

# Thrombocytopenia induced by diazoxide treatment in a toddler with Hyperinsulinism-Hyperammonemia syndrome: a rare side-effect

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Topic: Diabetes and insulin

## INTRODUCTION

- Diazoxide is the first-line drug for Hyperinsulinemia-Hyperammonemia(HI/HA) syndrome, a disease due to a mutation in the glutamate dehydrogenase-1(GLUD1) gene
- Diazoxide, an opener of the pancreatic  $\beta$ -cells KATP-channels reducing insulin release, is uncommonly associated with thrombocytopenia

## AIM

We describe a toddler with HI/HA syndrome who developed thrombocytopenia after starting on diazoxide treatment

## METHOD

- A 13-month-old boy presented with tonic-clonic seizures, loss of consciousness, staring and hypoglycaemia, Blood Glucose(BG) 32mg/dl (1.7mmol/l))
- Treatment: intravenous(iv) Dextrose and oral feeds. He continued to have asymptomatic hypoglycaemia, BGs <60mg/dl (3.3mmol/l).
- There was a history of sweating, restlessness, and upper limbs tremor the past four months
- Examination normal, no dysmorphic features
- Ht and Wt on 15<sup>th</sup> percentile, SGA, unrelated parents. Mother, 28 years-old is on treatment for epilepsy since a young age

## RESULTS

- Laboratory tests:** Hypoglycaemia screen (BG 36mg/dl (2mmol/l)), revealed inappropriately high insulin and C-peptide levels (17,8 $\mu$ U/ml and 3,3ng/ml respectively) (fig 1), no ketones in urine. HI/HA syndrome was suspected by a glucagon and protein-loading test that showed hypoglycaemia and hyperammonaemia (92mmol/l) (fig 2)
- Treatment (Tx) and further course:** Oral diazoxide (max dose 6.7mg/kg/d) and hydrochlorothiazide (7 mg/kg/d) were started; he was discharged home. On day 12 of diazoxide Tx he presented with a two-day history of petechial rash and nose bleeds (fig 3); Platelet count (PLT) was 2K/ $\mu$ L(NR 150-450K/ $\mu$ L). Tx with corticosteroids, iv platelets and immunoglobulin was given; diazoxide was discontinued. Thrombocytopenia ameliorated five days after diazoxide discontinuation (PLT 226 K/ $\mu$ L), but hypoglycaemia occurred. Octreotide and later lanreotide were initiated (fig 4). He has been well since with no hypoglycaemic episodes. Growth is on the 5<sup>th</sup> centile, development is normal.
- Genetic testing:** a novel mutation of HI/HA syndrome with variable penetrance was found to the patient, his mother and the maternal grandmother who is asymptomatic.

Figure 1. Graph showing inappropriate concentration of serum insulin and C-peptide for the level of blood glucose

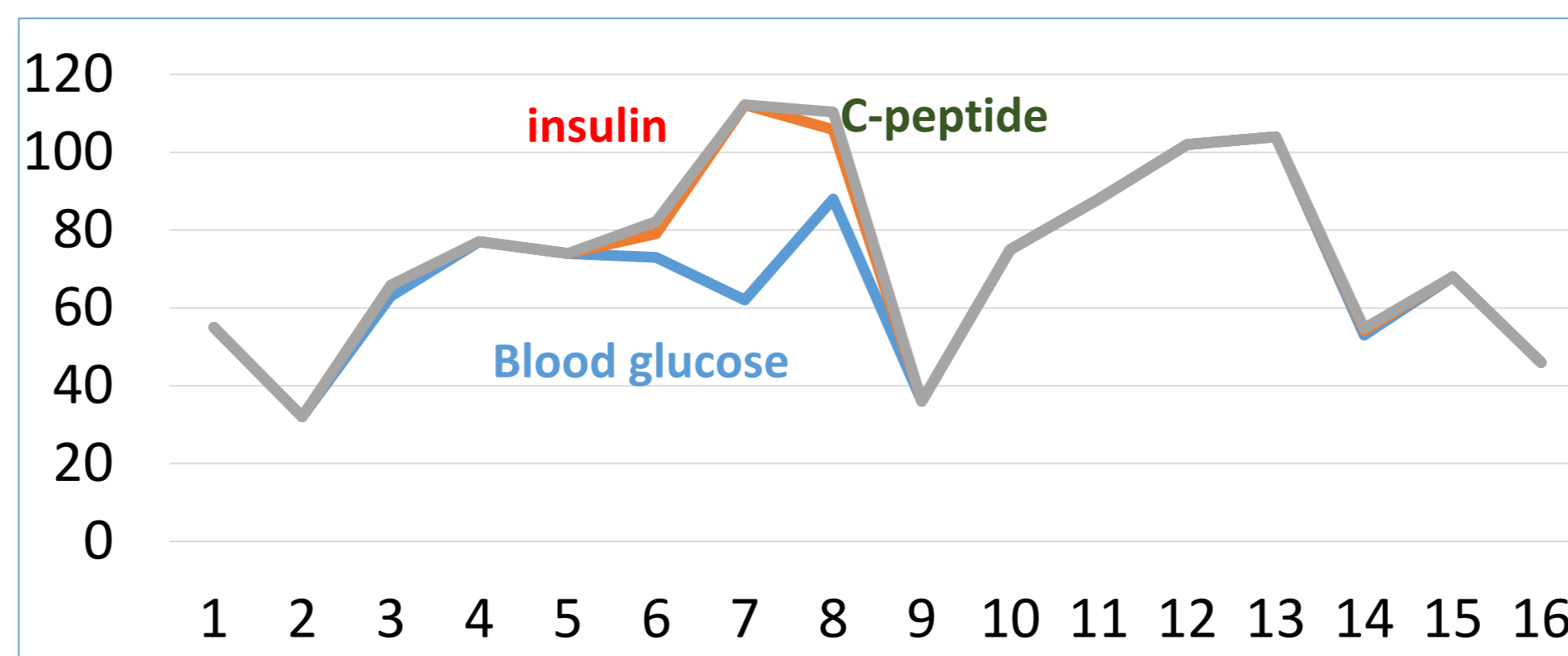


Figure 2. Protein loading test

Protein loading test	30'	+30'
Time (min)		
Glucose (70-100mg/dl)	68 (3.7mmol/l)	46 (2.5 mmol/l)
Insulin (2.6-24.9 $\mu$ U/ml)	4.6	9.6
NH3 (<35 $\mu$ mol/l)	82	82

