

# Severe Hypoglycemic Encephalopathy secondary to Refractory Hyperinsulinemic Hypoglycemia

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## Background

Congenital hyperinsulinism (HI) is caused by dysregulated insulin secretion from pancreatic beta cells leading to continued hypersecretion of insulin despite low plasma glucose.<sup>2</sup> It is a relatively rare disorder that affects about 1 in 25,000 to 50,000 live births and is the leading cause of severe, intractable hypoglycemia in pediatric patients.<sup>6</sup> One common cause of HI are variants in the subunits of the adenosine triphosphate sensitive potassium channel ( $K_{ATP}$ ) rendering the channels nonfunctional or absent resulting in hypersecretion of insulin.<sup>2</sup>

$K_{ATP}$ -HI is classified into focal disease vs diffuse disease.<sup>2</sup> Focal disease can be attributed to mutations in the ABCC8 gene that encodes for the sulfonylurea receptor 1 subunit (SUR-1) within the  $K_{ATP}$  channel.<sup>3</sup> This mutation, in conjunction with somatic loss of the maternal gene, renders the channel dysfunctional leading to hypersecretion of insulin. These patients are found to have hypoglycemia refractory to Diazoxide as it blocks the SUR-1 subunit allowing for hyperpolarization of the cell which decreases insulin secretion.<sup>5</sup>

Delay in diagnosis and treatment can lead to neurological damage and seizures secondary to prolonged hypoglycemia which can cause long term developmental delay. It is imperative that pediatricians recognize early signs of hypoglycemia and evaluate patients appropriately.

