Effect of 6 months therapy with Metreleptin in an African American boy with Congenital generalized lipodystrophy.

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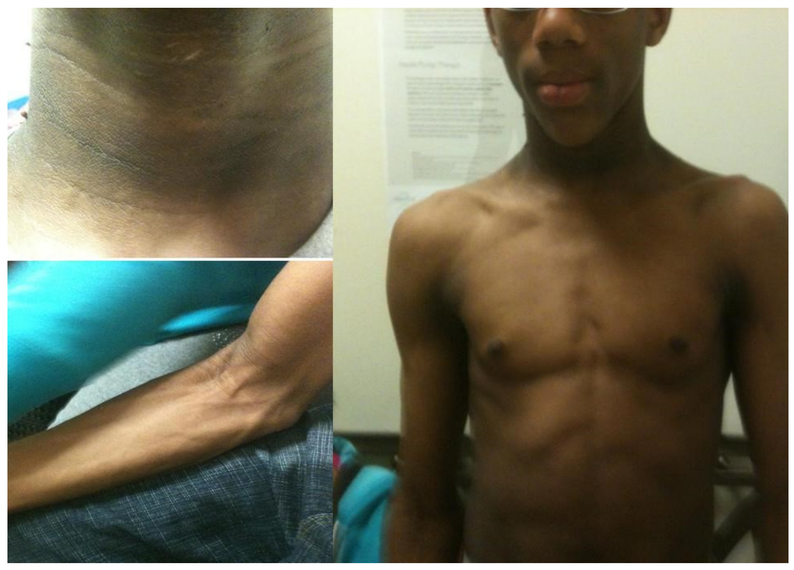
Background:

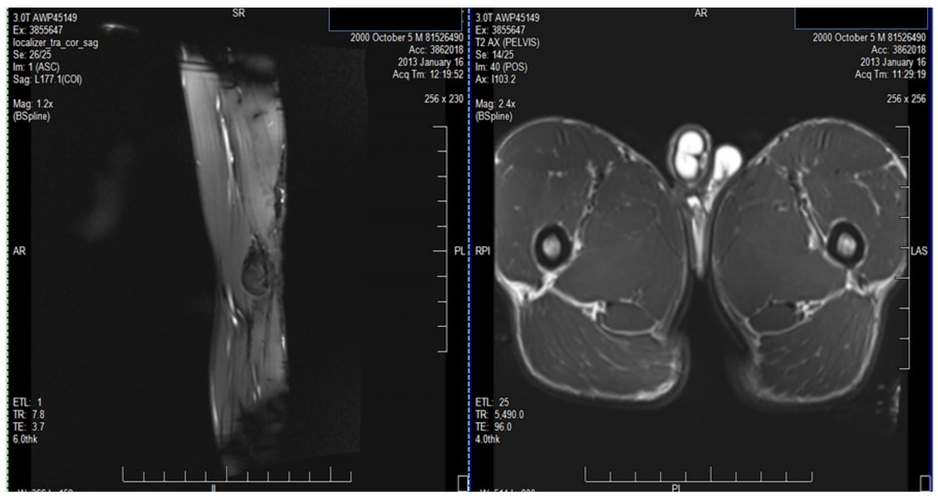
Congenital generalized lipodystrophy (CGL) is a rare autosomal recessive disorder which presents with near total lack of adipose tissue and extreme insulin resistant diabetes. Metreleptin, an analog of leptin was made through recombinant DNA technology. It was approved to treat CGL in February 2014.Our case represent successful use of Metreleptin in a child with diabetes developed secondary to CGL.

Case Presentation

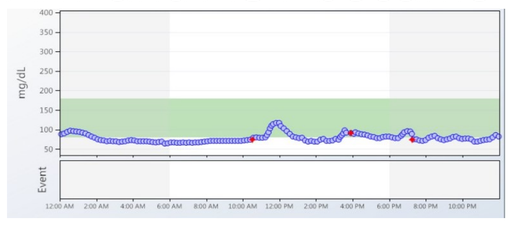
A 14-yr-old African-American boy was referred for evaluation of insulin dependent diabetes at 11 yr. of age. He was diagnosed with diabetes at 9 yr of age. Clinically, he was noted to have significant acanthosis nigricans, muscular extremities, acromegaloid features of the face and normal intellectual development. His BMI 23.2 kg/m^2 and blood pressure were normal.



Leptin level was low at 0.5 ng/ml (Nl. 1.4-16.5), Triglycerides (TG), ALT, AST were elevated and Hemoglobin A1c was 14.7%. Islet cell antibodies were negative. *AGPAT2* gene analysis revealed homozygous c.IVS4-2A>G mutation.
MRI revealed generalized muscle hypertrophy with markedly decreased subcutaneous and intra-abdominal fat, periarticular and intramedullary lytic bone lesions, and hepatomegaly.



Treatment with high doses of insulin up to 3 u/kg/day with addition of metformin was unsuccessful. After starting Metreleptin treatment within 1 month we were able to stop insulin therapy. At first it was necessary to increase Metreleptin dose from 2.5 mg to 10 mg daily but within 2 months of therapy dose was decreased to 1.5 mg daily and without any other medications his glucose levels became normal. HbA1c improved from 11 to 5.9% after 6 months of therapy. His TG, ALT and AST became normal as well.



	Reference value	2012 At the time of Insulin therapy 200 Units daily	2014 Before Leptin	2015 After 6 months of Leptin therapy
Glucose fasting mg/dl	65-99	328	235	119
C-peptide ng/ml	0.8-3.1	7.06	0.92	4.08
Hb A1c %	>6.5	14.7	11	5.9
Leptin ng/ml	1.4-16.5	0.5	1.3	1.3
AST U/L	12-32	34	19	28
ALT U/L	6-19	36	19	25
Cholesterol mg/dl	125-170	110	111	91
HDL mg/dl	35-75	36	41	41
LDL mg/dl	< 110	25	29	43
Triglycerides mg/dl	36-135	238	204	36

Conclusion

Diabetes secondary to congenital generalized lipodystrophy can be misdiagnosed in children as type 1 diabetes. Clinical keys were acanthosis nigricans and acromegalic facial features and muscular extremities. Metreleptin therapy may dramatically improve the metabolic complications in patients with CGL.

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