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Case Report

Acquired generalized lipodystrophy type 2-lawrence syndrome: a rare case report

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ABSTRACT

Lawrence syndrome (Acquired Generalized Lipodystrophy) is a rare disorder, characterized by various dermatological and systemic manifestations such as lipodystrophy, hypertriglyceridemia, hepatomegaly, acanthosis nigricans and acromegaloid features. Because of its rare occurrence we are reporting a case with similar manifestations in a 10 years old child.

Keywords: Acquired generalized lipodystrophy, Autoimmune hepatitis, Diabetes, Hyperglycemia, Lawrence syndrome, Leptins, Partial dystrophy

INTRODUCTION

Acquired Generalized Lipodystrophy (AGL) is characterized by selective loss of adipose tissue from large regions of the body that develops during childhood and adolescence associated with metabolic disturbances.[1] Ziegler originally described AGL in 1928 in an 11 years old girl. In 1946, Lawrence provided a detailed description and proposed '5 major diagnostic criteria' for the disease.[2]

CASE REPORT

A 10 years old hailing from West Bengal, male child, born out of non-consanguineous marriage, apparently alright till 8 years of age, presented with yellowish discoloration of eyes and skin, associated with abdominal pain for the past 20 days. Complaints of pain noted in the ankle region during walking. Also, complaints of voracious appetite since 1 year and loss of weight noted. There was no weight gain, but weight loss in spite of voracious appetite for the past 1 year. He also gave the history of jaundice 1 year ago, lasted for 20 days. The patient's vitals at the time of admission were temperature-afebrile, pulse-80/min, blood pressure 96/60 mmHg (100/70 mmHg) anthropometric measurements showed weight-21.5 kg (52.5% of expected), height-131cm (<150 cm) and Body Mass Index 12.54 kg/m^2 (Figure 1 and 2).

There was generalized loss of subcutaneous fat all over the body with prominent muscles and veins, giving masculine habitus all over the body except abdomen. Eyes, malar bones and ears appeared prominent. Icterus was present in the sclera, mucosa and skin. (Figure 3, 4 and 5) Acanthosis nigricans was observed in the axillae bilaterally. Abdomen was prominent with hepatomegaly of 12 cms, consistency being firm in nature. Laboratory examination revealed complete blood count, urine routine-microscopic examination and renal function test was within normal limit. Erythrocyte Sedimentation Rate-80 mm/1 hour, Fasting Blood Sugar- 101 mg/dl (70-110), Post prandial (2 hour) Blood Sugar- 180 mg/dl (126-140), Serum Fasting Insulin-110.93 mIU/L (2.6-11.1). Liver function test shows Serum total /direct bilirubin = 3.6/1.5 mg/dl Serum Alkaline phosphatase-626 IU/L(80-360), Serum Alanine Transaminase- 820 IU/L (up to55), Serum AST- 753 IU/L,

Serum Albumin-3.4 gm/dl (>3.5 gm/dl), GGT- 205 (12-43). HbA1C- 4.5%.

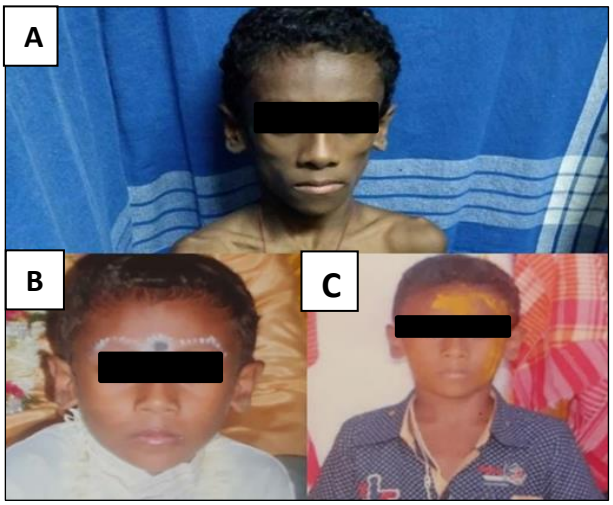

Figure 1: Clinical photographs of the patient. (A) Shows the face of the patient at 10 years of age revealing the loss of subcutaneous fat in cheeks. Prominent veins over the forehead, (B) Face of the patient at 3 years, (C) Face at 8 years denoting normal development and no loss of sub cutaneous fat.

