A rare autosomal recessive syndrome Beredenelli-Seip syndrome in a 14 months old male child is reported who presented with features of voracious appetite, muscular built, acromegalic features, phlebomegaly, enlarged external genitalia and hyperlipidemia.
Case report

A Rare Case Of Beredenelli- Seip Syndrome

Rana S K¹, Singh R², Kumar S²

¹Professor & Head, ²Associate Professors

Department of Pediatrics, SGRR Institute of Medical & Health Sciences, Dehradun-248001

Corresponding Author: Dr S K Rana
Email: drsudhirrana@gmail.com

ABSTRACT

A rare autosomal recessive syndrome Beredenelli-Seip syndrome in a 14 months old male child is reported who presented with features of voracious appetite, muscular build, acromegalic features, phlebomegaly, enlarged external genitalia and hyperlipidemia.

Key words: Congenital Generalized Lipodystrophy, Hypertriglyceridemia, Chromosome 9q34, Chromosome 11q13.

Introduction

Berardinelli - Seip Congenital Generalized Lipodystrophy (BSCL) a rare autosomal recessive inheritance pattern syndrome, characterized by generalized loss of body fat involving face, trunks and limb. It was first described in 1954 by Berardinelli in a 2-year-old Brazilian boy [1] and later by Seip in three patients. [2] There are approximately 250 cases registered all over the world, with greater frequency reported in some ethnic groups, mainly in Latin Americans and Arabians (individuals of Portuguese and Norwegian ancestry). [3] The estimated worldwide prevalence is 1 in 10 million populations. [4]

Clinically this syndrome is characterized by accelerated growth, muscular build, voracious appetite, increased metabolic rate and generalized lack of subcutaneous tissue (only mechanical adipose tissue is spared eg in orbit, palms, buccal region, tongue etc) in early childhood. Hyperinsulinemia, elevated serum triglycerides occur even in infancy along with decreased HDL levels even in early age. At the time of puberty abnormal glucose tolerance and diabetes occurs. Liver may undergo fatty changes and later cirrhosis and oesophageal varices.[5] Atherosclerosis, diabetic nephropathy and retinopathy may occur. An accumulation of fats in the heart can cause hypertrophic cardiomyopathy, which can lead to heart failure and sudden death.
Case Report
Our case was a 14 months old male, child third in birth order, was born to a 30 years old mother without a history of risk factors during antenatal period. Other two siblings were healthy. There was no H/O consanguinity, illness during neonatal or infancy period. Baby presented with features of voracious appetite and thin appearance. Other features included wise old man appearance with frontal bossing, prominent orbital ridge, kinky hair, lack of subcutaneous fat, well developed skeletal musculature, large hands and feet, prominent and tortuous prominent veins all over body, patulous and incompletely prolapsed anus, bilateral inguinal hernia and encysted hydrocele of cord, knobby joints and lumbosacral lordosis. External genitalia were large for the chronological age. Bone age was two years against chronological age of 14 months. Other examination including mental development and neurological examination was normal. There was no acanthosis nigricans, hepatic steatosis or diabetes in our case. [Fig 1,2]

Investigations: Routine blood examination, blood sugar, GTT studies, TSH, GH, S. electrolytes, LFT, RFT, S CPK levels, and S Calcium levels were within normal limits. Lipid profile was abnormal (Total triglyceride level: rose (491 mg/dl, HDL 24 mg/dl, and Cholesterol-117 mg/dl). Echocardiography and CT head and abdomen were within normal limits. Skin biopsy revealed absence of subcutaneous fat and USG of upper limb demonstrated generalized lack of subcutaneous fat. The child was advised to undergo blood insulin assay, karyotyping and hernitomy at higher centre and was discharged with dietary advice & calcium supplementation. Child was subsequently lost to follow up.

Discussion
The signs and symptoms of Berardinelli-Seip Congenital Generalized Lipodystrophy (BSCL) are apparent from birth or early infancy. Three major criteria or two major plus two or more minor criteria make a diagnosis of BSCL likely. Major criteria include lipatrophy affecting the trunk, limbs, and face; acromegaloid features; hepatomegaly; elevated serum triglycerides; and insulin resistance. Minor criteria include hypertrophic cardiomyopathy, psychomotor retardation, hirsutism, precocious puberty in females, bone cysts, and phlebomegaly.[6] In our case, three major criteria of acromegaloid features, generalized lipodystrophy and hypertriglycerideremia and minor criteria of phlebomegaly were met. The other features which have been reported in some case reports are: percussion myxoedema, infantile hypertrophic pyloric stenosis, cardiac rhythm disturbance, scoliosis, camptodactyly, dysplastic acetabulum [7] third ventricular dilatation, hypothalamic hamartomas [8], peripheral pulmonary stenosis [9], and sclerotic skeleton [10].

The basic defect in BSCL is in the 1-acylglycerol-3-phosphate-O-acyltransferase-2 (AGPAT2) gene on chromosome 9q34 in the type 1 variant and in the BSCL2 gene on chromosome 11q13 in the type 2 variant. [11]

The pathophysiology of lipodystrophies is still unknown. However, murine models of lipotrophic diabetes revealed that primary genetic alterations in fat development resulted in diabetes and dyslipidemia. Leptin deficiency, caused by the absence of adipose tissue, 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 adiponectin, 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. Berardinelli-Seip congenital lipodystrophy cases have a distinctive physical appearance. The combination of an almost total absence of adipose tissue and an overgrowth of muscle tissue makes these individuals appear very muscular. They also tend to have a large chin, prominent orbital ridges, and large hands and feet. Affected females may have clitoromegaly, and males also tend to have enlarged external genitalia. Many people with this disorder develop acanthosis nigricans which causes the skin in body folds and creases to become thick, dark, and velvety.

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 should 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 [12].

Source of drugs: Nil
Funding: Nil
Acknowledgement: Nil
Conflict of interest: Nil.

6.
References:

8. Photographs

Fig 1.
**Fig 2**: 14 months old male child with acromegalic appearance of face, hand and feet, prominent orbital ridge, kinky hair, generalized lack of subcutaneous fat, well developed skeletal musculature, large hands and feet, prominent and tortuous prominent veins all over body and enlarged external genitalia for age.