## Imaging

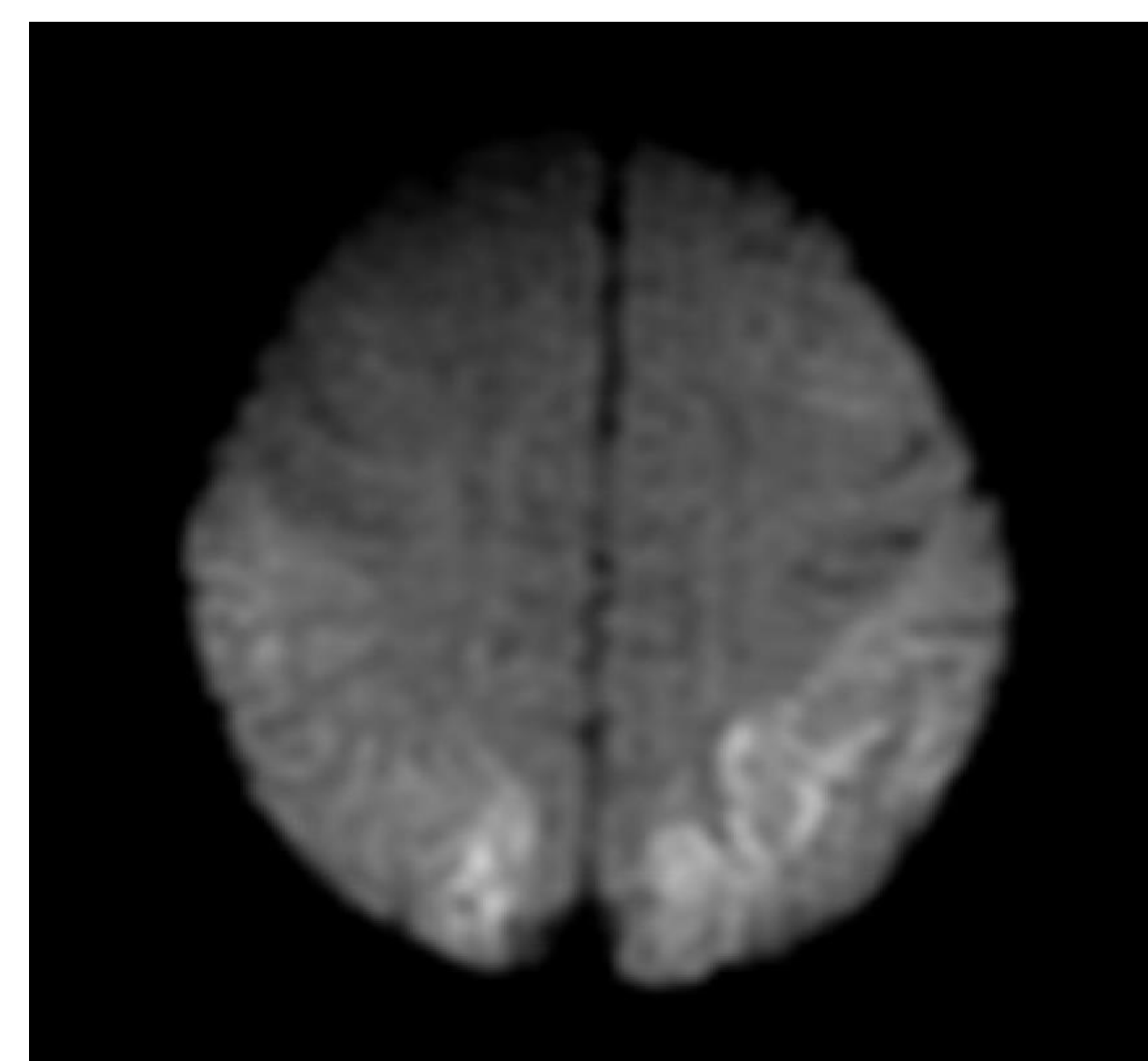
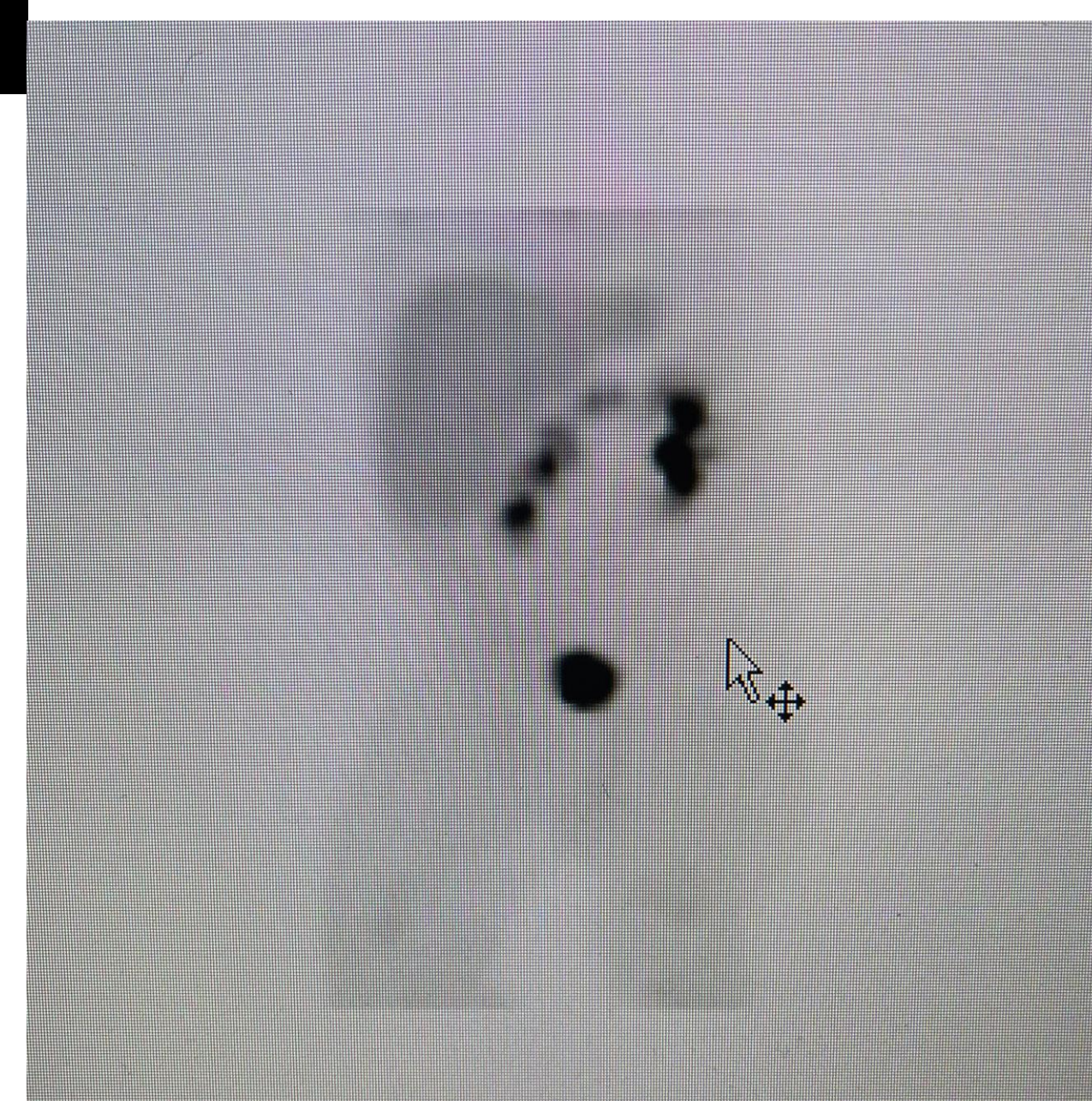


