems as they get older including an increased risk of developing dry skin, skin infections, atopic disease, psoriasis, autoimmune disease and premature aging of the skin. Young adults with Down's syndrome are more likely to develop truncal folliculitis on their presternal and interscapular area due to Malassezia folliculitis which responds well to oral itraconazole. Children with Down's syndrome are more likely to develop alopecia areata and hidradenitis suppurativa.

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28.3 Neurofibromatosis

This is a relatively common autosomal dominant condition but almost 50% of cases have no family history. It occurs in 1 in 3000 people. There are two main types of neurofibromatosis **(type 1 and type 2)**:

28.3.1 Neurofibromatosis Type 1 (von-Recklinghausen's = NF1)

NF1 represents 85% of all cases.

It is a rare (1 in 4000 births) autosomal dominant disease characterised by the presence of two or more of the following:

(a) Six or more *café-au-lait* spots greater than 5 cm in pre-pubertal children and greater than 15 cm in adults
(b) Axillary or inguinal freckling (70% of cases)
(c) Two or more neurofibromas
(d) Two or more Lisch nodules (small circle pigmented iris hamartomas—best seen with a slit lamp)—(90% of cases)
(e) Optic glioma
(f) A distinctive osseous lesion (e.g. sphenoid dysphasia or thinning of the long bone cortex)
(g) A first degree relative with NF1

Café-au-lait macules are usually the first sign of the disease and they appear in all children with NF1 by the age of 4. They are sharply defined, light brown macules, varying in size from 0.5 cm to 50 cm, but the majority are less than 10 cm in children.

Neurofibromas occur as a result of benign tumours surrounding nerves which present as soft, lilac-pink, sessile dome shaped or pedunculated tumours mostly on the trunk and limbs ranging in size from a few millimetres or several centimetres in diameter. They can be present in their hundreds (Fig. 28.1).

Elephantiasis neurofibromatosis is caused by neurofibromas of the nerves with associated overgrowth of subcutaneous tissue and skin which can produce gross disfigurement as depicted in the movie "The Elephant Man". However, most cases of NF1 are mild and never develop any major complications.

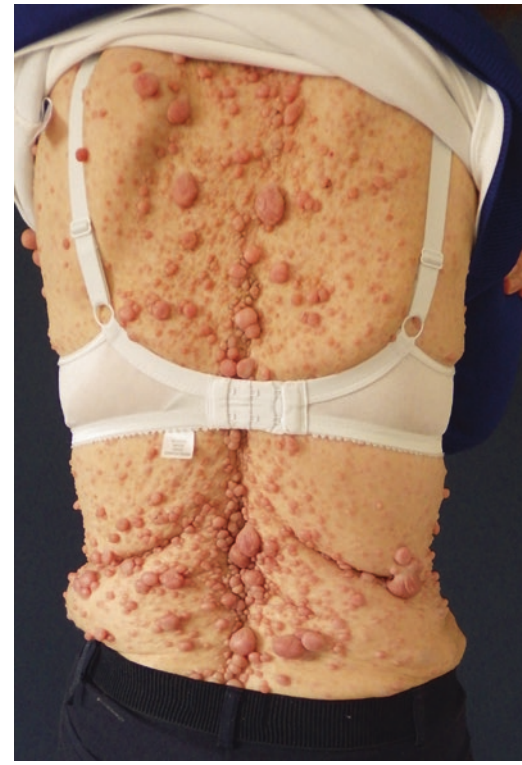

Fig. 28.1 Neurofibromatosis type 1

Neurological manifestations occur in 40% of patients especially intracranial tumours, spinal cord tumours **(which can lead to scoliosis)**, peripheral nerve tumours and epilepsy. This **can result** in both behavioural and learning difficulties. Some patients can have internal organ involvement with neurological, GI, GU or cardiovascular problems. Genetic counselling is important as 50% of children of parents with NF1 are likely to be affected by the disease.

28.3.2 Neurofibromatosis Type 2 (Bilateral Acoustic Neurofibromatosis)

This is a separate entity to NF1 with the affected gene on chromosome 22. Like NF1, patients can develop café-au-lait spots and cutaneous fibro-

mas but they also develop acoustic neuromas as well as other CNS tumours. The usual age of first symptoms (i.e. hearing and balance problems) is around 20-years of age (range 2–52) and cataracts are present in 80% of the cases.

