Online Journal of Health and Allied Sciences
Peer Reviewed, Open Access, Free Online Journal
Published Quarterly : Mangalore, South India : ISSN 0972-5997
Volume 9, Issue 4; Oct-Dec 2010

Case Report:
Berardinelli-Seip Syndrome

Sameer I Dal, Assistant Professor,
Hitesh Patel, Resident,
Department of Pediatrics, KT Children Hospital, PDU Medical College, Rajkot - 360 001, Gujarat, India

Address For Correspondence:
Dr. Sameer Dal,
Assistant Professor,
PDU Medical College,
Rajkot – 360 001.
E-mail: dal.sameer@gmail.com

Citation: Dal AI, Patel H. Berardinelli-Seip Syndrome. *Online J Health Allied Scs.* 2010;9(4):28
URL: http://www.ojhas.org/issue36/2010-4-28.htm
Open Access Archives: http://cogprints.org/view/subjects/OJHAS.html and http://openmed.nic.in/view/subjects/ojhas.html

Submitted: Oct 8, 2010; Accepted: Nov 3, 2010; Published: Jan 20, 2011

Abstract:
We have reported two cases of Berardinelli-syndrome in a family which is a rare autosomal recessive disorder of the adipose tissue, originally described by Berardinelli and Seip, has been reported in approximately 120 patients of various ethnic origins. Assuming that only 1 in 4 patients is reported.Patients present with acanthosis nigricans (dark velvety pigmentation of the skin) in the axilla, neck or groin, severe insulin resistance, high levels of serum insulin and serum triglycerides.The other clinical features consist of enlarged hands, feet and prominent mandible (acromegaloid features), increased sweating, umbilical hernia and lytic lesions (bone appear to be eaten-up on X-rays) in long bones of the upper and lower extremities (arms, forearm, hands, thigh, calf, legs and feet) such as humerus, femur, etc. Hepatomegaly from fatty liver is almost universal and may ultimately lead to cirrhosis. Splenomegaly is common. Nearly all patients have a prominent umbilicus or frank umbilical hernia. Females present with enlarged clitoris, increased body hair, absence of or irregular menstrual cycles, and polycystic ovaries (enlarged ovaries). Only a few affected women have had successful pregnancies, whereas affected men have normal fertility.
Key Words: Berardinelli-Siep syndrome; Lipodystrophy

