Acrodermatitis enteropathica

Synonym: Zinc deficiency syndrome

**Outline**

- This is a zinc deficiency whose main symptoms are dermatitis, alopecia and diarrhea.
- The main types are a congenital type (autosomal recessively inherited) and an acquired type that is caused by administration of parenteral central venous nutrition or excision of the digestive tract.
- Erythema and erosion form on the distal portions of the extremities, and on the genitalia and orifices (the periphery of the eyes and mouth, nares, and auditory meatus), presenting clinical features similar to psoriasis, seborrheic dermatitis and cutaneous candidiasis.

**Clinical features**

Dermatitis tends to occur on sites that have mechanical pressure, such as the distal portions of the extremities, the genitalia, and the facial orifices (the periphery of the eyes and mouth, nares, and auditory meatus; Fig. 17.14). Acrodermatitis enteropathica begins with papules, small blisters, or erythema accompanied by pustules, and progresses to erosion and crusts. Annular scaling is clinically observed, resembling psoriasis, impetigo, seborrheic dermatitis and cutaneous candidiasis. Nail deformity and peri-onychia occur.

Alopecia occurs in almost all cases, appearing on the occipital and temporal region of the head first and then spreading to the entire scalp and eyebrows. Diarrhea and vomiting recur.

**Pathogenesis**

The congenital type of acrodermatitis enteropathica is autosomal recessively inherited. It is caused by a mutation in the...
SLC39A4 gene on chromosome 8. SLC39A4 is a specific protein for transporting zinc and iron. Acquired zinc deficiency is caused mainly by prolonged parenteral central venous nutrition, excision of the digestive tract, or severe diarrhea or vomiting. It may be induced by the anti-rheumatoid drug oral penicillamine, or by deficiency of zinc in breast milk.

**Laboratory findings, Diagnosis**

Zinc levels are low in patients. In normal people, zinc levels are 60 to 130 \( \mu g/dl \) in serum, and 300 to 600 \( \mu g/day \) in urine. The alkaline phosphatase level in the blood is also low, because of the low zinc level.

**Differential diagnosis**

The eruptions resemble psoriasis, impetigo, seborrheic dermatitis and cutaneous candidiasis. Acrodermatitis enteropathica is a rare metabolic disease; however, dermatitis, diarrhea, and alopecia may also occur in congenital biotin metabolic disorder and essential fatty acid deficiency.

**Treatment**

Sufficient supply of zinc is essential.

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**2. Hemochromatosis**

*Synonym: Bronze diabetes*

**Outline**

- Excessive accumulation of iron in the body leads to organ failure from deposition of hemosiderin (an iron-binding protein) in various organs. It is caused hereditarily or by anemia, liver dysfunction, excessive intake of iron preparations, or excessive transfusions.
- Diffuse, brownish-blue-gray pigmentation occurs on sun-exposed areas and genitalia. Diabetes may occur as a complication. Abnormality is not seen in the central nervous system.
- Iron and increased ferritin are found in the serum by a blood test.
- Phlebotomy and iron chelator administration are the main treatments.

**Clinical features**

Diffuse, brownish-blue-gray pigmentation occurs in the skin as a result of marked deposition of hemosiderin, ferritin or melanin (Fig. 17.15). The sun-exposed areas of the body such as the face, dorsal hands, extensor surfaces of forearms, and genitalia are most severely affected. Atrophy and dryness are present. The axillary and pubic hair may become sparse. The symptoms progress gradually.

Liver dysfunction almost always accompanies the cutaneous
symptoms. Impaired hepatic function and hepatomegaly are found. Atrophy and dryness of the skin are present. Without proper treatment, liver cirrhosis may progress to hepatocellular carcinoma.

**Classification**

Hemochromatosis is divided into genetic hemochromatosis (autosomal recessively inherited) and secondary hemochromatosis (from excessive intake of iron).

**Pathogenesis**

In genetic hemochromatosis there is overabsorption of iron from the intestinal tract and of iron metabolic dysfunction in the endothelial system.

Secondary hemochromatosis may be caused by ① anemia accompanied by ineffective erythropoiesis (e.g., sideroblastic anemia, hemolytic anemia), ② liver disease (e.g., alcoholic cirrhosis), ③ excessive oral intake of iron (e.g., high intake of red wine, excessive intake of iron preparations), or ④ blood transfusion in large volumes.

**Pathology**

Hyperpigmentation of the skin is caused by increased dermal melanin and dermal hemosiderin within macrophages, seen as melanophages and siderophages. Iron deposits in the deep dermis. Dermal atrophy and pigmentation are present. Marked iron deposition can be found at the periphery of the sebaceous glands (Fig. 17.16).

**Laboratory findings, Diagnosis**

Serum iron, transferrin saturation and serum ferritin values increase from iron excess. UIBC is decreased. A liver biopsy is conducted for differential diagnosis.

**Treatment**

An iron chelator (deferoxamine) is administered. Symptomatic therapies are performed for organ failure. Alcohol intake is restricted.

### 3. Menkes disease

**Synonym:** Menkes kinky-hair disease

**Outline**

- This disease is an X-linked recessive disorder of copper metabolism.
- It is characterized by kinky hair and reduced skin pigmentation.

**Clinical features**

Congenital lack of a copper-dependent enzyme that is essential
for synthesis of melanin and keratin leads to reduced skin pigmentation. Hair is whitish and fragile (kinky hair). Babies with Menkes disease are born underweight and demonstrate convulsions and other neurological symptoms shortly after birth. Psychomotor retardation, muscular hypotonia, poor sucking, low body temperature, abnormality in the blood vessels in the whole body, and osteoporosis are present. Without proper treatment, most patients die before age 3.

**Pathogenesis**

Mutation in the gene that codes for copper-transporting ATPase (ATP7A) causes malabsorption of copper in the intestinal tract, resulting in copper insufficiency in the body. This leads to various symptoms. It is an X-linked recessive disorder; boys are most commonly affected.

**Treatment**

Parenteral copper salt is effective in mild cases. The gene responsible for Menkes disease has been identified; this may be useful for gene therapies.

**4. Calcinosis cutis**

Calcinosis cutis is a condition in which calcium deposits in large amounts to form firm, yellow to white papules or nodules. When the deposition is in the stomach, kidneys, lungs muscles, or in/under the skin and hypercalcemia is present, the cause is parathyroid tumor, excessive intake of vitamin D, or bone destruction caused by a tumor. Calcinosis cutis may appear as a symptom in systemic sclerosis and dermatomyositis, even in cases with normal serum calcium level (Fig. 17.17). There are also idiopathic cases: e.g. scrotal carcinosisis (Fig. 17.18).

**E. Vitamin deficiencies**

**1. Pellagra**

**Outline**

- It is caused by lack of B vitamins, especially niacin.
- The main symptoms are dermatitis, diarrhea and dementia.
- It most frequently occurs in recipients of isoniazid (INH), and in alcoholics and those who have had a gastrectomy or who have poor eating habits.
- Supplementation of niacin is the main treatment.

**Clinical features**

Symptoms of pellagra are characterized by the “3D’s”: