May 12th, 11:30 AM - 1:30 PM

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

Cintya Schweisberger

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

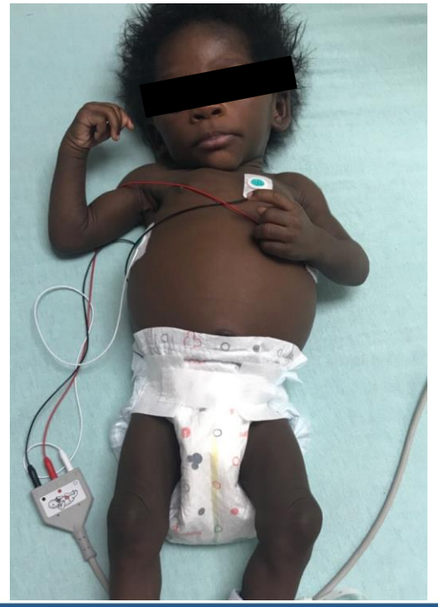
- 2-month-old SGA term female was noted to have poor weight gain, hyperphagia, and abdominal distension at a well child check
- She was admitted for failure to thrive with weight z-score of -2.17 and length z-score of -0.15
- Initial labs were notable for triglycerides 5,167 mg/dL, blood glucose 324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

1. Patni N, Garg A. Congenital generalized lipodystrophies--new insights into metabolic dysfunction. *Nat Rev Endocrinol*. 2015;11(9):522-534. doi:10.1038/nrendo.2015.123
2. Brown RJ, Oral EA, Cochran E, et al. Long-term effectiveness and safety of metreleptin in the treatment of patients with generalized lipodystrophy. *Endocrine*. 2018;60(3):479-489. doi:10.1007/s12020-018-1589-1
3. Kirel B, Bozdağ Ö, Köşger P, Aydoğdu SD, Alıncak E, Tekin N. A case of Donohue syndrome "Leprechaunism" with a novel mutation in the insulin receptor gene. *Turk Pediatri Ars*. 2017;52(4):226-230. Published 2017 Dec 1. doi:10.5152/TurkPediatriArs.2017.3193