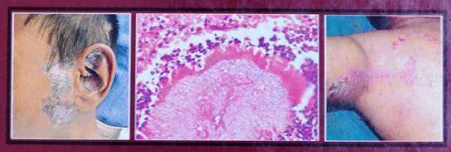
IADVL Textbook of Dermatology

FOURTH EDITION



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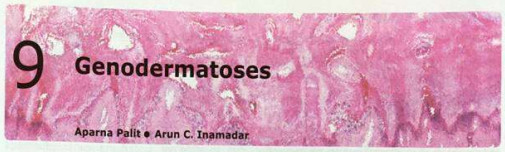

9 Genodermatoses

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KEY MESSAGE

- Genodermatoses are inherited genetic skin conditions, majority of which are lifelong, multisystem disorders.
- Four patterns of genetic transmission: autosomal dominant, autosomal recessive, X-linked dominant, X-linked recessive.
- All genodermatoses are associated with high morbidity because of the incurable nature and some are associated with increased mortality.
- Definitive diagnosis of most of the genodermatoses is difficult in resource-poor set up; hence clinical acumen of the physician, pedigree chart of the affected family and making appropriate diagnostic algorithm for each group of disorder are the helpful means to reach a provisional diagnosis. Definitive diagnosis is possible only by genetic studies.
- Management is symptomatic in most of the disorders. Genetic counselling and prenatal diagnostic facilities bring a ray of hope to the affected families.

INTRODUCTION

Patients with genodermatoses constitute a significant section in dermatological practice. The majority of these are lifelong, multisystem disorders. Some carry the risks of malignancy and premature death. Many genodermatoses cause cosmetic disfigurement, and patients present to the dermatologist for their unusual appearance. Management of these disorders is not only limited to the diagnosis of the particular disease but also probing into the family tree to know the inheritance pattern, providing options for prenatal diagnosis to the parents, and genetic counseling to prevent further such occurrence. With this background, it is understandable that a basic knowledge of genetics is essential to the dermatologist. The discussions in the following section include the principles of genetic transmission of diseases and the terms related to it.

PRINCIPLES OF GENETIC TRANSMISSION

Transmission of characters through generations is determined by genes located on the chromosomes. Such transmission may or may not follow Mendelian laws. As a broad group, these are categorized as inherited disorders. A familial disorder is recognized by occurrence of a character in a family clearly in excess of its expected occurrence in the same population.[1] A congenital character is the one present at or before birth.[1] Congenital and familial conditions do not necessarily imply genetic transmission. Non-Mendelian inherited disorders such as psoriasis and atopic dermatitis are quite common and show familial clustering frequently.[2]

The genotype of an individual indicates the characters transmitted through the genes. The physical expression of these characters is designated as phenotype. Autosomal characters are borne by autosomes (22 pairs of chromosomes) and sex-linked characters are carried by sex chromosomes (X/Y). Genes are located at particular chromosome loci as alleles. Two different alleles at a particular locus of a chromosome pair indicate heterozygosity, whereas identical alleles at a locus indicate homozygosity. Males with the expression of X-linked characters (unpaired alleles) are termed as hemizygous.[2] A dominant character is defined as the one whose phenotypic expression is possible in the heterozygous state. A recessive character manifests only in the homozygous state.

Four major patterns of genetic transmission are possible: (1) autosomal dominant (AD), (2) autosomal recessive (AR), (3) X-linked dominant (X-L-D), and (4) X-linked recessive (X-L-R). Sex-linked transmission may also occur through Y chromosomes (holandric transmission).