Lawrence-Seip Syndrome: A rare case report

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Abstract:
Lawrence-Seip syndrome (Acquired Generalised 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.

Key words: Lawrence-Seip syndrome, Acquired Generalised Lipodystrophy, hypertriglyceridemia, acanthosis nigricans.

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 mentally sluggish (IQ-82, Borderline) male child, born out of non-consanguineous marriage, apparently alright till 9 years of age, presented with progressive loss of fat from face, chest, upper back and both extremities, difficulty to seat in squatting position and voracious appetite since 1 year.

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The patient’s vitals at presentation were temperature-afebrile, pulse-80/min, blood pressure 96/60 mmHg (100/70 mmHg) anthropometric measurements showed weight-21 kg (52.5% of expected), height-135 cm (>150 cm) less than arm span-136 cm (same as height), abdominal circumference-58cm (appropriate for age) and Body Mass Index 11.53 kg/m2. Whole body examination showed prominent eyeballs and malar eminence, sunken cheeks, large ears, recessed chin, beak-like nose, over-crowded teeth and hypertrichosis over face, giving gaunt appearance; presence of prominent muscles and subcutaneous veins giving masculine habitus all over body; acanthosis nigricans over both axillae, cubital fossae, popliteal fossae with mottled pigmentation bilaterally symmetrical over neck, axillae, cubital fossae, groin, popliteal fossae and trunk; pot belly with mild hepatomegaly (2cm below the right costal margin). Laboratory examination revealed complete blood count, urine routine-microscopic examination and renal function test was within normal limit. Erythrocyte Sedimentation Rate-14 mm/1st hr, Fasting Blood Sugar- 101 mg/dl (70-110), Post prandial (2hr) Blood Sugar- 118 mg/dl
(126-140), Serum Fasting Insulin-176.93 mIU/L (2.6-11.1). Serum biochemistry profile revealed liver function test was within normal limit except Serum Alkaline phosphatase-626 IU/L(80-360), Serum Alanine Transaminase-157 IU/L (upto55), Serum Albumin-2.89 gm/dl (>3.5 gm/dl). Lipid profile revealed serum Triglyceride-1617 mg/dl (50-150), Serum High Density Lipoprotein 20 mg/dl (>55), Serum Low Density Lipoprotein-169 mg/dl (60-150), Serum Very low Density Lipoprotein-323.4 mg/dl (upto30). Thyroid function test revealed T3-213.9 ng/dl (104-190), T4-9.295 microg/dl (4.5-12.5), TSH-3.186 mIU/l(0.5-4.3). Anti Streptolysin-O Titre and C-Reactive Protein were positive and Rheumatoid factor, Serum HIV, Serum Hepatitis B surface Antigen were negative. Abdominal ultrasound showed mild hepatomegaly(18cm). Chest X-ray revealed no abnormality.

**FIGURE-1(a):** Face at 9 yrs of age  
**FIGURE-1(b):** Face at 10 yrs of age, showing sunken cheeks and hypertrichosis giving gaunt appearance  
**FIGURE 2:** Masculine habitus with prominent muscles and superficial veins, acanthosis nigricans with mottled pigmentation over neck, axillae and cubital fossae, protruberant abdomen

**FIGURE 3:** USG Abdomen shows mild hepatomegaly (18cm)

**FIGURE 4:** Histopathology of acanthosis nigricans showing basket wave appearance hyperkeratosis and papillomatous projection of dermis
Histopathological examination from cubital fossa was suggestive of acanthosis nigricans. The patient was started on Atorvastatin (20mg) and Metformin (500mg), and is under regular follow up and treatment of Endocrinologist, Paediatrician and Dermatologist. **Discussion:** 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-Seip syndrome**³.

**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, hepatosplenomegaly, panniculitis prior to onset, associated autoimmune disease.

**Laboratory**:
- Diabetes Mellitus/ Impaired Glucose tolerance, severe hyperinsulinemia (fasting and postprandial), increase serum triglyceride &/or decreased HDL, reduced S. Leptin &/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. 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. 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. Acanthosis nigricans begins in childhood involving the neck, axillae, groin, umbilicus, and nipples. There may be localized or generalized hyperpigmentation, eruptive xanthoma, telangiectasias, mild palmoplantar keratoderma, curly hair, mild hirsutism, and occasional alopecia. Muscular hypertrophy with prominent superficial veins, acromegalic facial and acral features, voracious appetite, increased basal metabolic rate, heat intolerance, accelerated growth, advanced bone and dental age, osteosclerotic and lytic skeletal changes, masculine features in female. Metabolic syndrome is less severe than with CGL, in contrast to liver sequelae, which are often lethal. 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 levels⁴. True or pseudo clitoromegaly, polycystic ovarian syndrome, menstrual irregularities may be seen. Premature coronary artery or carotid or peripheral vascular disease may be seen. 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. Some patients may develop cirrhosis with portal hypertension and esophageal varices, moderate to massive splenomegaly. **Subtypes:** Type 1: AGL with panniculitis, Type 2: AGL with Autoimmune Disease, Type 3: Idiopathic AGL. In our patients, onset of symptoms was at the age of 9 yrs and absent family history of similar complaints rules out congenital or familial lipodystrophy. Normal renal function tests rules 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.
Absence of history of intolerance to heat or increased sweating, any painful nodules, joint pain, photosensitivity, muscle pain, muscle weakness favors the diagnosis of type 3 AGL (idiopathic). Our patient presented with generalized loss of subcutaneous fat, prominent thigh muscles, acanthosis nigricans, generalized hyperpigmentation, prominent subcutaneous veins, protuberant abdomen and hepatosplenomegaly; with raised serum transaminases, raised serum fasting insulin, hypertriglyceridemia, hyperlipidemia and low HDL cholesterol levels. Low fat diet should be recommended. Fibrates are efficacious in lowering serum triglycerides levels, used alone or in combination with low-dose statins. A new option for therapy is Leptin, an adipocyte hormone, which may improve insulin resistance, hyperglycemia, dyslipidemia and hepatic steatosis. Our patient was started on Atorvastatin (20mg) and Metformin (500mg) once a day with strict dietary fat restriction, and is under regular follow up and treatment of Endocrinologist, Paediatrician and Dermatologist.

References: