PCSK1 Loss-of-function Heterozygosity as Cause of Hypoglycemia in Infancy: A Case Report

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CASE PRESENTATION

- Endocrinology consulted for a three-month-old female due to hypoglycemia.
- Admitted to inpatient pediatric gastroenterology service for the past month for diarrhea.
- Despite improvement in her congenital diarrhea, the patient required a glucose infusion rate of up to 9 mg/kg/min to maintain euglycemia.

INITIAL CRITICAL SAMPLE

Blood glucose	52 mg/dL
Insulin	2.6 mU/L
Beta-hydroxybutyrate	0.1 mmol/L
Cortisol	1.30 mcg/dL*
Growth hormone	3.79 ng/mL

*patient subsequently passed an ACTH stimulation test

GENETIC TESTING RESULTS

Compound heterozygosity for loss-of-function mutations in Proprotein Convertase Subtilisin Kexin 1 (PCSK1)

- c.595C>T, p.Arg199*
  - (previously reported)[1]
- c.914G>A, p.Trp305*
  - (not previously reported)

GLUCAGON STIMULATION TEST

Time	00:55	01:05	01:16
Blood glucose (mg/dL)	52	Glucagon administration	109

- Pro-insulin level was 126.4 pmol/L at the time of a blood glucose of 58 mg/dL.
- Trial of diazoxide resulted in resolution of hypoglycemia.
- Diazoxide administration did not worsen the patient's underlying congenital diarrhea.[2]

DISCUSSION

This case describes a presentation of PCSK 1 loss-of-function different than failure to thrive in infancy followed by obesity, as is frequently described.[3] This is an example of the wide variability in endocrinopathies that may be seen with PCSK1 deficiency. It also highlights the utility of diazoxide as management of reactive hypoglycemia due to elevated proinsulin levels.

CONCLUSION

PCSK-1 loss-of-function presents with a variety of endocrinopathies, warranting further phenotypic description of particular genotypes.

REFERENCES

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