H. Other metabolic disorders

1. Fabry’s disease

Synonym: Angiokeratoma corporis diffusum (Fabry)

This is an X-linked recessive lysosomal storage disorder. The pathogenesis is absence or marked reduction of α-galactosidase activity caused by genetic mutation (Figs. 17.26 and 17.27). Trihexosylceramide fails to be degraded because of a lack of this enzyme, resulting in deposition in the blood vessels, causing dysfunction (Fig. 17.28). Multiple angiokeratoma, small papules of 2 mm to 3 mm in diameter accompanied by telangiectasia, occur, mostly on the abdominal and lumbar regions (“bathing trunk” distribution). Renal failure, cerebrovascular disorder, heart failure and breathing difficulty occur, with most patients dying at about age 40. Clinical features of Fabry’s disease differ greatly from case to case. Enzyme replacement therapies have been attempted in recent years.

2. Kanzaki disease

Synonym: Angiokeratoma corporis diffusum (Kanzaki)

This is a lysosomal storage disorder. Enzyme deficiency results from mutation in the N-acetyl-α-d-galactosaminidase gene on chromosome 22. This disorder of glycoprotein metabolism is autosomal recessively inherited. The cutaneous symptoms resemble those of Fabry’s disease: Small multiple angiokeratomas occur on the whole body, particularly on the lumbar region (Fig. 17.29). Oligohidrosis, sensory nerve failure, and hearing impairment are present. The prognosis is good.

3. Gouty tophus

Multiple nodules of 5 mm to 30 mm in diameter occur on the auriculae, finger and toe joints, elbows, knees and Achilles tendons. The skin becomes tense and thin, with yellowish-white tone in subcutaneous areas. When the skin is broken, a chalk-like substance containing uric acid crystals is excreted. Gouty tophus heals with scarring after ulceration.

Gout is caused by hyperuricemia; uric acid is hyperproduced and/or underexcreted. Acute gouty arthritis tends to present as intense pain in the great toe that gradually spreads to the other joints. Joint swelling and tenderness are present. Peripheral areas swell and become dark red, and these changes are accompanied by burning sensation, fever, leukocytosis, and elevated erythrocyte sedimentation rate.
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Synonym: Hyalinosis cutis et mucosae

Hyaline-like substances deposit in cutaneous membranes to form wart-like nodules and papules on the eyelids and eyelash regions, and white nodules in the oral cavity. Nodules in the glottis cause hoarseness. Cases caused by autosomal recessively inherited mutation in the extracellular matrix protein 1 (ECM1) gene on chromosome 1q21 have been reported in recent years.

This autosomal recessively inherited disorder is caused by mutation of the phenylalanine hydroxylase (PAH) gene, which codes for an enzyme that metabolizes phenylalanine into tyrosine. Reduced skin pigmentation, brownish hair color, and mental developmental delay result from the atic dysfunction. In Japan, Guthrie newborn mass screening is conducted for phenylketonuria. The incidence is 1 in 60,000 to 1 in 80,000. Maintaining a phenylalanine-restricted diet until about age 3 prevents cerebral disorder. The skin and hair color returns to normal by dietary supplementation of tyrosine.