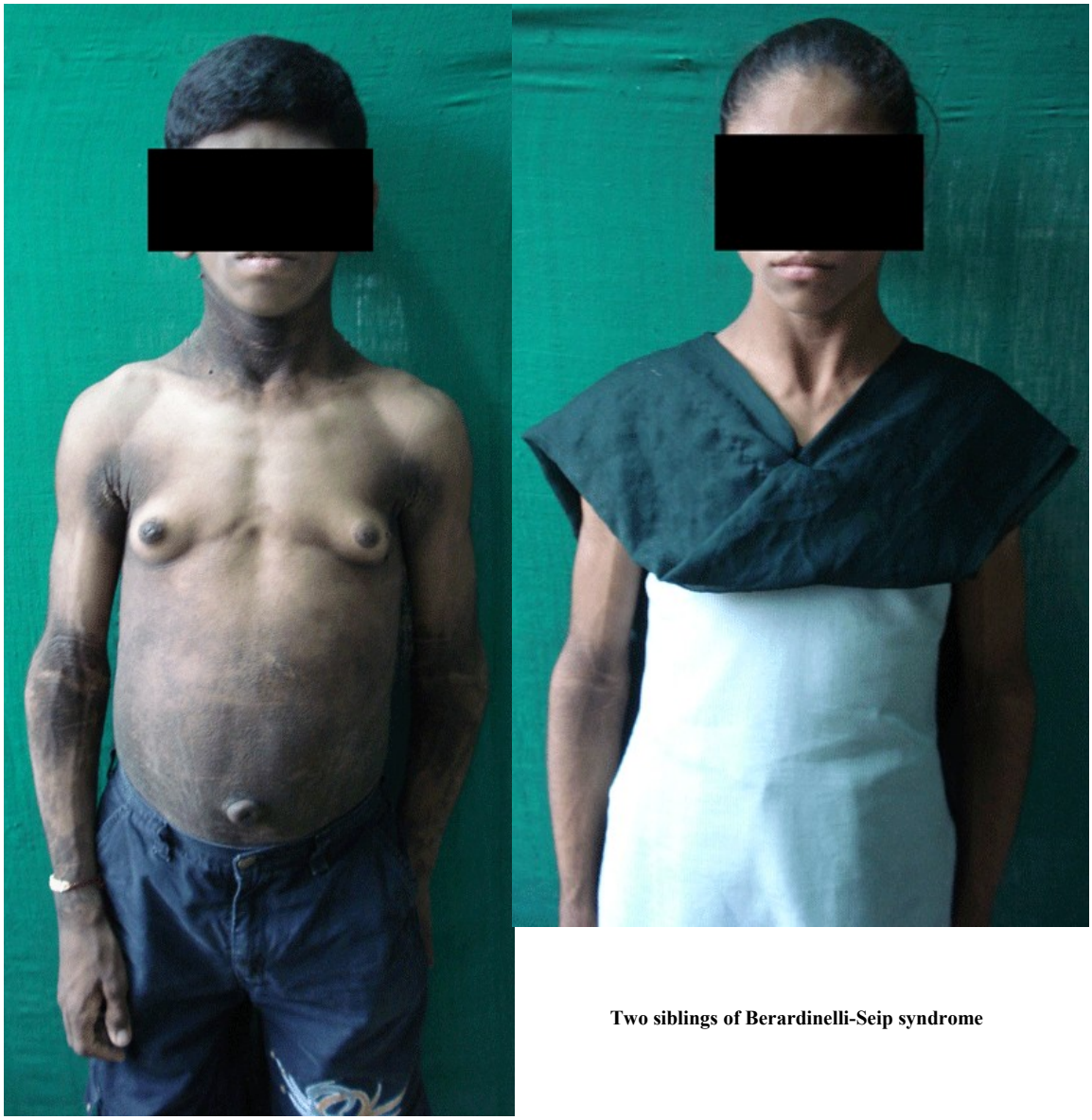
Introduction:
Berardinelli-Seip syndrome or 'Congenital generalized lipodystrophy' is an autosomal recessive disorder characterized by the generalized complete absence of subcutaneous fat and the presence of muscle hypertrophy, hyperlipemia, diabetes mellitus,acanthosis nigricans and hepatosplenomegaly with cirrhosis. Approximately 120 patients of various ethnic backgrounds have been reported.[1]

Case Report:
Two siblings - a 12 year old boy and his 15 year old sister, born out of second degree consanguineous marriage, presented with abnormal facial features and gradually increasing dark discoloration of skin. On examination, the boy had

- Coarse facies
- Large hands and feet
- Generalized loss of subcutaneous fat,prominent musculatures over face and limbs
- Acanthosis nigricans over flexural areas,including neck, axilla, elbow, waist and knee
- Abdominal distension
- Hepatosplenomegaly
- Mild ascites
- Evidence of cirrhotic stigma (Gyneomastia,testicular atrophy and clubbing)
- Biochemical parameters revealed hyperlipidemia(Serum cholesterol 296 mg/dl, triglycerides 172 mg/dl, LDL194 mg/dl, HDL 30 mg/dl)
- Blood glucose was also high (FBS 160mg/dL, PPBS 220mg/dL)
- Ultra sound Abdomen confirmed the cirrhosis & ascites

His sister had similar clinical feature like:

- Generalized loss of subcutaneous fat with muscular prominence
- Adenoid facies with hypertrophied pharyngeal tonsils
- Short stature
- But no evidence of cirrhotic stigma
- Acanthosis nigricans was present,but to a lesser extent
- Blood sugar and lipid profile were also abnormal
- Intelligence Quotient of both were subnormal



Two siblings of Berardinelli-Seip syndrome

Discussion:

Lipodystrophies represent a heterogeneous group of diseases characterized by generalized or partial alterations in body fat development or distribution and insulin resistance. The other cardinal clinical signs of these syndromes are acanthosis nigricans, frequent hypergonadism in females, muscular hypertrophy and liver steatosis.[2] Lipodystrophies are classified as congenital or acquired (depending on origin) and, generalized or partial (based on clinical pattern).

