Doi: 10.32677/IJCR.2015.v01.i01.006 **Case report**

Berardinelli - Seip Congenital Lipodystrophy - An infantile presentation

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ABSTRACT

Berardinelli – Seip congenital lipodystrophy (BSCL) is an inherited form of generalized lipodystrophy characterized by loss of subcutaneous fat, hypertriglyceridemia, insulin resistance and acanthosis nigricans. Rare cases of BSCL type 2 present during infancy or early childhood. It is caused by mutation in Seipin gene. It is a severe phenotype with premature death occurring in 15% cases. We present such a rare case of BSCL in a five month old infant.

Key words: *Hypertriglyceridemia, Insulin resistance, Lipodystrophy, Phlebomegaly*

Berardinelli - Seip congenital lipodystrophy (BSCL) is an autosomal recessive disorder characterized by generalized complete absence of subcutaneous fat and the presence of muscle hypertrophy, hyperlipidemia, diabetes mellitus, acanthosis nigricans and hepatosplenomegaly with cirrhosis. Approximately 300 patients have been registered in various ethnic origins [1]. BSCL has been classified into 3 groups which are BSCL1, BSCL2 and BSCLX. BSCL 1 is due to defective 1-acylglycerol-3-phosphate-O-Acyltransferase-2 (AGPAT) gene on chromosome 9q34 where as in BSCL2 the gene involved is Seipin gene located on chromosome 11q13. BSCLX doesn't show evidence of either mutation. In all forms of congenital generalized lipodystrophy, there is complete absence of subcutaneous fat and abnormal fat storage in muscle and liver with various metabolic problems. The estimated prevalence of this rare disease is 0.25 in 100,000 populations and only 12 cases of BSCL have been reported in India [2].

CASE REPORT

A five month old male baby (figure 1) born out of 2nd degree consanguinous marriage presented with enlarged stubby hands and feet, abdominal distension and absence of fat pad affecting face, trunk and limbs since birth. There was no history of feeding intolerance, vomiting, loose motions convulsions His antenatal, natal and postnatal history was non-contributory with no significant family history. He was exclusive breast fed till date and was accepting feeds well. On examination, baby was conscious, active and stable vital signs. On general examination, he had coarse facies, enlarged prominent veins all over his body (figure 2), and yellowish nodules over knee, and elbow. On systemic examination, he had hepatosplenomegaly while rest of the systemic examination was non-significant.

His routine laboratory investigations including complete blood count, C reactive protein, serum electrolytes, and renal and liver function tests were within normal limits. His fasting blood sugar was high (225 mg/dl). His total serum protein was elevated (10.08 gm/dl), and serum albumin was 4.08 gm/dl. Yellowish nodules over the body were suggestive of xanthoma; therefore, his serum lipid profile was sent. His serum was milky white with elevated triglyceride (TG) levels (figure 3). Serum TG was 1845 mg/dl, serum cholesterol was 148 mg/dl, LDL cholesterol was 88 mg/dl, and total cholesterol to HDL cholesterol ratio - 7.4. Investigations done to

establish the cause of hyperglycemia showed high serum insulin level (14.12 μIU/ml), and HbA1C (15.7%). Ultrasonography of abdomen revealed fatty liver, and chest X-ray was showing cardiomegaly with CT ratio 62%; however, echocardiography revealed no structural abnormality.

