A 13-year-old boy, the offspring of first cousins, presented with long-standing, brown-black, hyperpigmented, velvety, hyperkeratotic plaques over both ankles, axillae, neck, and groin (Figure 1). His face was acromegaloïd and he had a generalized paucity of subcutaneous fat (Figure 2). His muscles were prominent and his abdomen distended (Figure 3). In addition, he was hirsute and his genitalia were enlarged. A paternal uncle has had similar skin lesions since he was a child.

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Denouement and Discussion

Generalized Lipodystrophy

Figure 1. The axilla appears hyperpigmented and velvety, characteristic of acanthosis nigricans.

Figure 2. The face is acromegaloid and the neck shows changes of acanthosis nigricans.

Figure 3. The muscles are prominent and the abdomen is distended secondary to hepatomegaly.

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everalized lipodystrophy, also known as lipoatrophic diabetes, is a progressive multisystem disorder characterized by the loss of subcutaneous and other body fat. The congenital form of generalized lipodystrophy, known as the Lawrence-Seip syndrome, has its onset in the first 2 years of life and is inherited in an autosomal recessive fashion. A sporadic, acquired generalized form has its onset in the first to third decades of life. Partial acquired lipodystrophy occurs sporadically and is characterized by the loss of fat in localized areas.

Individuals affected with the generalized form of lipodystrophy develop a cadaveric appearance with acromegalic face and prominent muscles, the result of accelerated growth and the loss of subcutaneous fat. A complete loss of body fat does not occur in generalized lipodystrophy. There seems to be preservation of fat in sites where loss of body fat does not occur in generalized lipodystrophy, known as the Lawrence-Seip syndrome, has its onset in the first 2 years of life and is inherited in an autosomal recessive fashion. A sporadic, acquired generalized form has its onset in the first to third decades of life. Partial acquired lipodystrophy occurs sporadically and is characterized by the loss of fat in localized areas.

Acanthosis nigricans invariably develops in affected individuals as a symmetric dermatosis with a hyperpigmented, velvety appearance that gives a sandpaper-like sensation on palpation. The sites of predilection of acanthosis nigricans include the neck, groin, axillae, and inframammary areas. Affected areas over the knees, elbows, and knuckles have a pebbly feel, more common in the acquired form of the disease. Acanthosis nigricans is associated with other disorders that include obesity, endocrinopathies, autoimmune metabolic diseases, and malignant neoplasms, many of which also feature insulin resistance.

ENDOCRINE ABNORMALITIES

Hyperinsulinism, a hallmark of lipodystrophy, is due to heterogeneous defects in insulin binding, receptor expression, receptor kinase function, or postreceptor signaling. There is resistance to ketone production secondary to a paucity of stored fat and elevated circulating insulin levels. The presence of hypothalamic releasing factors in the serum of some patients with lipodystrophy suggests a lack of hypothalamic regulation. The acromegalic appearance of these patients suggests elevated growth hormone secretion, but their circulating levels of growth hormone and insulin growth factor-I may be normal, high, or low. The bone age is usually advanced. Thyroid and adrenal function are generally normal. Plasma glucagon levels range from normal to markedly elevated.

MANAGEMENT

The treatment of generalized lipodystrophy is supportive. Caloric restriction may improve hyperlipidemia and carbohydrate tolerance. Good control of blood glucose levels is very difficult to achieve because of the underlying insulin resistance. In one report, the selective dopaminergic blocking agent, pimozide, reversed the physical abnormalities as well as the biochemical disturbances.

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