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Cintya Schweisberger

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Metreleptin and Metformin Use in an Infant with Congenital Generalized Lipodystrophy Secondary to AGPAT2 Mutation

Cintya Schweisberger, DO; Jill Jacobson, MD; Emily Paprocki, DO

Children's Mercy Kansas City

Background

- Congenital Generalized Lipodystrophy (CGL) is characterized by widespread fat loss and severe metabolic abnormalities ⁽¹⁾
- Metreleptin, a synthetic leptin analog, is shown to decrease fasting triglycerides, fasting glucose, and HbA1c ⁽²⁾
- Metformin use in infants has only been described in a few case reports of CGL and Donohue syndrome ⁽³⁾ (insulin receptor mutation), and there is no established dosing for this age group

Case

- 2-month-old SGA term female was noted to have poor weight gain, hyperphagia, and abdominal distension at a well child check
- She was admitted for failure to thrive with weight z-score of -2.17 and length z-score of -0.15
- Initial labs were notable for triglycerides 5,167 mg/dL, blood glucose 324 mg/dL, ALT 212 units/L, AST 215 units/L, elevated random insulin level of 257 mIU/mL, and HbA1c 8.9% (Table 1)

Clinical Course

- Day 1: Started on detemir 1.0 units/kg/day (titrated to a maximum dose of 4.4 units/kg/day)
- Day 3: Started on metformin suspension 50 mg/kg/day
- Day 4: Triglycerides, glucoses, and LFTs decreased (Table 1)
- Discharged home on glargine 0.7 units/kg/day (insurance denied detemir) and metformin
- Genetic evaluation revealed that she was homozygous for a pathogenic variant in the AGPAT2 gene
- 1 month follow up: Started on subcutaneous metreleptin and glargine discontinued
- 3 month follow up: Triglycerides improved, normal LFTs, and normal glucoses while on 0.056 mg/kg/day of subcutaneous metreleptin and metformin
- She had improved growth and met all developmental milestones

Labs

Table 1	Day 1	Day 4	3 months
Triglycerides (mg/dL)	5,167	758	229
HDL (mg/dL)	10	-	-
Glucose (mg/dL)	324	113-138	62-114
HgbA1c (%)	8.9	-	-
Insulin (mIU/mL)	257	-	-
AST (units/L)	215	119	51
ALT (units/L)	212	124	48
Leptin (ng/mL)	0.3	-	-
Adiponectin (mcg/mL)	<0.2	-	-
Bicarbonate (mmol/L)	17	-	-



Conclusion

- Leptin is important in regulation of lipid and glucose metabolism, and patients with CGL are deficient due to lack of adipose tissue
- Metabolic abnormalities, including stabilization of glucoses and improved hypertriglyceridemia, in our patient markedly improved with initiation of metreleptin, metformin, and insulin
- Medications were well tolerated without side effects
- We present successful dosing of these treatment modalities without adverse reactions in an infant with CGL

References

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