GLUCAGON CHALLENGE TEST - RECURRENT HYPOGLYCEMIA

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GUIDE :

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Measurement of thyroid hormones –hypothyroidism

Measurement of cortisol – Addisons disease

Measurement of C-peptide – type of Diabetes

Measurement of LH, FSH and estradiol, testosterone – Pubertal disorders

Measurement of GH levels – GHD

Can measurement of insulin levels ALONE at time of hypoglycemia – make a diagnosis of hyperinsulinemia?

Problems with insulin assay

nsulin concentration measured in peripheral plasma may be up to 90% ower than the initial peak plasma concentration within 30 minutes (intra nd extra vascular distribution, clearance by liver on passage)

lemolysis (difficult sample drawing) – enzyme release from RBC – destroys

to n 4 deg celsi aximum for one day

eference	Cut – off
elson	2 µU/mL
perling text book of pediatric ndocrinology	5 µU/mL
rook text book of pediatric ndocrinology	EVEN DETECTABLE INSULIN AT THE TIME OF HYPOGLYCEMIA IS HYPERINSULINEMIA

What is the alternative then?

- IGFBP-1 – not available in India
- Ketone test[illegible] practically useful but some pit falls
  - Poor fat [illegible]res – cannot mount ketotic response

Am J Dis Child. 1984 Feb;138(2):168-71.

Ketonuria does not exclude hyperinsulinemic hypoglycemia.

Wolfsdorf JI, Sadeghi-Nejad A, Senior B.

- Glucagon [illegible]ge test

CASE 1

laster H one and half year old male child

resented with seizures on d4 of life : CBG :33mg/dL

hypoglycemic seizures noted in 5th month, 6th
7th month a year of age...

arly morning hypoglycemia episodes
o ily history of hypoglycemia or early diabetes

n examination – No nical markers
nthropometry – n growth
ght SD sc eight SD score -1.5, target height SD score -1.3)

upervised fast test done:

CRITICAL SAMPLES	Value	Interpretation
FASTING BLOOD GLUCOSE	46mg/dL	LOW
BLOOD KETONES	NEGATIVE	Non Ketotic
Serum GH	1.2 ng/mL	Low
SERUM CORTISOL	25.3 µg/dL	Normal
SERUM INSULIN	7. 8 µU/mL	Elevated
SERUM AMMONIA	86 µg/dL	Normal

it hyperinsuline GH deficiency?

Glucagon challenge test done

- Basal Blood sugar – 46 mg/dL

- glucagon [illegible] g given IV – No Dextrose bolus given

- [illegible]epeat Blood suga[illegible] at 30 minutes – 84 mg/dL

This is hyperinsu[illegible]ia – child started on diazoxide after [illegible]king blo[illegible]netic studies

Home monitoring of blood glucose

Prior to Diazoxide therapy (morning)

- 34
- 65
- 45
- 73
- 56
- 32
- 65
- 54
- 76

After Diazoxide (10 mg/kg) Morning

- 76
- 84
- 89
- 82
- 90
- 79
- 100
- 95

CASE 2

aster B – 2 year old developmentally normal male child

esented with low sugar in D2 of life

ince then

arie work up. Previ ritical sample taken – ketones negative, insulin 31 µIU/m

n ex nination: Short

eight SD score -2.5
Target height SD sco 1.3
Weight SD score -1
logic short

CASE 2

CRITICAL SAMPLES	Value	Interpretation
FASTING BLOOD GLUCOSE	43 mg/dL	Low
BLOOD KETONES	Negative	Non-ketotic
GROWTH HORMONE	1.4ng/mL	Low
SERUM CORTISOL	27.7 µg/dL	Normal
SERUM INSULIN	0.2µU/mL	Below the cut-off, but detectable

Previous FAO scre work-up twice – Negative

Is it GH defici Hyperinsulinemia?