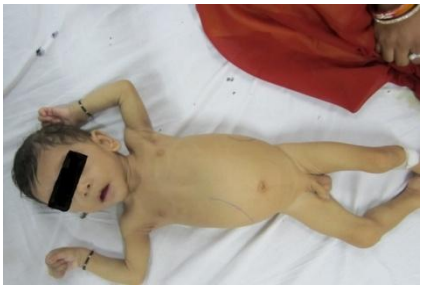

Figure 1 - Distended abdomen with loss of buccal fat pad and course facies

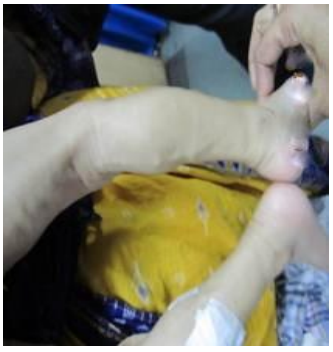

Figure 2 - prominent superficial veins over lower limbs

Figure 3 - milky white serum compared with normal serum

Biopsy of nodules over knee was done and sent for histopathological examination which was suggestive of xanthoma. X-ray of limbs did not show presence of bone cysts. Genetic diagnosis could not be done in this patient due to non-availability of this facility in our set up. Since, he had three of the major criteria; he was diagnosed with BSCL and as the clinical presentation was during infancy with more severe form it was presumed to be type 2 BSCL.

DISCUSSION

Clinical presentation of our patient was consistent with Berardinelli – Seip Congenital lipodystrophy - 2 variety; although, diagnosis could not be confirmed by genetic analysis. BSCL type 2 is a rare autosomal recessive disorder caused by mutation in the Seipin gene which equally affects males and females. BSCL 1 is a less severe form and can present between 2nd and 3rd decade where as BSCL2 presents in neonatal period, infancy and early childhood. Major criteria for diagnosis of BSCL are lipoatrophy, acromegaloid features, hepatomegaly, elevated serum triglycerides, and insulin resistance. Minor criteria are hypertrophic cardiomyopathy, psychomotor retardation, hirsuitism, precocious puberty and bone cysts. Diagnosis requires presence of three major criteria or two major and two minor criteria to be fulfilled [3].

The BSCL-2 locus (Seipin gene) is identified within 2.5 Mb interval flanked by markers D11S4076 and D11S4080 on chromosome 11q13 [1]. Seipin gene plays a role in lipid droplet formation and adipocyte differentiation [4]. Marked lipodystrophy occurs at birth or early infancy [5]. Lipodystrophies produce distinctive facies and a well defined musculature with prominent superficial veins (phlebomegaly) is one of the earliest manifestations. Anabolic features are observed at birth with enlarged visceral organs. Even toddlers have hyperplasia of pharyngeal tonsils and adenoids. Later during childhood, acanthosis nigricans develop on extensive areas of skin most prominently on elbows, knees, waist, neck and axilla and can diminish or disappear during puberty [4]. Other skin manifestations are eruptive xanthoma and hirsuitism.

Only few patients develop diabetes during infancy but most often diabetes develops during teenage year. Hyperlipidemia usually precedes diabetes in these patients and diabetes is usually insulin resistant and ketosis is absent despite poor control. Other features are enlarged hands, feet and prominent mandible (acromegaloid features). Lytic lesions may present in long bones of upper and lower extremities [6]. Congenital generalized

lipodystrophy with lytic lesions in bone is also termed as Brunzell Syndrome. Females present with enlarged clitoris, increased body hair, absence of or irregular menstrual cycles and polycystic ovaries. Mental subnormality and low IQ commonly is seen more commonly in BSCL type 2 variant than in BSCL1. Cardiomegaly is frequently observed with muscular hypertrophy and arterial hypertension [7].

Treatment of acanthosis nigricans is done by Etretinate. Dietary fish oil is also useful [8]. Use of medium chain triglyceride can result in improving hypertriglyceridemia, hepatomegaly and insulin resistance. But it has no effect on lipoatrophy. Fibre content of diet should be higher and easily digestible carbohydrates should be restricted [9]. Patients should be provided with rigid meal schedule as they have limited ability to store energy. Leptin replacement can reverse metabolic complications in majority of the children with BSCL and with insulin resistance or dyslipidemia before development of overt diabetes [10]. Patients can survive upto young adulthood or early middle age. Common causes of death are renal failure, upper GI bleeding due to esophageal varices resulting from hepatic failure [11].

CONCLUSION

BSCL type 2 is an adipose tissue disorder characterized by abnormal fat distribution with metabolic problems. Patients with this condition should be regularly followed up and monitored for metabolic derangements. During follow up visits, tanner's staging, neurological, endocrinological, cardiovascular, ophthalmologic and orthopedic evaluation should be done. Patients should consume low fat diet and regular physical exercise should be encouraged to postpone metabolic problems.

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