Neonatal presentation of Persistent Hyperinsulinemic Hypoglycemia of Infancy

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Case Summary

Alfa Begum, a 2-month-old female baby, 3rd issue of her consanguineous parents hailing from Sylhet was admitted into Dhaka Shishu (Children) hospital (DSH) with the complaints of repeated episodes of convulsion, excessive sleepiness and weakness since 25th days of her life. Convulsion was generalized tonic-clonic in nature, persisted for 1-2 minutes, had been occurring several times in a day specially during early morning associated with excessive sweating. She had no history of birth asphyxia, fever, repeated vomiting, loose motion or family history of such type of illness.

For these complaints she was admitted and treated in local hospitals 3 times before this episode as a case of persistent hypoglycemia. But as convulsion was not cured so she was admitted here for further evaluation and better management.

Alfa born at term by LUCS with birth weight 4 kg without any perinatal complications. Mother, a 30 years old lady had no history of Diabetes Mellitus, Hypertension or taking any oral hypoglycemic agent during her pregnancy period. Now she is on mixed feeding, breastfeeding along with formula milk since 25 days of life.

During admission, Alfa was found to be lethargic, afebrile, anicteric, having rounded face but there was no facial dysmorphism. Vitals revealed, Heart Rate: 150/min, Respiratory Rate: 30/min, Temp: 98ºF, Dehydration: absent, CRT <3sec without any active convulsion .

Anthropometrically, Weight: 6 kg (falls on 95th centile), Length: 55 cm(0n 5th centile), OFC: 38cm.

Chest shape was normal with symmetrical movement. Air entry was good without any added sound. Heart sounds (1st and 2nd) were normal and audible in all four areas.

Abdomen was slightly distended and umbilicus was healthy. Liver was palpable, 3 cm from Right costal margin, firm in consistency, sharp border and smooth surface without splenomegaly or ascites. Genitalia was normal. Other systemic examination findings were normal.

Alfa Begum, 2 months old infant

(photo is given with parents permission)

So our provisional Diagnosis was Glycogen Storage Disease (type-I) and Differential Diagnosis was- 1. Galactosemia

2. Congenital Hyperinsulinemia

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Blood Sugar Monitoring Chart (mmol/L) after admission

8am	10am	12pm	2pm	4pm	6pm	8pm	10pm	12am	4am	6am
1.0	1.6	0.6	2.3	2.3	1.4	1.3	1.0	1.0	0.8	1.4
1.2	1.0	1.0	3.9	1.4	1.0	5.2	3.5	1.5	0.6	1.0

Investigations Done (in Sylhet) before admission at BSH

1.CBC : Hb= 14.9 gm/dl, TC = 7.2 x10^9 /L
DC: N= 40%, L= 51%, M= 5%, E= 4%,
Platelet= 2,63,000/cmm

2. RBS: 1.9 mmol/L

3. S.Ca : 7.21 mg/dl

4. SGPT: 45 U/L

5. S.Lactate: 2 mmol/L

6. S.Ammonia: 120 µmol/L

7. USG of whole abdomen: Normal

8. S.Lipid profile:

Total Cholesterol: 135 mg/dl

HDL Cholesterol: 58 mg/dl

LDL Cholesterol: 115 mg/dl

Triglyceride :136 mg/dl

After admission in our hospital Lactose free milk along with I/V fluid, Inj. Hydrocortisone were added, and following investigations were done.

1. CBC

Hb- 12.7 gm/dl
TC = 11.36 x10^9 /L
DC, N=37%, L=51%
Platelet= 2,89,000/cumm

2. RBS: 1.6 mmol/L

3. S.Electrolytes:

Na: 144 mmol/L
K: 5.87 mmol/L
Cl: 104 mmol/L

4. S.Ca: 2.6 mmol/L

5. ABG: pH: 7.45
pCO$_2$: 26.6 mm Hg
pO$_2$: 86.5 mm Hg
HCO$_3^-$: 18.7 mmol/L
BE : -3.6

6. Fasting Blood Sugar: 1.2 mmol/L

7. S.Ammonia: 77 µmol/L

8. S.Lactate: 2 mmol/L

9. Urine R/M/E: Normal

As hypoglycemia was not corrected so, consultation had taken from Department of Gastroentrology and Hepatology and they Advised to do Liver function test, Urinary metabolites, Galactose-1-PO$_4$ Uridyl-transferase assay. Then the Investigations revealed:

