Lipodystrophy, Congenital Generalized, Type 1

Alternative Names
CGL1
Berardinelli-Seip Congenital Lipodystrophy, Type 1
BSCL1
Lipodystrophy, Berardinelli-Seip Congenital, Type 1
Brunzell Syndrome, AGPAT2-Related

Record Category
Disease phenotype

WHO-ICD
Endocrine, nutritional and metabolic diseases > Metabolic disorders

Incidence per 100,000 Live Births
2-5

OMIM Number
608594

Mode of Inheritance
Autosomal recessive

Gene Map Locus
9q34.3

Description
Congenital generalized lipodystrophy (CGL; Berardinelli-Seip syndrome) is an autosomal recessive disorder is characterized by the almost complete absence of body fat deposition and is usually evident at birth or during early infancy. In addition, the syndrome often includes the following features: organomegaly, muscle hypertrophy, acanthosis nigricans, hyperandrogenism, hyperlipidemia, and hyperinsulinemia or insulin-resistant diabetes.

The disease has an extremely rare incidence. Estimates indicate an incidence of about 2-3 cases per 1 million live births.

Molecular Genetics
There is evidence that congenital generalized lipodystrophy type 1 is caused by mutations in the gene encoding 1-acylglycerol-3-phosphate O-acyltransferase-2 (AGPAT2).

Epidemiology in the Arab World
Algeria
Van Maldergem et al. (2002) described an Algerian female patient with Berardinelli- Seip congenital lipodystrophy, type 1 (BSCL1) as there was evidence for cosegregation with chromosome 9q. Her parents were consanguineous. Phenotypic evaluation was based on the history, physical examination, and review of medical records. She had delayed onset of BSCL1 that appeared at age of 23 years. Hypertriglyceridaemia, hepatomegaly, hypertrophic cardiomyopathy, and diabetes mellitus were observed in the patient. The patient had normal intelligence. Van Maldergem et al. (2002) found that the origin of BSCL1 patients cold be from sub-Saharan Africa and Maghreb countries and that this type of BSCL occurs in females more than males.

Egypt
Soliman et al. (1995) described the case of a 2-year-old Egyptian female with Seip-Berardinelli Lipodystrophy. The patient showed pubertal LH and FSH responses to GnRH stimulation. Not surprisingly, this patient presented with developed breasts, a large clitoris, and hypertrophied labia [Also see: Oman > Soliman et al., 1995].

Morocco
Van Maldergem et al. (2002) studied two Moroccan females from two consanguineous families with Berardinelli- Seip congenital lipodystrophy, type 1 (BSCL1) as there was evidence for cosegregation with chromosome 9q. Phenotypic evaluation was based on the history, physical examination, and review of medical records. The disease appeared since birth in both females who also presented

hypertriglyceridemia and hepatomegaly with normal intelligence.

Oman

Soliman et al. (1995) did a study on three children diagnosed with Seip-Berardinelli Lipodystrophy (SBLD) to investigate the relationship between their endocrine function (using radio-immunoassay technique) and their growth and sexual maturation. The children had advanced skeletal age, but were not uniformly tall. In addition, the children were normal with respect to their peak growth hormone responses to high dose of clonidine, thyroid function, 8 a.m. serum cortisol levels, as well as hypothalamic pituitary CT scan images. An Omani female (Case 1) presented with delayed sexual maturation, and investigations revealed bone age of 15 years, low serum estradiol concentration, prepubertal response of LH and FSH to gonadotrophin releasing hormone (GnRH) stimulation test, but normal concentrations of prolactin, testosterone, and 24-hr urinary concentrations of 17-ketosteroid. The Omani male patient (Case 2) had glandular hypospadias with chordee, and normal testicular size and consistency. His endocrine evaluation revealed normal testosterone response to human chorionic gonadotrophin stimulation. Soliman and colleagues (1995) were unable to correlate any hormonal abnormality with the advanced skeletal age in these children, and concluded that the growth and sexual maturation in these patients might vary between being either delayed or advanced [Also see: Egypt > Soliman et al., 1995].

Heathcote et al. (2002) identified 16 subjects with congenital generalized lipodystrophy from 11 consanguineous sibships in Oman originating from three different geographical areas (groups A, B, and C). The evaluation of the main clinical and biological characteristics of subjects revealed no obvious differences between subjects in groups A and B, but a variable expression of the disease in group C. Affected individuals in group C had lipodystrophy and muscle hypertrophy as common features but did not show significant developmental delay, acanthosis nigricans, or childhood-onset insulin resistance. In addition, all individuals in group C and none in groups A and B were affected by cardiomegaly and hypertrophic pyloric stenosis. Group C also showed reduced exercise tolerance, percussion myoedema in skeletal muscle (the production of a dimple in the muscle after pressing on the surface), and disturbance of cardiac rhythm and cardiomyopathy. In 2002, Rajab et al. 17 children with congenital generalized lipodystrophy from 12 consanguineous sibships; including those analyzed by Heathcote et al. (2002). All children had widespread absence of adipose tissue from infancy together with apparent muscle hypertrophy and hepatomegaly. They did not appear to represent a single homogenous entity, and it was possible to sub-classify the cases into two distinct groups. In the first group of seven cases, the features were similar to other published cases with acanthosis nigricans, raised insulin levels, and insulin resistance. In this group, there was an association between the degree of acanthosis nigricans and the severity of the disorder. Three years later, Rajab et al. (2005) undertook a study to estimate the prevalence of commonly diagnosed autosomal recessive diseases in Oman from a hospital-based register in years 1993 to 2002. The study revealed that congenital generalized lipodystrophy was diagnosed in 18 patients, with an observed incidence of 1 in 25,000 births.

Palestine

Agarwal et al. (2003) analyzed a consanguineous family from Palestine with congenital generalized lipodystrophy. Of a total of three siblings, a 9-year-old female was homozygous for the disease. The onset of the disease occurred at 6 years of age and the patient also developed diabetes mellitus.

Tunisia

Van Maldergem et al. (2002) described a Tunisian female with Berardinelli- Seip congenital lipodystrophy, type 1 (BSCL1) as there was evidence for cosegregation with chromosome 9q. Her parents were consanguineous. Phenotypic evaluation was based on the history, physical examination, and review of medical records. The disease started at birth in her case. Hypertriglyceridemia and hepatomegaly were observed. The patient had normal intelligence.

United Arab Emirates

Agarwal et al. (2003) analyzed a consanguineous family of African origin from the United Arab Emirates with congenital generalized lipodystrophy. Of a total of seven siblings, a 7-year-old male was homozygous for the disease.

References

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Related CTGA Records

1-@Acylglycerol-3-Phosphate O-Acyltransferase 2
BSCL2 Gene
Diabetes Mellitus, Noninsulin-Dependent
Lipodystrophy, Congenital Generalized Type 2

External Links

http://www.emedicine.com/med/topic3523.htm
http://www.genetests.org/profiles/bscl
http://www.orpha.net/data/patho/GB/uk-berard.pdf

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