28.4 Tuberous Sclerosis

Tuberous sclerosis is an autosomal dominant disorder of hamartoma formation in many organs especially in skin, brain, eyes, kidney and heart. It is uncommon with an incidence of 1 in 10,000. Approximately 60–70% of cases are thought to be new mutations. The typical skin lesions are as follows:

(a) Angiofibromas—these usually appear from the age of 3–10 years old. They are firm, discreet, reddish brown, telangectatic papules ranging from 1 mm to 10 mm in diameter on the cheeks and chin and often mistaken for acne (Fig. 28.2).
(b) Shagreen patch—this is an irregular, thick, macular, papular, soft skin coloured plaque usually in the lumbo-sacral area that causes no symptoms (Fig. 28.3)
(c) Periungual fibromas—these appear at or after puberty as smooth, firm, fleshy, warty benign growths arising from the proximal nail folds and can grow to 5 mm or 10 mm long (Fig. 28.4a, b).
(d) Ash leaf-shaped white macules—these are white ovoid macules measuring 1–3 cm usually on the trunk or limbs (Fig. 28.5). They are usually the first cutaneous sign of tuberous sclerosis. They may be present at birth or shortly after and can be a clue to the diagnosis in a child with epilepsy. However, these macules are often seen in normal babies without tuberous sclerosis.

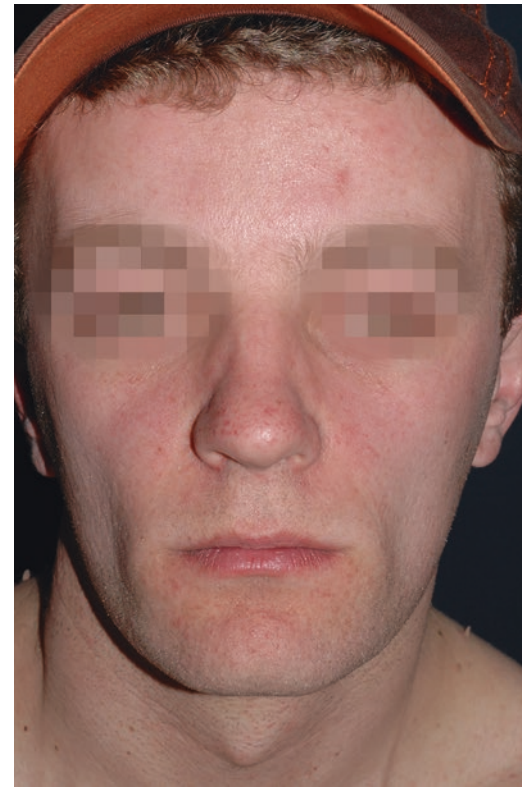

Fig. 28.2 Tuberous sclerosis with tiny angiofibroma on the nose

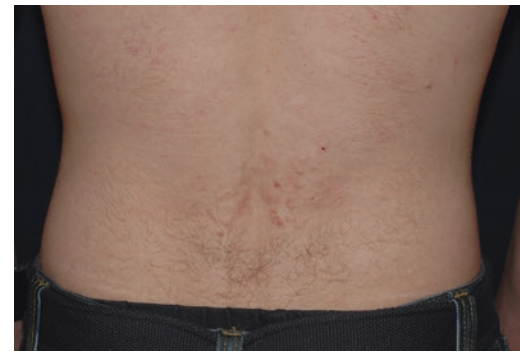

Fig. 28.3 Tuberous sclerosis with a Shagreen patch

60–70% of patients with tuberous sclerosis will have epilepsy, intellectual disabilities and developmental delay which may be present from birth or develop in adolescence or early adult life. Tumours may also occur in the heart, kidney, lungs, GI tract and brains.

