

Case Report: Berardinelli-Seip congenital generalized lipodystrophy - A case report and literature review

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Vol. 10, No. 1 (2006-10 - 2006-12)

Curr Pediatr Res 2006; 10 (1 & 2): 41-44

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Key words: congenital generalized lipodystrophy, acanthosis nigricans, acromegaly, insulin resistance

Accepted February 23, 2006

Abstract

Congenital generalized lipodystrophy (GLD) is a rare autosomal recessive disease characterized by near absence of adipose tissue from birth or early infancy and severe insulin resistance.

Since Berardinelli described a very rare case of congenital generalized lipodystrophy, nearly 120 cases have been reported in the literature. We report a case of GLD which, to the best of our knowledge, is the first Saudi child. The earlier case from Saudi Arabia was a Yemeni.

Case report

A 9 month old girl was referred to our clinic for her unusual facial features. This girl was born in another hospital at term after spontaneous vaginal delivery, and postnatal period was reportedly uneventful. She was discharged along with her mother the next day. She remained well throughout except for her unusual facies. The parents are first degree cousins and have another 2 ½ year old normal male child. There is no family history of similar condition.

On examination, she had generalized lipoatrophy with no fat noted or felt over the buttocks and the limbs. She had low anterior hair line, empty cheeks, prominent orbital ridges and large ears (Fig. 1). There was obvious muscular hypertrophy, particularly of the calf and thigh muscles (Fig. 2). The hands and feet were large (Fig. 3) with prominent veins and a hyperpigmented macule was seen over the right upper arm (Fig. 4). She also had cliteromegaly (Fig. 5). There were neither acanthosis nigricans nor hepato splenomegaly. Her growth parameters: Height, Weight & Head circumference at 9 months were 72 cms (50th- 75th centiles), 8 Kgs (25th-50th centiles), 44.5 cms (50th centiles) and at 17 months were 82 cms (75th centiles), 11.3 Kgs (75th centiles), 48 cms (75th – 90th centiles) respectively. Growth parameters at birth were not available. Her parents and a sibling (2 ½ year old male) were examined and found to be normal. Complete ophthalmic examination revealed no abnormality. Her formal developmental assessment (DDST) done at 14 months of age showed gross motor, language and social skills were appropriate for age, while she showed some delay in fine motor skills. The results of radiological and biochemical tests are shown in Table I. These showed high triglyceride levels and very low serum Leptin levels. DNA studies were not feasible.

The differential diagnosis varies from infants to older children. In the infant, one should consider Short syndrome, neonatal progeroid syndrome, Neurometabolic lysosomal storage disorders (Gauchers type2, Krabbe disease) and Russel-Silver diencephalic syndrome. In an older child, the differentiation from Dunningan-lipodystrophy, Rabson-Mendenhall syndrome and Insulin dependent Diabetes Mellitus should be considered [3].

There are major and minor diagnostic features in GLD. The major features include: lipoatrophy affecting trunk and limbs, muscular hypertrophy and secondary phlebomegaly. Empty cheeks may be absent at birth and appear during the first months of life.

1. Acromegaloid features: prognathism, salient orbital ridges, enlarged hands and feet, macrogenitosomia, gigantism and advanced bone age.
2. Hepatomegaly: secondary to fatty liver.
3. Elevated serum concentration of triglycerides, sometimes with hypercholesterolemia.
4. Insulin resistance: elevated serum concentration of insulin and C peptide in the first years of life, overt diabetes mellitus in second decade, acanthosis nigricans of neck, groin and axillae. The minor features include:
 - a. Hypertrophic cardiomyopathy which may be present in infancy or develop later in life.
 - b. psychomotor or mental retardation.
 - c. hirsutism with low frontal and posterior hair lines and hypertrichosis of the trunk.
 - d. precocious puberty in female and
 - e. bone cysts of epiphyseal and metaphyseal re gions which are often diagnosed in second decade

[1].

Fig.1: Empty cheeks, low frontal hairline,prominent orbital ridges and large ears



Fig. 2: Hypertrophied calf and thigh muscles



Fig. 3: Large hands and feet



Fig. 4: Hyperpigmented macule



Fig. 5: Cliteromegaly



Fig.6: Prominent ventricular system and basal subarachnoid cisterns



Table I: Results of Radiological and biochemical tests

Investigation	Results
Skeletal survey Bone age	Normal
Chronological age 9 months 17 months	Bone age 9-10 months 25-26 months
Chest Xray, ECG	Normal
Echocardiography	Normal
Ultrasound Abdomen	Slightly enlarged liver measuring 11.35cms, otherwise normal structures including ovaries
CT Brain	Prominent ventricular system, basal arachnoid cisterns, cistern magna and sylvian fissures
Complete blood count	Normal
Renal function tests	Normal
Serum cholesterol	3.7mmol/l (3.2-6.2)*
Serum Triglycerides	2.26 mmol/l (0.4-2.0)
Seum Insulin	11.73 IU/ml (7-34)
Pituitary hormones	Normal
Thyroid function tests	Normal
Alanine aminotransferase	39 U/l (6-37)
Aspartate aminotransferase	39 U/l (10-31)
Gglutamyl transfere	42 U/l (7-32)

Rest of Liver function tests	Normal
Fasting blood sugar	4.7 mmol/l
HbA1c	5.3% (4.3-5.8)
Serum 17-OH progesterone	Normal
Serum cortisol	Normal
Serum Leptin	0.25 ng/ml (control 18- 37.4)

Reference ranges are shown in brackets

The other features which have been reported in some case reports are: perussion myxoedema, infantile hypertrophic pyloric stenosis, cardiac rhythm disturbance, scoliosis, camptodactyly, dysplastic acetabulum [2] third ventricular dilatation, hypothalamic hamartomas [3], peripheral pulmonary stenosis [4], and sclerotic skeleton [5].

Complications of this syndrome include hypertrophic cardiomyopathy, fatty liver with hepatic dysfunction, endocrine disturbances, bone cysts and spontaneous fractures. Mental retardation is observed in a majority of BSCL2 patients.

The treatment comprises of restriction of total fat intake between 20% and 30%, which is often sufficient to maintain a normal triglycerides serum concentration. Hypercholesterolemia is rarely in the range requiring anticholesterol drugs. Medium chain triglycerides may provide an additional effect and should be used when low fat diet alone is insufficient. The other drugs, including fenfluramine, have no proven efficiency and should be avoided. The patient will have to be followed in a diabetology clinic for possible retinal, peripheral nerve and renal complications once every six months. Cardiac and liver ultrasound need to be repeated every six months. Special education will be required for most BSCL2 patients [1].

Anna Rajab et al had reported genetic heterogeneity in 17 patients with Congenital Generalised Lipodystrophy from Oman [2]. They described a distinct phenotypic subgroup which showed no significant developmental delay, no acanthosis nigricans, no early childhood onset of insulin resistance or hyperlipidemia in preschool age. The height and bone age were advanced in infancy but dropped to below average from second year of life. Except for hyperlipidemia, our patient seems to fit the above mentioned phenotypic subgroup. However the other features of this group, namely pyloric stenosis, premature ventricular contractions, pulmonary artery stenosis, hypertrophy of uterus or urinary bladder and esophageal dysmotility were not seen in our patient.

Acknowledgement

The authors thank Professor M Salih for revising the manuscript.

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