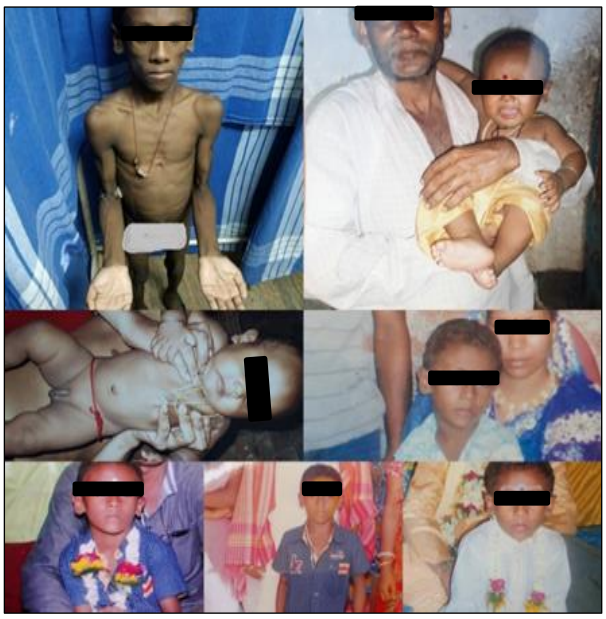

Figure 2: Clinical photographs of the patient at various age groups shows the severe progression of the disease over the years in form of generalized loss of subcutaneous fat.

Childhood pictures of the patient demonstrate that there is no loss of subcutaneous fat in the early ages denoting the acquired nature and the slow progression of the disease.

Lipid profile revealed Total cholesterol- 175 mg dl, serum Triglyceride- 450 mg/dl (50-150), Serum High Density Lipoprotein 18 mg/dl (>55), Serum Low Density Lipoprotein- 110 mg/dl (60-150), Serum Very Low-Density Lipoprotein- 95 mg/dl (up to30). Thyroid function test normal.

Figure 3: Lateral of the patient masculine habitus with prominent muscles and superficial veins acanthosis, nigricans.

Rheumatoid factor, Serum HIV, Serum Hepatitis B Surface Antigen, HCV, HAV, ANA profile were negative. Wilson workup negative. LKM antibodies- 72 (>45) highly positive.

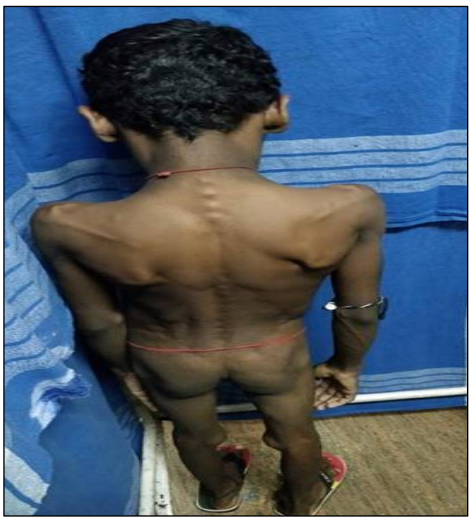

Figure 4: Back of the patient masculine habitus with prominent muscles and superficial veins acanthosis, nigricans.

Abdominal ultrasound (Figure 6) showed mild hepatomegaly (16 cm), with diffusely altered echo texture. Chest X-ray revealed no abnormality. Liver biopsy done which confirmed the presence of steatohepatitis with the features of macro vesicular steatosis, and Grade 2 hepatocellular ballooning.

During the hospital stay, the patient developed persistent hyperglycaemia episodes. The patient was started on Atorvastatin (20 mg) and Metformin (500 mg), and paediatric endocrinologist opinion taken. Advised to start steroids Prednisolone (40 mg) for 2weeks, tapering dose and 5 mg OD to continue, along with Azathioprine 25 mg for 2 weeks followed by 40 mg to continue.