Congenital generalized lipodystrophy (Berardinelli-Seip syndrome) is transmitted as an autosomal recessive trait and is linked to two genetic loci, on chromosomes 9q34 and 11q13. [2,3] Recently, the 11q13 locus has been identified as the BSCL2 gene, encoding seipin, a protein of unknown function mainly expressed in brain.[4]

The pathophysiology of lipodystrophies is still unknown. However, murine models of lipoatrophic diabetes revealed that primary genetic alterations in fat development resulted in diabetes and dyslipidemia.[5] Leptin deficiency, caused by the absence of adiposetissue, could be an important determinant of the metabolic abnormalities since exogenous administration or transgenic overexpression of leptin has been shown to markedly improve insulin sensitivity, glycemic control, dyslipidemia and hepatic steatosis in mice. Similarly, the defect in adinopectin, another fat derived hormone, has recently been shown to be involved in insulin resistance.[6]

Males and females are equally affected and the clinical manifestations are obvious from birth, because of the lack of subcutaneous fat. Fat cells are present but are reduced in number and size, containing little fat. Anabolic features are observed at birth, with enlarged visceral organs. Toddlers may have potentially dangerous hyperplasia of pharyngeal tonsils and adenoids. Lipodystrophies produce a distinctive facies. A well defined musculature with prominent superficial veins is one of the earliest manifestations. Clitoral or penile hypertrophy has been evident at birth, but genitomegaly is not apparent after puberty. The earliest skin manifestations include acanthosis nigricans, eruptive xanthomas and hirsutism. All patients have acanthosis nigricans to some degree.[7]

Acanthosis nigricans can diminish and disappear with puberty and is said to be prominent on the elbows, knees, waist, neck and axilla. Acromegalic gigantism with advanced dentition is an early and constant feature.

The growth rate is most marked in the first 4 years, and these children may attain 90 percent of their adult growth within the first 10 years of their life. Growth subsequently slows and adults are normal or short stature. Females have a masculine habitus with marked muscularity. Liver disease with fatty steatosis and cirrhosis is another constant feature. Hepatosplenomegaly tends to produce a markedly protuberant abdomen.

Diabetes mellitus usually begins in teenage years. The diabetes is insulin resistant and despite poor control ketosis is absent. Hyperlipidemia usually precedes the diabetes. An increased basal metabolic rate is a frequent finding. Intelligence may range from normal to subnormal. Kidneys may be enlarged without apparent histologic cause and renal failure may ensue. Cardiomegaly is frequently observed with muscular hypertrophy and ventricular dysfunction.

Common causes of death renal failure and GI hemorrhage from oesophageal varices in association with hepatic failure.Patients survive into young adulthood or early middle age.

Treatment for acanthosis nigricans can be accomplished with etretinate (beginning at 75 mg/day and increased gradually to 0.5 mg/kg/day after 10-12 weeks).[8] Dietary fish oil may also be useful in acanthosis nigricans.

Substitution of eucaloric medium chain triglycerides for long chain fatty acids can lead to improvement of chylomicronemia, xanthomatosis, hypertriglyceridemia, hepatomegaly, and carbohydrate tolerance hyperinsulinemia, but not lipoatrophy. The limited ability to store energy as fat means patients must maintain a rigid special diet with 4 regular sized meals each day and avoid large meals. Easily digestible carbohydrate should be restricted and dietary fibre is important.[9]

References:

1. Garg A. Lipodystrophies. *Am J Med* 2000;108:143.
2. Janaki VR, Premlatha S, Rao NR, Thambiah AS. Lawrence Seip syndrome. *Br J Dermatol* 1980;103(6):693-696.
3. Garg A, Wilson R, Barnea R et al. A gene for congenital generalized lipodystrophy maps to chromosome 9q34. *J Clin Endocrinol Metab* 1999;84(9):3390-3394.
4. Magre J, Delepine M, Khallouf E et al. Identification of the gene altered in Berardinelli Seip congenital lipodystrophy on chromosome 11q13. *Nat Genet* 2001;28(4):365-370.
5. Van Maldergem L, Magre J, Khallouf E et al. Genotype phenotype relationships in Berardinelli Seip congenital lipodystrophy. *J Med Genet* 2002;39(10):722-733.
6. Bhayana S, Hegele RA. The molecular basis of genetic lipodystrophies. *Clin Biochem* 2002;35(3):171-177.
7. Schwartz RA. Acanthosis nigricans. *J Am Acad Dermatol* 1994;31(1):1-19.
8. Mork NJ, Rajka G, Halse J. Treatment of acanthosis nigricans with etretinate in a patient with generalized lipodystrophy. *Acta Derm Venereol* 1986;66(2):173-174.
9. Seip M, Trygstad O. Generalised lipodystrophy, congenital and acquired. *Acta Paediatr Suppl* 1996;413:2-28.