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## **Congenital Generalized Lipodystrophy in a 4-year-old Chinese Girl**

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*Congenital generalized lipodystrophy (CGL) is a rare autosomal recessive disorder characterized by near complete absence of adipose tissue since birth and insulin resistance. The diagnosis is made on the basis of lack of body fat, muscular hypertrophy, acanthosis nigricans, hirsutism, hepatomegaly with fatty liver, hyperlipidemia and hyperglycemia with insulin resistance. We describe a 4-year-old Chinese girl with the clinical features of CGL.*

**Key words:** lipodystrophy, hypertriglyceridemia.

Generalized lipodystrophy is a rare condition of the lipid and carbohydrate metabolism clinically characterized by varying degree of fat loss in adipose tissues. Currently, lipodystrophy can be divided into

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congenital and acquired types, based on the age at presentation and pattern of inheritance.

Congenital generalized lipodystrophy (CGL) is a rare disease, which is also referred to as Berardinelli-Seip syndrome characterized by loss of adipose tissue, long extremities, acromegalic appearance, accelerated growth, hypertrophic cardiomyopathy, hepatosplenomegaly, insulin resistance, dyslipidemia (increase in triglycerides, decrease in HDL). It is known that dyslipidemia is a risk factor for the development of type 2 diabetes mellitus and cardiovascular disease (1,2).

Here we report a Chinese girl with CGL, treated with a special diet characterized by calorie restriction and partial substitution of long-chain triglycerides with medium-chain triglycerides.

### **Case Report**

A 4-year-old Chinese girl was full-term, normal delivery infant with birth weight 3.05 Kg, birth length 51 cm. Her parents were healthy and normal in height (paternal 172 cm, maternal 161 cm). There was no significant family history or no accidental use of contraceptive pills. Since birth, she had extreme lack of body fat and a muscular appearance, progressive hypertrichosis and her face displayed abnormality. She had mild impairment of intellectual function and performed poorly at school.

Physical examination revealed a height of

114.4 cm (>97th centile) and a weight of 20 kg (>97th centile). There was generalized loss of fat from the face, trunk and extremities. She had coarse, acromegaloid features, marked acanthosis nigricans over the neck and axillae, dry and thick hair, abdominal wall, umbilical hernia, severe hepatosplenomegaly, prominent muscles and veins with normal genitalia.

**Laboratory values:** Triglycerides of 2.02 mmol/L (normal range 0.3-1.8), serum total cholesterol of 2.92 mmol/L (<5.2), high-density lipoprotein cholesterol of 0.69 mmol/L (>0.9), low-density lipoprotein cholesterol 1.22 mmol/L (<0.8), GPT 96 U/L (<40), GOT 76 U/L (<50), fasting serum glucose 81.9 mg/dL (80-120), insulin 33.74 mIU/L (<15). FGIR (means a fasting glucose to insulin ratio) was elevated at 2.4 (FGIR < 7 is suggestive of insulin resistance). DHEA and DHEAS levels were increased at 14.78 µg/dL and 313.3 µg/dL (DHEA and DHEAS were determined with a commercially available EIA kit, DSL UK Ltd. Intra- and interassay coefficients of variation were 10.7% and 8.0% for DHEA, respectively, as well as 5.3% and 5.0% for DHEAS, respectively. At this age, normal values were  $<154 \pm 2.8$  µg/dL for DHEAS and  $<8.3 \pm 1.7$  µg/dL for DHEA). Testosterone, baseline LH and FSH were normal. B ultrasound showed severe diffuse hepato-splenomegaly and hepatic steatosis visceral fat lack. Bone age was advanced.

Saturated fats and long-chain triglycerides were replaced with soluble fibers, unsaturated fats and medium-chain triglycerides (such as plant oil instead of animal oil). After six months, the serum triglyceride concentration decreased from 2.02 mmol/L to 1.35 mmol/L.

## Discussion

Congenital generalized lipodystrophy is a rare autosomal recessive disease with a preva-

lence of less than one case per 12 million individuals(3). It affects all ethnic groups although many of these cases have involved individuals of Portuguese or Norwegian ancestry. Worldwide, over 200 cases have been reported. Enlargement of the hands, feet and mandible, loss of adipose tissue, accelerated growth, voracious appetite, increased basal energy expenditure and advanced bone age, acanthosis nigricans, moderate to severe mental retardation, insulin resistance, severe hyperinsulinemia, hypertriglyceridemia and low levels of high-density lipoprotein cholesterol, umbilical hernia and hepatosplenomegaly are characteristic(4). The present case had loss of fat, acromegaloid appearance, acanthosis nigricans, mild mental retardation, umbilical hernia, hepatosplenomegaly, hyperinsulinemia and hypertriglyceridemia. Clinical features and serum biochemistry were compatible with the diagnosis of CGL.

The genetic heterogeneity of CGL, as well as the existence stages of the disease, explains the differences among the main clinical findings of the patients reported previously(5,6). These studies have reported mutations in two unrelated genes-BSC12 (which encodes a protein seipin, whose function is still unknown) and AGPAT2 (which encodes 1-acylglycerol-3-phosphate O-acyltransferase 2)-in patients with CGL belonging to pedigrees linked to human chromosomes 11 q13 and 9q34, thus contributing to the elucidation of mechanisms involved in adipose tissue disorders that results in peripheral insulin resistance, diabetes mellitus and dyslipidemia.

Premature adrenarche has been defined as the appearance of pubic hair and the production of significant quantities of DHEA and DHEAS because of the early maturation of the adrenal zonal reticularis before 8 years of age in girls(7). In this case, the DHEA and

DHEAS levels in her serum were significantly higher than the normal range in her age. These results showed that she had premature adrenarche. The previous study reported that exaggerated premature adrenarche appears to be an early sign of polycystic ovary syndrome (PCOS)(8). Eventually, premature adrenarche may result in an important locus association with the development of irregular menarche cycles, polycystic ovaries and sterility in women with CGL.

The treatment of CGL is not well established. Recent studies have proposed replacement with leptin, a protein produced by the adipose tissue, which has yielded promising results in controlling lipid and carbohydrate metabolic disorders, but the effects were quite limited(9,10). The limited ability to store energy as fat means patients with CGL must maintain a rigid special diet with 4 regular-sized meals each day. In this case, her serum triglyceride concentration decreased after six months of given a special diet characterized by calorie restriction and partial substitution of long-chain triglycerides with medium-chain triglycerides as reported previously(1).

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