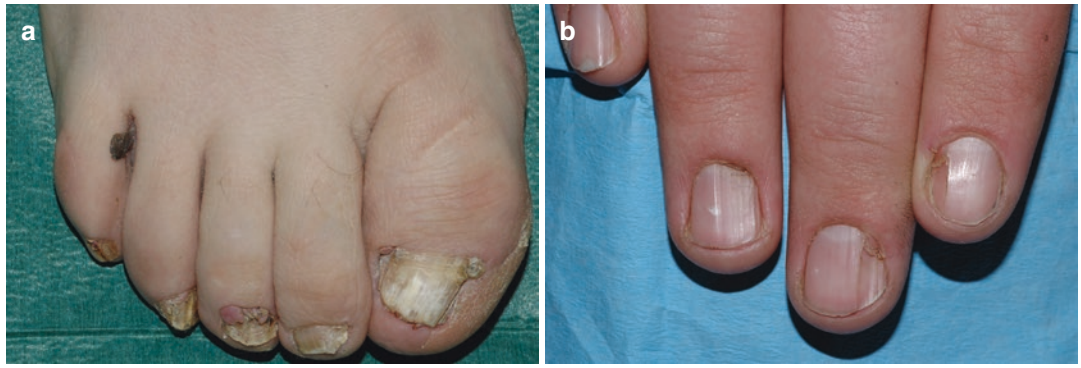

Fig. 28.4 Tuberous sclerosis: (**a**) periungueal fibroma with possible fungal nail infection, and (**b**) periungueal fibroma with secondary nail dystrophy

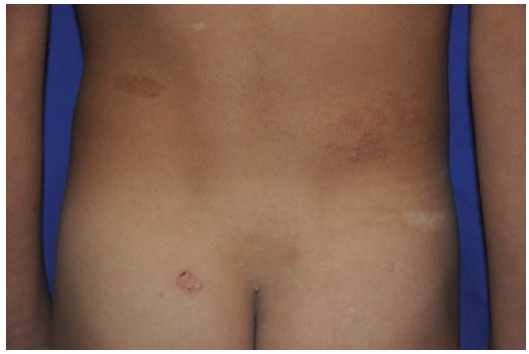

Fig. 28.5 Cafe au lait spots, ovoid white (ash leaf) macules and Shagreen patch in tuberous sclerosis. Photo courtesy of Dr Myriam Raquel González Oviedo

28.5 Ehlers-Danlos Syndrome

Ehlers-Danlos syndrome is a genetic connective tissue disorder resulting in fragile and hyperelastic skin, hypermobile and easily dislocatable joints**,** scoliosis and fragile blood vessels (easy bruising). Internal organs may be involved including the heart valve (mitral valve prolapse) GI, GU, eyes, spine and gums. The skin feels soft and boggy. Some patients may have hyper-mobile joints without skin involvement. Clinical features including osteoarthritis, usually first appear in young adults.

28.6 Darier's Disease

This is a rare autosomal dominant disease that causes a disruption of keratinosation resulting in various abnormal skin and nail manifestations. Patients often have a family history of Darier's disease. They usually present in late childhood or in early adult life with greasy, scaly papules on the face and trunk in a seborrhoeic dermatitis pattern. It can sometimes spread in a dermatomal distribution. It can also affect the flexures. It may be mistaken for other skin conditions such as acne, psoriasis and seborrhoeic dermatitis. Subtle signs such as longitudinal red or white streaks on the nails and palmer pits may help make the diagnosis. Histology is usually characteristic in Darier's disease.

The clinical features are variable with many patients having mild disease while others may have extensive disease. Patients with Darier are more prone to skin bacterial and viral infections such as widespread herpes simplex.

Treatment will depend on the severity of the disease. Mild cases may only require emollients and photo protection. More troublesome cases may require topical or oral retinoids.

28.7 Albinism

Albinism is an autosomal recessive (but some forms are X-linked) genetic deficiency of melanin pigment production. Oculocutaneous albinism (OCA) affects the eyes, hair and skin, whereas only the eyes are affected in ocular albinism (OA). While most people with albinism have very light or white skin and hair, levels of pigmentation can vary depending on the type of albinism. OA, which is much less common, involves only the eyes, while skin and hair may appear similar or slightly lighter than that of other family members.

Approximately 1 in 17,000 people in Europe have one of the types of albinism, although it is much more common in East Africa. Lack of pigment results in severe visual problems and makes the patient particularly sensitive to UVL damage and skin cancer. Sun glasses and sun protection for the skin with high SPF sun blocks, hats and appropriate clothing is vital from birth. Life expectancy is not affected provided the patient does not succumb to skin cancer.

Very rare genodermatoses such as **Epidermolysis bullosa** are covered in other chapters (see Chap. 23) or should be reviewed in major text books in dermatology (see Chap. 67).

28.8 Conclusion

Genodermatoses are genetic skin conditions which can be classified into these three categories: chromosomal defect, a single gene defect or can be polygenetic. The condition may be inherited or due to a new mutation. Early diagnosis is important to limit morbidity and mortality. Genetic counselling is vital if the affected person is planning a family.