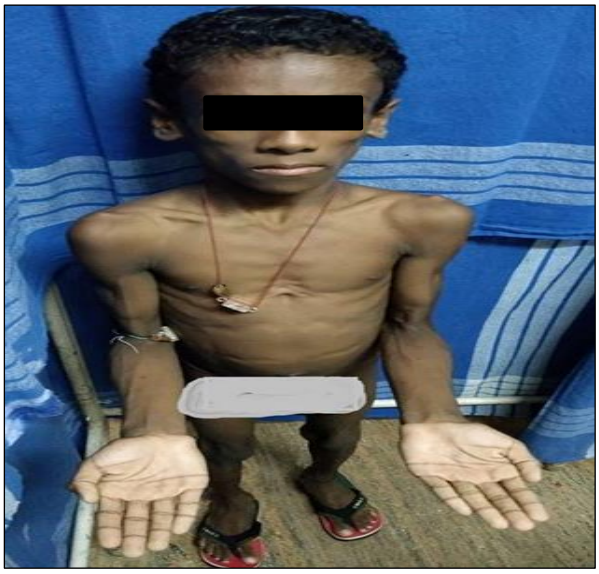

Figure 5: Front view of the patient masculine habitus with prominent muscles and superficial veins acanthosis, nigricans.

Patient was also advised LEPTIN protocol 0.06 mg/kg sc followed by 0.02 mg/kg sc. This patient could not avail benefit of leptin therapy (not available in India), so author had option of only steroids, metformin and immunomodulators to treat this patient.

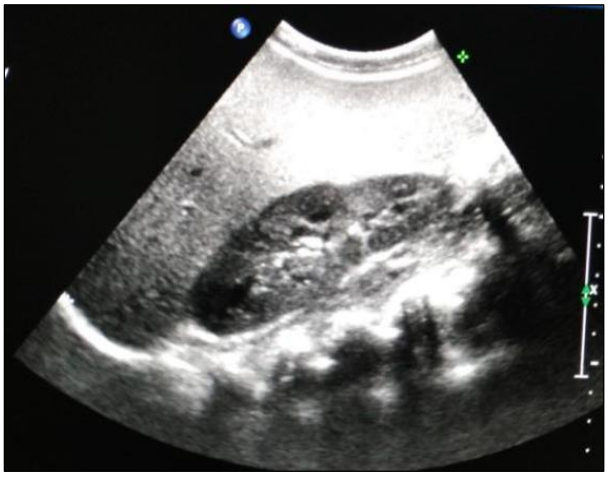

Figure 6: USG abdomen shows mild hepatomegaly.

DISCUSSION

About 50 cases of AGL have been reported in the literature since 1946, when Lawrence first described this syndrome.[3] Typical findings include extreme paucity of subcutaneous adipose tissue, insulin resistance accompanied by hyperinsulinemia, and diabetes mellitus. A mostly mild anabolic syndrome might occur, depending on the onset of the disease. However, most clinical features of AGL are common to the more frequent CGL, but the acquired form presents a different clinical course and pathophysiologic triggering events.[4]

Lawrence-Seip Syndrome is a lipodystrophy disorder in which autoimmune disease, viral/ bacterial infections and panniculitis are suspected to be the etiological antecedent suggesting immunologically mediated fat cell lysis leading secondary compensatory metabolic changes via the hypothalamic-pituitary dysfunction.

Criteria for diagnosing the Lawrence syndrome[5]

Essential criteria

Selective loss fat involving large regions of the body beginning during childhood or adolescence.

Supportive criteria

Clinical loss of subcutaneous fat from palms and soles, acanthosis nigricans, hepato-splenomegaly, panniculitis prior to onset associated autoimmune disease.