Glucagon challenge test done

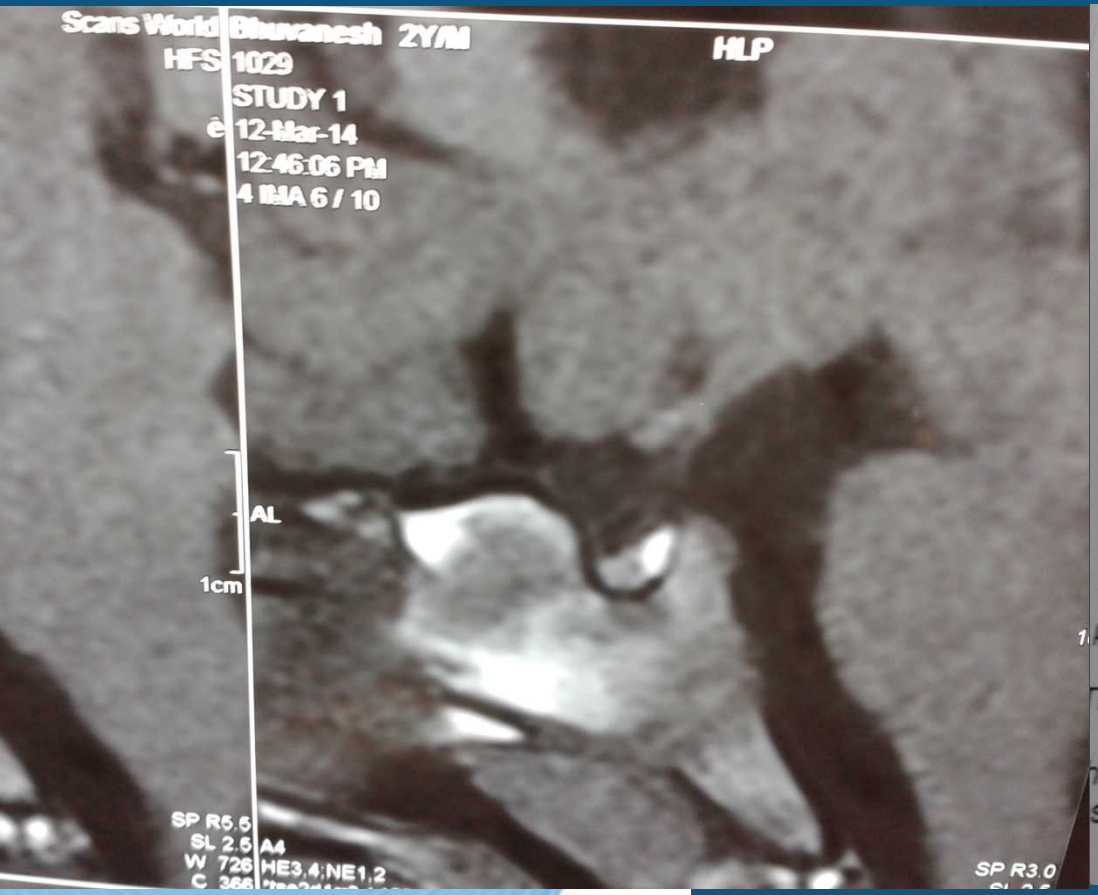
- Basal Blood sugar – 42 mg/dL

- inj glucagon … given IV – No Dextrose bolus given

- Repeat Blood sugar … t 30 minutes – 40 mg/dL

This is NOT hypo… emia – GH deficiency more likely

MRI Brain



SCANS WORLD

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MASTER. BHUVANESH [2y/M]

Procedure done on : 12/03/2014
Reported on : 12/03/2014

Ref. By: Dr.K.P. HEMCHAND.,MD(Ped)PDCC.,

SW/NB/MRI: 21029

WIDEBORE 48 CHANNEL 1.5T MRI – BRAIN

Sequences:

T2W : AXIAL
DWI, ADC MAPPING
T1 W: SAGITTAL
T2 W FLAIR : CORONAL
SWI : AXIAL
PC ANGIOGRA

Brain:

Anterior pituitary gland measures 2.7 x 3.0 x 11.1 mm, volume 44 mm³ reduced.

Posterior pituitary gland measures 3.7 x 2.0 x 7.0 mm, volume 26 mm³, normal.

