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Editorial

Skin: a window to dysmorphic syndromes

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The term "dysmorphology" was coined by Smith (1926-1981), a pediatrician, in the 1960's to describe the study of human congenital malformations, particularly those affecting the morphology (the anatomy) of the individual. Dysmorphology literally means, "the study of abnormal form." Today as a scientific discipline, dysmorphology combines concepts, knowledge, and techniques from the fields of embryology, clinical genetics and pediatrics and deals with people having congenital abnormalities and their families.[1]

Certain terms have been evolved to describe the dysmorphic features like malformations, deformation, disruption, syndrome, sequence and association.[2] A dysmorphic syndrome is a recognized pattern of two or more anomalies in an individual. Most of syndromes comprise of one or more major anomalies together with a variable number of minor anomalies.

It is estimated that 2-3% of all live-born infants show one or more significant malformations and by the end of first postnatal year, this figure doubles by the discovery of new anomalies not present at the time of birth.[2]

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Most malformations are defects of blastogenesis and are genetically controlled. These can be monogenic, polygenic, chromosomal, microdeletion syndromes or result from teratogens i.e. drugs e.g. retinoids, thalidomide, hormones etc., infections including herpes simplex, varicella-zoster, cytomegalovirus, rubella, HIV, toxoplasmosis, syphilis etc., maternal disease e.g. diabetes mellitus, nutritional deficiencies; environmental toxins; ionizing radiations or can be sporadic.[2,3]

At present more than 3500 dysmorphic syndromes have been described and the list is ever increasing.[3,4] It is estimated that skin is affected in more than 1000 such syndromes. Because of easy visibility, accessibility and large surface area skin can provide a lot of information and help. Hence a meticulous examination of integument may open a window to the final diagnosis.

Diversity and heterogeneity of cutaneous features can be broadly categorized as: 1. changes of skin texture e.g. ichthyosis, palmoplantar keratoderma, cutis laxa, cutis hyperelastica, signs of skin ageing, blistering, dystrophic scarring/keloid formation, aplasia cutis etc.; 2. pigmentary changes e.g. lentigines, freckles, café-au-lait macules, hypopigmentary changes (albinism, vitiligo, ash-leaf macules), changes along Blaschko lines; 3. vascular defects e.g. port-wine stain, hemangioma, poikiloderma, telangiectasia, cutis

Table 1 Different categories of skin signs with a few examples of dysmorphic syndromes [modified from Smithson and Winter[3]].

Category of skin malformation	*Examples*
Altered texture of skin	
Ichthyosis	Sjogren-Larssen syndrome, trichothyodystrophy
Palmoplantar keratoderma	Papillon-Lefevre syndrome
Cutis aplasia	Adams-Oliver syndrome
Hypoplastic/atrophic skin	Goltz syndrome
Loss of subcutaneous fat	Progeria
Epidermolysis bullosa	Bart syndrome
Pigmentary changes	
Depigmentation, following the lines of Blaschko	Hypomelanosis of Ito
Café-au-lait patches	Neurofibromatosis type 1
Whorled hyperpigmentation	Incontinentia pigmenti
Piebaldism	
Vascular defects	
Telangiectasia	Ataxia telangiectasia, hereditary hemorrhagic telangiectasia
Asymmetrical varicosities of limbs	Klippel-Trenaunay-Weber syndrome
Characteristic hemangioma of the philtrum of the upper lip	Macrocephaly cutis marmarata syndrome
Tumours	
Cutaneous haemangiomata	Bannayan-Zonana syndrome
Fleshy papules on face	Murray-Puretic syndrome (or juvenile hyaline fibromatosis)
Multiple naevoid basal cell carcinomas	Gorlin syndrome
Hair abnormalities	
Sparse hair	Dubowitz syndrome
Generalized hirsutism	De Lange syndrome
Trichorrhexis nodosa	Trichothiodystrophy
Nail abnormalities	
Rudimentary nails	Nail-patella syndrome
Sweating abnormalities	Ectodermal dysplasia
Others	

marmorata etc.; 4. cutaneous tumours e.g. epidermal/sebaceous nevi, hemangioma, neurofibroma, angiofibroma, adnexal tumours etc.; 5. hair changes e.g. abnormal patterns of hair growth (localized/diffuse, scarring/nonscarring alopecia, hypertrichosis, hirsutism), texture (hair shaft defects) and pigmentation (poliosis, premature greying) etc; 6. other changes affecting nails, sweat glands etc. **Table 1** depicts a few such examples.[4]

Diagnosing a dysmorphic syndrome is very important since it determines which investigations should be done, how the patient should be managed; long-term prognosis and estimated genetic risk and advice to family. When a newborn is identified with one or more malformations, a detailed history with particular emphasis on family history and antenatal and perinatal history and physical examination should be undertaken. Clinical experience, extent of reading and observational skills are vital to reach the diagnosis but other tools e.g. clinical photographs, specialized development charts, laboratory investigations and electronic databases are also helpful.[1,2,3] The London Dysmorphology Database and On Line Mendelian Inheritance in Man, are two such sites which can be searched for this purpose by using combinations of handles/key features.[4,5]

Besides an easy clinical evaluation, skin is an organ easy to biopsy. In addition to the light microscopy and electron microscopy, fibroblasts can be cultured and used for biochemical testing and specialized tests for genetic analysis, mutation studies etc.[1,3]

When a dermatologist is called for opinion about a congenital malformation, he should be wary that this anomaly might be just the tip of a syndromic iceberg. Sometimes it may not be possible to reach the final diagnosis and a regular follow up reveals the mystery. Similarly, the help of other specialties may be sought for the diagnosis and management.

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