- **S. Bilirubin:** 0.26 mg/dl
- **SGPT:** 56 U/L
- **SGOT:** 45 U/L
- **S. Alkaline Phosphatase:** 245 U/L
- **Prothrombin Time:** 10 seconds
- **APTT:** 38 seconds
- **Galactose-1-PO Uridyl-transferase assay:** Not done due to financial constraint

As diagnosis was not conclusive yet, so next Consultation had taken from Department of Endocrinology and patient was transferred to endocrinology department for further evaluation and management. Then our initial Plan of management was-

- Monitor blood sugar 2 hourly and maintain chart
- Breast feeding 2 hourly along with Inf.10% baby saline (400 ml)
- Inj. Hydrocortisone was omitted

Blood and Urine for ketone body along with Urine for reducing substance were sent, which revealed

- Urine for Ketone Body & Reducing substance: Negative
- Blood for ketone body: Nil

Then we had planned to do : (Critical sample)

S. Cortisol, S. ATCH, S. Insulin level and Corresponding Blood sugar and Free Fatty Acid, which revealed

- **S.Cortisol: 9.18 µg/dl (4.3-22.4)**
- **Plasma ACTH: 9.38 pg/ml (7.2-63.3)**
- **Fasting Insulin: 29 µIU/ml (normal-<2mU/L)**
- **Corresponding Blood Sugar: 0.9 mmol/L**

So, our final diagnosis was **Persistent Hyperinsulinemic Hypoglycemia of Infancy (PHHI)**

Finally the following Treatment was given to the baby

a) Tab. Diazoxide (50mg):

(5-20 mg/kg/day) dose was adjusted according to blood sugar level

1/2 + 0 + 1/2 for 3 days
1/2 + 1/2 + 1/2 for 5 days
1 + 0 + 1 was continued

b) Advised for frequent feeding to maintain glucose level.

Within 2 weeks, patient has achieved normal sugar level as well as become convulsion free. So, patient was discharged with advice.

Blood Sugar Monitoring Chart (mmol/L) after 2 weeks of treatment

8 am	10 am	12 pm	2 pm	4 pm	6 pm	8 pm	10 pm	12 am	4 am	6 am
6.3	3.7	3.5	4.4	4.5	3.7	3.8	4.4	4.5	3.3	5.6
5.3	4.0	4.4	4.3	7.2	5.7	5.2	3.5	4.3	3.4	3.8

1st Follow-up visit: (14 days after discharge)

The patient was afebrile, Heart Rate:110/min, Respiratory Rate:28/min having no edema or convulsion. Her weight was 6.2 kg (no excess weight gain), neck control was achieved. Investigation revealed

RBS: 5 mmol/L

CBC: Hb= 11.4 gm/dl, TC = 6.2 x10^9 /L

DC: N= 40%, L= 55%, M= 2%, E= 3%,

Platelet= 2,25,000/cmm

2nd Follow-up visit (1 month later in local hospital):

The child had no further convulsion, vitals were within normal limit, having no other complaints and blood sugar was maintained with oral diazoxide (1 tab twice daily).