Figure 3. Patient with purpuric rash on head and limbs

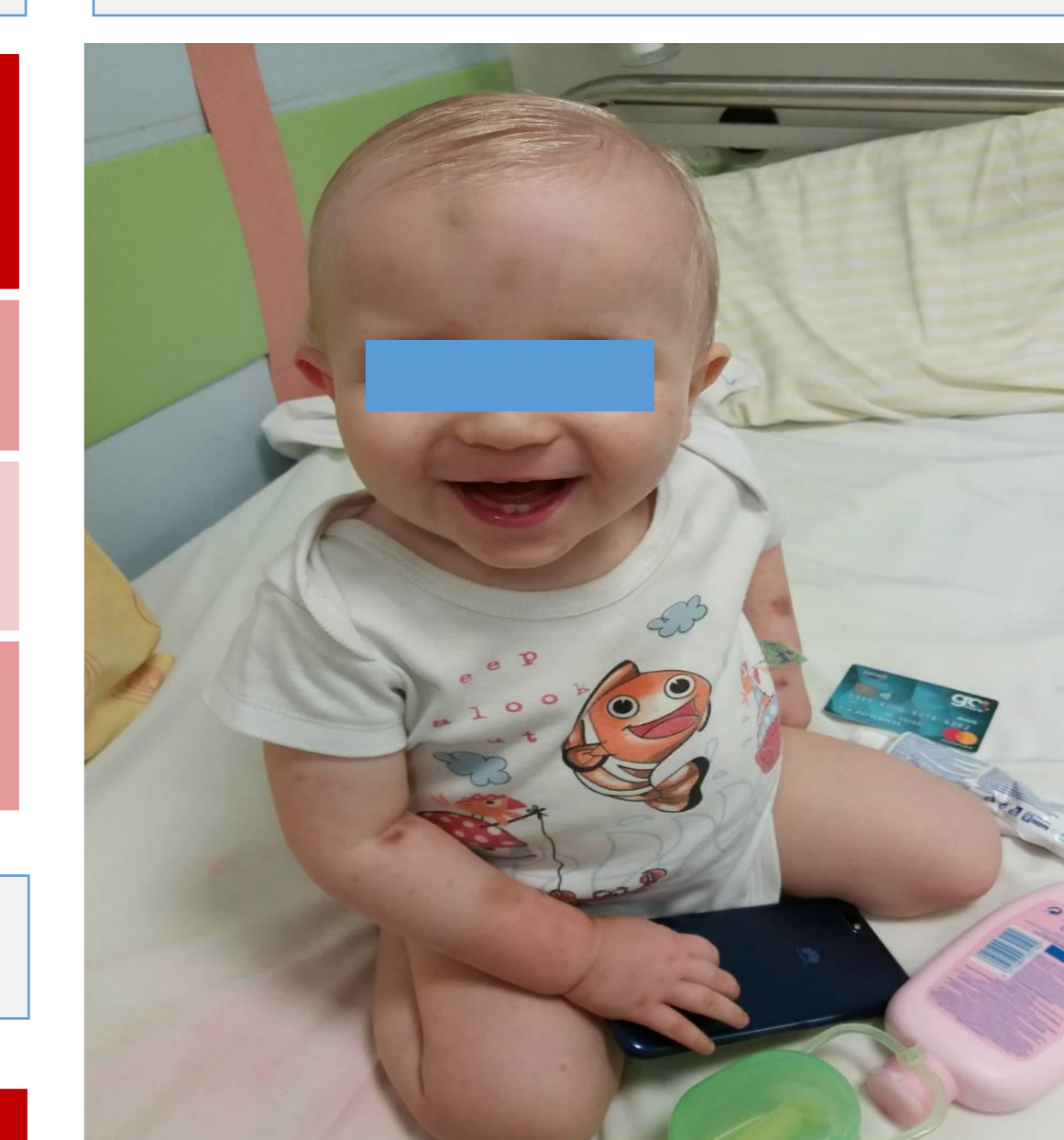


Figure 4. Platelet count and treatment course

Day of Admission	Day 12	Day 12	Day 12	Day 13	Day 15	Day 20	Day 22	Day 50
PLT K/ $\mu$ L	2	13	24	44	226	791	628	
Glucose (70-100mg/dl)	77	97		92		84		
Insulin (2.6-24.9 $\mu$ U/ml)				19.6				
C-peptide (1,1-4, 4 ng/ml)				3.18				
Treatment	Diazoxide stopped	Iv methylprednisolone iv platelets immunoglobulin			Oral prednisolone		Started Octreotide	Started Lanreotide



## CONCLUSIONS

- Diazoxide is a well-tolerated, first - line oral medication for hyperinsulinaemic hypoglycaemia**
- Thrombocytopenia is a rare side effect**
- Second-line treatment with other agents, such as octreotide/lanreotide, may be required**
- A full blood count should be obtained periodically**

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