characterized by periodontal disease (Figs. 15.17-1 and 15.17-2). It is autosomal recessively inherited.

10. Richner-Hanhart syndrome

The three major characteristics are painful palmoplantar keratosis, photophobia, and mental retardation. It is autosomal recessively inherited. The pathogenesis is a reduced activity of tyrosine aminotransferase.

11. Náxos disease

Keratosis, cardiac myopathy of the right ventricle, cardiac enlargement, and palmoplantar keratosis are present. Cases with mutation in the plakoglobin gene have been reported.

c. Other hereditary keratoses

1. Darier’s disease

Synonym: Keratosis follicularis

Outline

• Keratotic papules of 2 mm to 5 mm in diameter appear, mainly on seborrheic and intertriginous areas. The condition is aggravated by perspiration in summer.
• The pathogenesis is genetic mutation in SERCA2, the calcium pump of keratinocytes. It is autosomal dominantly inherited.
• The characteristic pathological findings are acantholysis, lacunae, corps ronds, and grains.

Clinical features

Darier’s disease first occurs in infancy and continues through adolescence. Multiple dark brown keratotic papules of 2 mm to 5 mm in diameter covered by thick crusts occur in the seborrheic and intertriginous areas such as the neck, axillary fossae, sternal region, inframammary region, abdomen and groin (Figs. 15.18-1 and 15.18-2). The papules may be moist and give off a bad odor. On the perspiratory intertriginous areas, papules coalesce and condyloma-like proliferation occurs. The following occur: keratosis in the palms and soles, verrucous keratosis in the dorsal surfaces of hands and feet, punctuate depression in the palms, enanthema, deformity of nails, and sometimes nervous symptoms such as mental retardation and epilepsy. Bacterial or viral infection (e.g., Kaposi’s varicelliform eruption) may occur secondarily.

Pathogenesis

Darier’s disease is caused by mutation in the ATP2A2 gene, which codes for the SERCA2 calcium pump. That pump controls the calcium concentration in the cytoplasm of keratinocytes.
A. Hereditary keratoses

Since calcium regulates intercellular adhesion and differentiation of keratinocytes, the genetic mutation promotes keratinization and abnormal formation of desmosomes and keratin fiber complex, leading to abnormal dyskeratosis and acantholysis.

Pathology

Darier’s disease is characterized by dyskeratosis. Therefore, corps ronds (large round cells with a basophilic pyknotic nucleus and bright cytoplasm) and grains (long, thin cells that resemble parakeratotic cells and stain dark) are found in the granular layer. There is acantholysis, its accompanying lacunae formation, and villi formation in which dermal papillae extend upwards into the lacunae (Fig. 15.19).

Differential diagnosis

Darier’s disease should be differentiated from acanthosis nigricans, Hailey-Hailey disease and seborrheic dermatitis.

Treatment

The symptoms are improved temporarily by oral retinoid. Urea ointments are also useful. Secondary infections and sun exposure should be avoided.

2. Erythrokeratodermia

Localized keratotic lesions accompanied by flush may be produced in infancy; erythrokeratodermia is the generic term for these clinical conditions. There are various clinical features and causative genes (Fig. 15.20). The following are the major types of erythrokeratodermia.

1. Progressive symmetric erythrokeratodermia
   It is autosomal dominantly inherited. In some cases, mutation in the gene coding for loricrin has been identified. Localized, sharply circumscribed flushing and keratotic lesions are present. The extremities are most commonly affected. It often appears symmetrically. The lesions extend with time. The main treatment is oral retinoid.

2. Erythrokeratodermia variabilis
   It is autosomal dominantly inherited. In some cases, mutation in the gene coding for connexin has been identified. Localized, sharply circumscribed flushing and keratotic lesions appear in infants under 1 year old. The lesions occur symmetrically on the face, trunk and extremities, and tend to extend and coalesce. They disappear in several days to several weeks, recurring on different sites. Scaling is marked and gives the skin an unwashed appearance, but there are no subjective symptoms. The main treatment is oral retinoid.

Skin fragility syndrome—See Chapter 14.