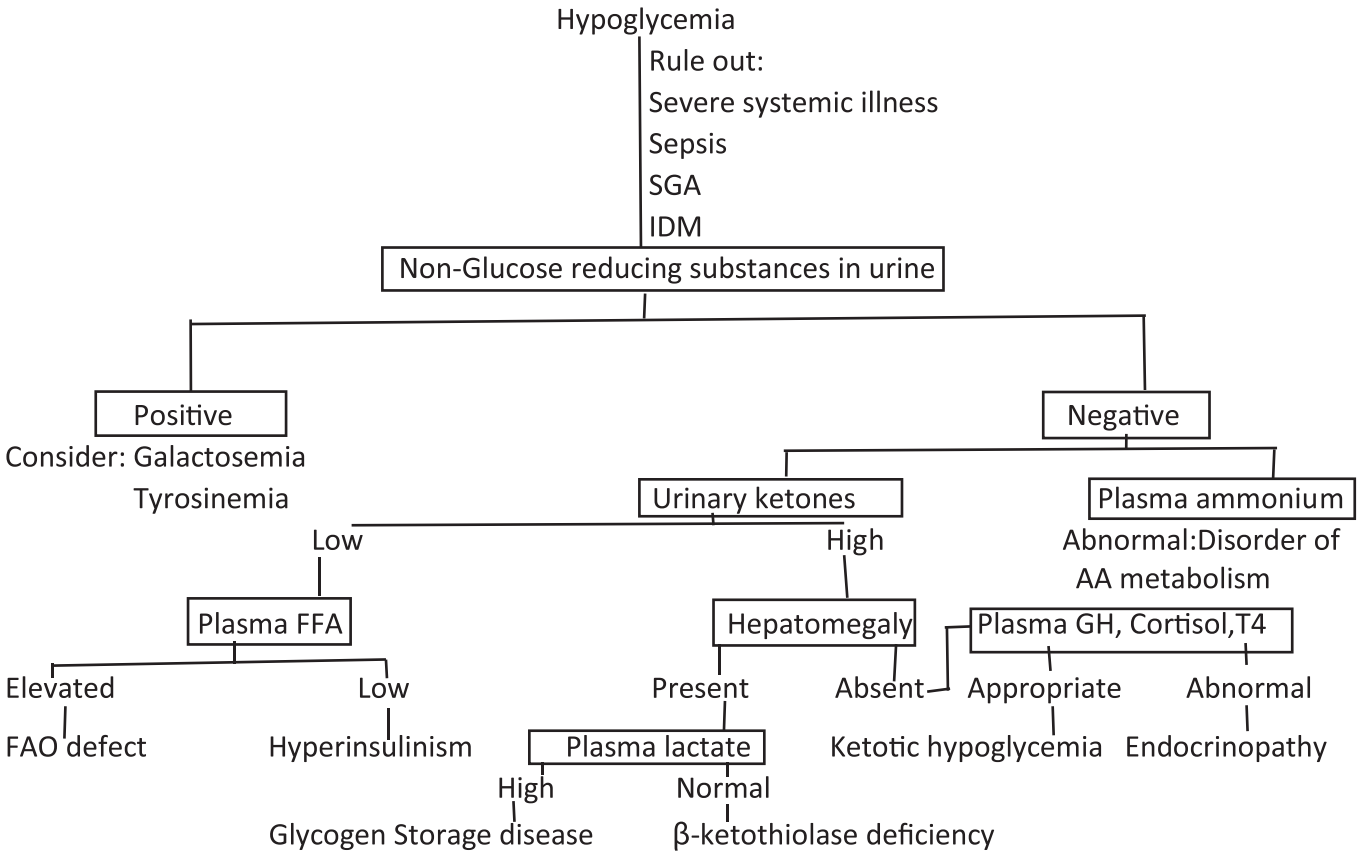
3rd Follow-up visit (2 months later): Patient had no further convulsion, normal blood sugar was maintained, developmental milestones were normal.

Alfa at 6 months of age can sit with support (photo is given with parents' permission)

Our Next Follow-up plan was 3 monthly for 1 year, 6 monthly for 3 years, yearly for life long.

Discussion

Persistent Hyperinsulinemic Hypoglycemia in Infancy (PHHI) is the most common cause of persistent and recurrent hypoglycemia in the neonatal and infancy periods.[1]



Flowchart: Approach to a case of Hypoglycemia[2]

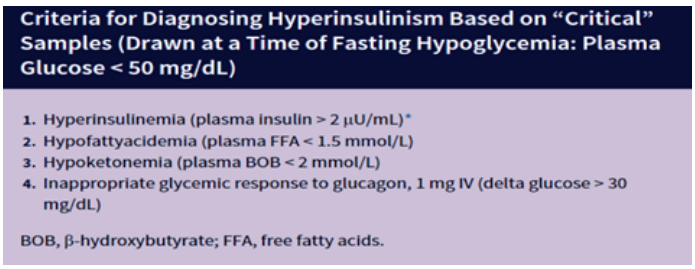


Fig. Diagnosis of Hyperinsulinemia of infancy.[3]

Management[4]

- Frequent feeding through oral/nasogastric route.
- **Pharmacological interventions:**
  - Diazoxide
  - Somatostatin analogs: Octreotide
  - Calcium channel blocker: Nifidipine
  - Glucagon
- **Surgical interventions:**
  - Partial Pancreatectomy
  - Total Pancreatectomy followed by insulin supplementation.

Complications: Neurological sequelae of hypoglycemia (25-50%): Seizures, developmental delay, permanent brain damage, impaired bonding & socialization.[5]

Prognosis: The prognosis is good in case of asymptomatic neonates with early diagnosis and appropriate treatment.[6]

Delayed diagnosis and non-responder patients have poor prognosis for subsequent normal intellectual development.[7]

Conclusion

- Appropriate approach to hypoglycemia makes early diagnosis and favourable outcome.
- PHHI is the most common cause of persistent and recurrent hypoglycemia.
- Permanent neurological sequelae occur in 25-50% of patient<6 months old with severe recurrent symptomatic hypoglycemia.
- No role of corticosteroid in management of PHHI.[8]

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