CASE REPORT

CONGENITAL HYPERINSULINISM (HYPERAMMONEMIA HYPERINSULINISM)

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HOW TO CITE THIS ARTICLE:
Garuda Rama. "Congenital Hyperinsulinism (Hyperammonemia Hyperinsulinism)". Journal of Evidence based Medicine and Healthcare; Volume 2, Issue 9, March 02, 2015; Page: 1339-1342.

ABSTRACT: **BACKGROUND:** Congenital hyperinsulinism causing hypoglycemia. **CASE CHARACTERISTICS**: 1yr child with hypoglycemic convulsion. **OBSERVATION:** High insulin levels on fasting, hyperammonemia, diffuse hyperplasia of pancreas on PET dopa scan. **OUTCOME:** Good response to frequent glucose feeds and diazoxide. **MESSAGE:** Any child presenting with convulsion needs blood sugar estimation and hypoglycemia if any, should be thoroughly investigated. Congenital hyperinsulinism comprises a group of different genetic disorders with the common finding of recurrent episodes of hyperinsulinemic hypoglycemia due to inappropriate secretion of insulin by pancreatic β-islet cells. Hyperammonemia hyperinsulinism is due to type-3 diffuse hyperinsulinism transmitted as autosomal dominant due to mutation in glutamate dehydrogenase gain of function mutation.[1, 2]
KEYWORDS: Hyperammonemia hyperinsulinism, hyperplasia of pancreas.

CASE REPORT: A 1-year old girl with wt 7.5kg and ht 75cm presented to emergency room with seizure. It was not associated with fever. There was history of repeated seizures from 7 months of age, treated with anticonvulsants. She was not investigated. Born out of non-consanguineous marriage, her developmental history was normal. On physical exam, there were no dysmorphic features, no features of hypothyroidism or hypopituitarism. Cardio-vascular and respiratory systems were normal. Per abdomen, there was no organomegaly. She was investigated thoroughly for hypoglycemic convulsion. Random blood sugar was 27mg/dl, WBC 8600/mm,^{3} DC: P 30%, L 62%, E 4%, M 4%, MCV 68fL, Platelets 407000/mm,^{3} Serum Ca 10.2 mg/dl, Na 140mEq/L, K 4.3mEq/L, Cl 100mEq/L, HCO3 23.8mEq/L, pH 7.495, Creatinine 0.2mg/dl, LFT normal, Serum lactate 23mmol/L, Ammonia 454umol/L. Thyroid function tests were normal. Metabolic screening was negative.

Hormonal study on fasting hypoglycemia showed high levels of insulin with C peptide;[3]

Serum Insulin : 17.40uu/ml (normal < 2)

Serum C peptide : 2.15uu/ml (normal < 0.6)

Serum cortisol : 29.54ug/dl (normal 4-22)

Serum growth hormone : 6.38ng/ml (normal 1-13)

Ultrasound abdomen and CT brain normal.

PET Dopa scan: Congenital Hyperinsulinism is divided histologically into 2 types, focal and diffuse and PET Dopa scan helps to distinguish them [4]. In this case, PET Dopa scan of pancreas showed diffuse hyperplasia of β-cells suggestive of diffuse hyperinsulinism.(see figure)

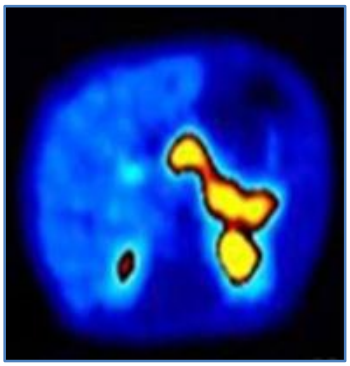

Figure 1

In view of elevated serum insulin and ammonia with diffuse hyperplasia of pancreatic β-cells, a diagnosis of hypoglycemia due to hyperammonemia hyperinsulinism was confirmed. She was treated with IV bolus of glucose. After stabilisation of blood glucose, she was put on high carbohydrate frequent feeds [3] and tab Diazoxide 50mg once daily. She responded well and was discharged. On follow up, she is asymptomatic and blood sugar was well maintained.

DISCUSSION: In infancy, hypoglycemia due to hyperinsulinism is more common [2] than insulinoma. There are 4 types of hyperinsulinism.

1. Transient neonatal hyperinsulinism.
2. Focal hyperinsulinism due to SUR 1 or Kir 6.2 mutation.
3. Diffuse hyperinsulinism. This has two variants, autosomal recessive and dominant.
   AR: SUR-1mutation, Kir 6.2 mutation, congenital disorder of glycosylation, short chain acyl co-enzyme dehydrogenase deficiency.
   AD: glucokinase gain of function mutation, hyperammonemia hyperinsulinism (glutamate dehydrogenase gain of function mutation). [2]
4. Wiedman Beckwith syndrome.

In hyperinsulinism, hypoglycemic episodes develop from birth to late infancy. In this case, the child had hypoglycemic episodes from 7 months of age and is found to have diffuse hyperplasia of pancreatic β-cells on PET Dopa scan, with elevated levels of serum ammonia and insulin. She comes under type-3 diffuse hyperinsulinism (hyperammonemia hyperinsulinemia) due to glutamate dehydrogenase gain of mutation. High insulin levels occur in this condition due to increased activity of glutamate dehydrogenase resulting in defective regulation of insulin secretion. [2] Other metabolic conditions are excluded. Hypoglycemia should be treated by IV bolus glucose promptly to prevent brain damage and intellectual disability.[5] These patients need frequent glucose feeds to maintain glucose levels.[3] Drugs like glucagon, diazoxide, somatostatin analogues and nifedipine are useful to raise blood sugar.[6] Glucagon raises blood sugar by

promoting glycogenolysis and is useful as an emergency treatment but not appropriate for long term management. Diazoxide is an antihypertensive antidiuretic benzothiazide and acts on pancreatic β-cells, opens K-ATP channels and inhibits insulin secretion. Side effects of diazoxide are hirsutism, salt and fluid retention and rarely pulmonary hypertension. Somatostatin analogues or nifedipine are used if they don't respond to diazoxide. Studies have shown, such patients respond well to diazoxide. Hence this patient was put on frequent high carbohydrate feeds with diazoxide and monitored for hirsutism and fluid retention. She responded well, with no side effects. Those who do not respond to medical management may benefit from partial pancreatectomy in focal hyperinsulinism and subtotal pancreatectomy in diffuse hyperinsulinism.[7]

CONCLUSION: Any child presenting with convulsion should be tested for hypoglycemia and if found so, should be further investigated.

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Date of Submission: 14/02/2015.
Date of Peer Review: 15/02/2015.
Date of Acceptance: 18/02/2015.
Date of Publishing: 27/02/2015.