Fig. 1 Fairly symmetric cortical restricted diffusion in bilateral occipital and parietal lobes consistent with findings seen in cases of severe hypoglycemic encephalopathy

Fig. 2 18 FDOPA PET scan showing areas of uptake in the body and head of the pancreas



## Case

3 day old AGA female discharged at 24 hrs of age following normal labor and delivery

Presented to PCP the next day with lethargy, decreased PO feeds  
Seizure in office, POC BG 22

Transferred to ER where hypoglycemia workup for sepsis, pituitary and adrenal causes was negative

Critical sample obtained: low BG 30 mg/dL, inappropriately elevated serum insulin of 34.4 uIU/mL and suppressed BOH <0.2 mmol/L, consistent with HI

MRI concerning for severe hypoglycemic encephalopathy  
EEG showed subclinical seizures refractory to multiple epileptic medications

Despite dextrose infusions (up to 24mcg/kg/min) & max dose Diazoxide 15 mg/kg/day she remained hypoglycemic and was transferred to a HI center

Genetic testing revealed c.502C>T pathogenic variant in the ABCC 8 gene, consistent with focal disease resistant to diazoxide

18 FDOPA PET scan showed significant uptake in the body/head junction of the pancreas and focal lesion was resected via pancreatectomy. Hypoglycemia persisted

Second surgery was performed with unclear margins, hypoglycemia persisted. Started on Octreotide and continuous overnight SoCal (glucose) mixed with breast milk