Laboratory of diabetes Mellitus/ Impaired Glucose tolerance, severe hyperinsulinemia (fasting and postprandial), increase serum triglyceride and/or decreased HDL, reduced S. Leptin and/or adiponectin level, anthropometric or MRI evidence of large region of fat loss, MRI evidence of preserved bone marrow fat. The disease usually begins insidiously over months to years in childhood and adolescence, rarely after 30 years of age.[5,6] Rarely, loss of fat can occur rapidly from one part of the body, followed by quiescent phase for several months or years and reactivate to involve rest of the body. Thus, some patients diagnosed initially as localized or partial lipodystrophy subsequently may develop generalized loss of subcutaneous fat leading to the diagnosis of AGL.[7]

There is lack of Bichat's fat pad(Empty cheek sign) in the preauricular region, resulting in cadaveric facies, total absence of subcutaneous fat and other metabolically active adipose tissue, preservation of fat deposits in 'mechanical' sites-orbit, palms, soles, tongue, breast, vulva, periarticular and epidural region.[8]

Acanthosis nigricans begins in childhood involving the neck, axillae, groin, umbilicus, and nipples.[9] There may be localized or generalized hyperpigmentation, mild hirsutism, and occasional alopecia.[10] Muscular hypertrophy with prominent superficial veins, acromegalic facial and acral features, voracious appetite, increased basal metabolic rate, heat intolerance, osteosclerotic and lytic skeletal changes, masculine features in female.[11]

Metabolic syndrome is less severe than with CGL, in contrast to liver sequelae, which are often lethal.[12] Insulin resistant Diabetes Mellitus shows severe fasting and postprandial hyperinsulinemia, impaired glucose tolerance, hypertriglyceridemia and sequelae chylomicronemia, pancreatitis, hyperlipidemia, low HDL cholesterol levels, low plasma Leptin levels.[13] True or pseudo clitoromegaly, polycystic ovarian syndrome, menstrual irregularities may be seen. Premature coronary artery or carotid or peripheral vascular disease may be seen.[14]

Renal and CNS abnormalities are usually absent. Hepatomegaly is commonly observed in patients with elevation of serum transaminases due to hepatic steatosis or non-alcoholic steatohepatitis.[15] Some patients may develop cirrhosis with portal hypertension and oesophageal varices, moderate to massive splenomegaly.

Subtypes[16]

Type 1: AGL with panniculitis,
Type 2: AGL with Autoimmune Disease
Type 3: Idiopathic AGL

In this patient, onset of symptoms was at the age of 8 years and absent family history of similar complaints rules out congenital or familial lipodystrophy. Normal renal function tests rule out Barraquer-Simons syndrome. Bilateral presentation rules out Poland's syndrome. Absence of muscle wasting, sclerodermatous changes, cataracts and other signs of premature aging rules out Progeria-type syndromes. Cockayne syndrome was ruled out because of absence of growth delay, retinal abnormalities and photosensitivity. Association of DM, hepatitis and AGL can be explained by the autoimmune basis. This case belonged to type 2. This patient presented with generalized loss of subcutaneous fat, acanthosis nigricans, prominent subcutaneous veins, protuberant abdomen and hepatosplenomegaly; hyperglycemia, jaundice; with raised serum transaminases, raised serum fasting insulin, hypertriglyceridemia, hyperlipidemia and low HDL cholesterol levels.

Low fat diet should be recommended.[17] Fibrates are efficacious in lowering serum triglycerides levels, used alone or in combination with low-dose statins.[18,19] A new option for therapy is Leptin, an adipocyte hormone.[20,21] Metreleptin (recombinant leptin) treatment of 51 children with lipodystrophies with low leptin levels, a significant improvement was noted in all glycemic control, triglyceride levels, steatohepatitis markers, etc., over 1-year treatment period and effects of treatment continued over 5 years of therapy.[22]

CONCLUSION

This report shows an uncommon case in which AGL is accompanied by autoimmune hepatitis and diabetes mellitus. The insufficient adipose tissue mass leads to excess energy storage in ectopic fat storage organs that finally results in insulin resistance and diabetes.

Coexistence of AGL and diabetes mellitus, although very rare, presents as a totally different disease phenotype. Two conditions in combination can pose significant treatment challenge with regard to both the glycaemic control and the dyslipidaemia. In the absence of metreleptin therapy, a combination of drugs including insulin, metformin, pioglitazone, statins and fibrates could be required at various stages of disease course.

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