The cerebral hemispheric parenchyma is normal. Normal grey-white matter diffe
present. No focal lesions are seen.

The corona radiata and centrum semiovales are normal. No focus of demyelination is

e caudate and lentiform nuclei and the thalami are normal. The corpus callosum,
sterior commisures are normal.

A diagnosis of G
hypoch
iency was arrived at – child has been
on GH –
des since then.

CASE 3

aster S was a 3 months baby.

e had documented three episodes of hypoglycaemia.

elivered as a preterm baby – Non consanguineous parents.

d failure to with height SD score of -4.5, weight SD score of -5.6.

ad si nificant risk facto and classical features of sepsis

ed in PICU – requ ed a GIR 12 mg/kg/min to maintain sugars

o clinical markers of ocrine dysfunction.

s are normal.

CASE 3

ritical sample taken in view of persistent hypoglycemia

EM work-up negative, FAO work-up negative, lactate and pyruvate normal

CRITICAL SAMPLES	Value	Interpretation
BLOOD GLUCOSE	38 mg/dL	Hypoglycemia
BLOOD KETONES	Negative	Non-ketotic
GROWTH HORMONE	12.6ng/mL	N growth hormone
SERUM CORTISOL	12.5 µg/dL	Cortisol replete
SERUM INSULIN	1.3µU/mL	Detectable, but below the text book cut-off of 2µU/mL

Glucagon challenge test done

- Basal Blood sugar – 40 mg/dL

- Inj glucagon 30ug/kg given IV – No Dextrose bolus given

- Repeat Blood sugar at minutes – 76 mg/dL

This is hyperinsulinemia robably transient related to sepsis

nfection was treated o subsequent hypoglycemia

ear of age evelopmental milestones and normal ctivity

Case	Screening test	Diagnostic test	Confirmatory evidence
Master H Permanent PHHI	Elevated insulin (7.8 µU/mL) Low GH (1.2 ng/mL) Negative ketones	Increment of glucose > 30 mg/dl with glucagon	Response to Diazoxide Genetic tests (awaited)
Master B GHD	Varied insulin levels (0.2 µU/mL and 31 µU/mL) Low GH (1.4 ng/mL)	No Increment of glucose with glucagon	MRI – hypoplastic pituitary Response to GH
Master S Transient Hyperinsulinemia	Marginally elevated insulin (1.3 µU/mL) Normal GH (12.6 ng/mL)	Increment of glucose > 30 mg/dl with glucagon	Evidence of sepsis After treating sepsis, no hypoglycemia

Maintenance of glucose homeostasis

INSULIN EFFECTS

- ↓ GLUCOSE UPTAKE
- ↓ LIPOLYSIS
- ↓ KETOGENESIS
- ↓ GLUCONEOGENESIS
- ↓ GLYCOGENOLYSIS

COUNTER REGULATORY HARMONE EFFECTS

1. Glucagon
2. Adrenaline
3. Cortisol
4. Growth hormone

↓ BLOOD GLUCOSE ↑

GLUCAGON STIMULATION TEST

Baseline Venous Blood sugar - Hypoglycemic

30 microgram/kg glucagon injected iv – No dextrose bolus

After an hour venous blood sugar levels checked

INCREMENT OF GLUCOSE > 30 mg/dl

appropriate conservation of liver
rcogen with hypoglycemia

dicates suppression of liver
rcogenolysis by excessive insulin

INCREMENT OF GLUCOSE < 30 mg/dl

No liver glycogen - depleted

Not due to excess insulin

PRACTICAL ASPECTS

- Glucagon stimulation test - - Must be done in ER/ PICU (back-up)
- All resuscitative measures must be kept handy
- Glucagon – cost hr 700/-, available easily
- Venous sugar, don't restrict to CBG

To summarize

- Three cases of ambiguous cause of hypoglycemia - Glucagon challenge – gave the answer
- Simple safe and cost effective test
- Simple test for extensive confirmatory investigation (MRI/ genetic test) and avoidy tedious treatment
- All ER-rooms must be equipped with glucagon and be used judiciously

THANK YOU