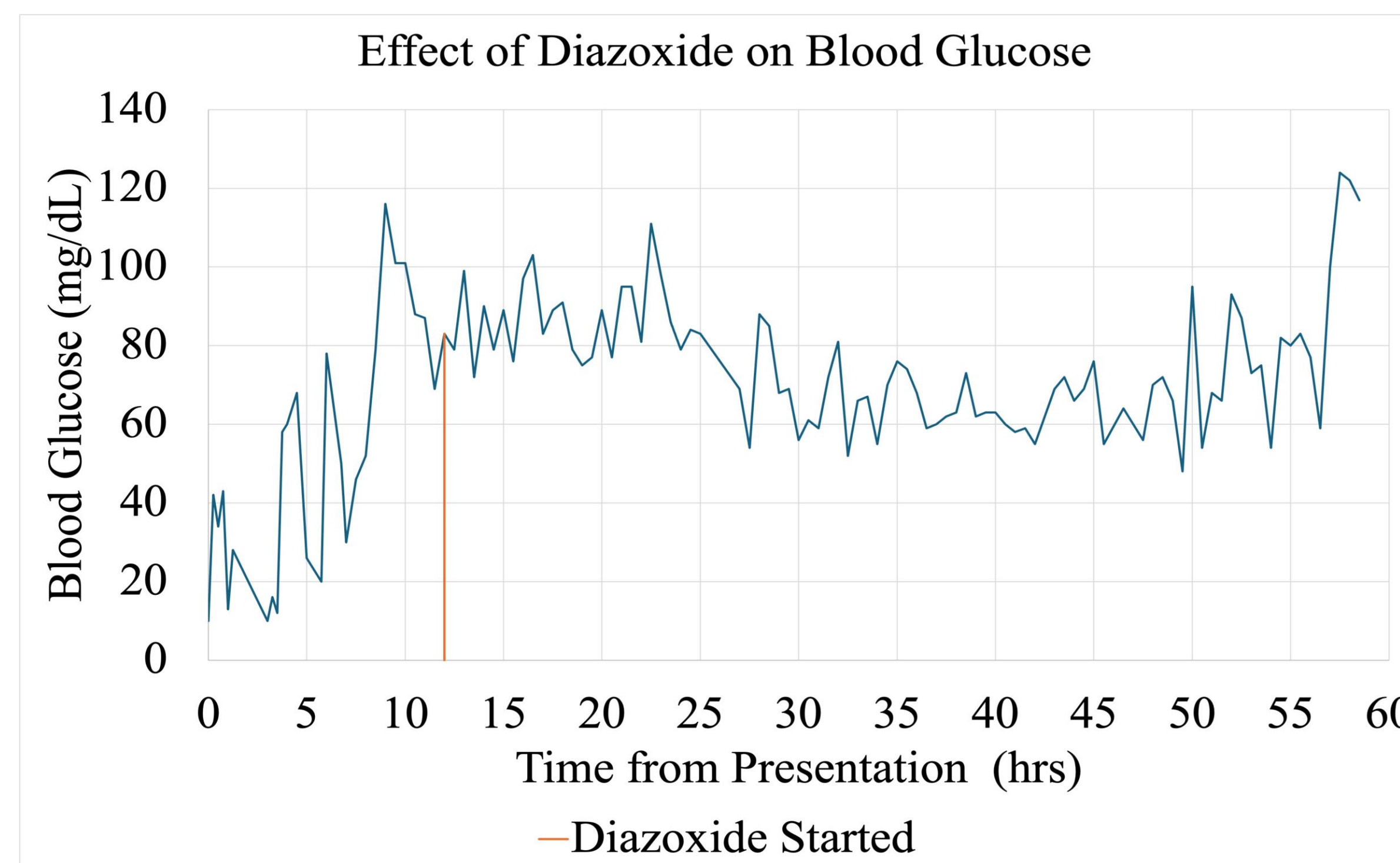


Fig 3. Blood glucose levels remained low despite the initiation of diazoxide treatment, showing this patient's HI was refractory to diazoxide

## Discussion

This case highlights the importance of early diagnosis and treatment in patients with CHI to prevent long-term developmental consequences and is a cautionary tale of the unanticipated consequences of early discharge. Due to the prolonged hypoglycemia this patient experienced prior to admission, leading to seizures and MRI changes consistent with hypoglycemic encephalopathy. Because she was discharged early from the hospital, the early warning signs of hypoglycemia, like poor feedings, were not witnessed by medical staff. Although CHI is a rare condition, it can lead to long term complications for patients if diagnosis and treatment is delayed.

Knowing that undiagnosed hypoglycemia will lead to brain damage pediatricians need to consider what we can do to ensure our patients safety. Options to consider: infants be monitored in the hospital for longer periods after birth; Or check BG on all infants prior to dc; and/or be diligent to educate families of warning signs for hypoglycemia and when to seek treatment.

## References

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