Recurrent Hypoglycemia-Not every low sugar is hyperinsulinemia

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INTRODUCTION AND OBJECTIVES

- Recurrent hypoglycemia is a life threatening condition. And its early diagnosis and correct diagnosis can be crucial to entail survival of the child.
- To review this case with respect to the clinical scenario and critical pathways we should remember while investigating a case of recurrent hypoglycemia.

METHODS

- A 5 year old, Pakistani origin, male child presented to the Pediatric Endocrine clinic with chief complaint of recurrent hypoglycemia.
- Patient had presented to Emergency room with an episode of documented hypoglycemia(blood sugar 2.2 mmol/l).Patient was given some IV fluids, stabilised and sent home without any critical sample saved.
- There was past history of documented recurrent hypoglycemia associated with high fever, vomiting, diarrhea. There was also history of sweating episodes.
- Child was first born, product of non-consanguineous marriage, full term with average birth weight. There was history of neonatal intensive care stay for pneumonia and respiratory distress with h/o one episode of convulsion related with hypoglycemia.
- There was a positive history of diagnosed with Dextrocardia and Situs inversus.
- The patient had been apparently evaluated previously by Pediatricians at various hospitals locally and in their home country for hypoglycemia including extensively for hyperinsulinemia (but never correlated).The parents had been even given glucometer to keep a measure of glucose levels and instructions for taking sugar in case of hypoglycemia.
- He had been also diagnosed with autism because of poor school performance and poor attention span.
- Clinical examination -Anthropometry -Weight at 10th percentile CDC and Height at 50th percentile CDC
- General examination revealed conscious, alert, thin built child with a sallow complexion, frequent eye blinking because of dry eyes and pallor.
- Significant generalized hyperpigmentation mainly on face, palmar creases, knuckles, elbows and oral mucosa was noted.
- No lymphadenopathy/signs of any fungal infection noticed.
- Mild to moderate development delay (predominant speech) was present.
- Rest of the systemic exam was normal other than the systemic finding related to situs inversus and dextrocardia

LAB RESULTS-TABLE 1

Serum	Initial	After 3 months
Glucose, Fasting, mmol/L (3.33 - 5.55)	2.36	4.56
Sodium, mmol/L (136 – 145)	136.00	138.00
Potassium, mmol/L (3.5 - 5.1)	5.11	4.5
Chloride, mmol/L (98 – 107)	97.90	101.80
Bicarbonate,mmol/L (22 – 29)	18.90	22.00
Plasma Adrenocorticotropic Hormone (ACTH), pmol/L (1.6 - 13.9)	445.10	400
Cortisol AM, nmol/L (171 – 536)	0.500	-
Free Triiodothyronine (FT3) pmol/L (3.69 - 8.46)	6.52	5.24
Free Thyroxine (FT4), pmol/L (12.3 - 22.8)	12.65	19.11
Thyroid Stimulating Hormone (TSH), mIU/L (0.7 - 5.97)	13.86	4.15
Thyroglobulin Antibody IU/mL (0 – 38)	135.50	118.10
Thyroperoxidase (TPO) Antibodies, IU/mL (0 – 13)	10.06	9.71

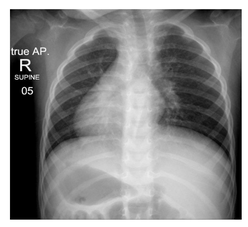
OTHER INITIAL LAB RESULTS-TABLE 2

HORMONES	VALUES
ALDOSTERONE, ng/dL Lying down position : 3.0 - 16.0 Standing upright position : 7.0 -30.0	21.1
PLASMA RENIN ACTIVITY ng/mL/hr Lying position: 0.15 - 2.33 Standing position: 0.10 - 6.56	8.54
ALDOSTERONE / RENIN RATIO < OR = 20	2.47
ANDROSTENEDIONE,ng/M l0-7 years 0.1 - 0.2 ng/mL	<0.3
Insulin, pmol/L 17.8 - 173	1.45
C-Peptide, nmol/L 0.37 - 1.47	0.04
Parathyroid hormone (PTH), pmol/L (1.59 - 6.89)	3.01
INSULIN LIKE GROWTHFACTOR -1 52.0 - 297.0 ng/mL	50.9
HUMAN GROWTH HORMONE < or = 3.00 ng/mL	0.61

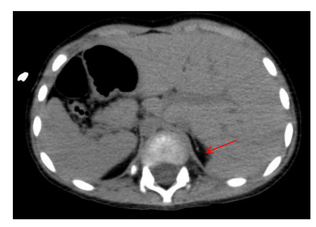
LAB RESULTS

- CBC had shown initial low hemoglobin and iron deficiency anemia which was later corrected after iron supplements.
- Liver and renal functions were found to be normal.
- Autoantibodies against adrenal glands and serum levelsfor light chain fatty acids could not be performed.

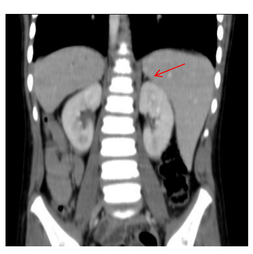
RADIOLOGY

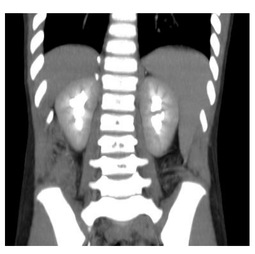


A.Dextrocardia and situs inversus



B.Plain CT Scan - Left Adrenal Calcification





C.Coronal Contrast CT Scan – Thinned out adrenals and left adrenal calcification

MANAGEMENT

- The child was diagnosed as a case of primary adrenocortical insufficiency or Addisons disease and started immediately on age and body surface area appropriate dose of hydrocortisone. Patient was also continued on thyroid replacement with thyroxine 25 µg once a day.
- On follow-up at 3 and 6 months, patient showed significant improvement. Blood pressure, and electrolytes and thyriod within normal range, pigmentation had significantly reduced and patient showed weight gain and most importantly there were no further reported cases of hypoglycemia.
- Patient was educated about the need to double dose of steroids in times of stress,infection, illness.

CONCLUSIONS

- Addison's disease is a rare endocrine disease in which there is destruction of the adrenal cortex with resultant inadequate secretion of the adrenal cortical hormones-cortisol, aldosterone and androgens.(1)
- Primary adrenal insufficiency can be a life-threatening disorder particularly in stressful situation, since cortisol secretion cannot be increased on demand at all(1)
- Addison's disease has an incidence of 0.8 per million and a prevalence of 40-110 per million in the USA and European countries.(2)
- The presence of recurrent hypoglycemia ,hyperpigmentation, along with electrolyte abnormalities of hyponatremia and hyperkalemia led to the suspicion of Primary adrenal insufficiency.
- Out of these signs ,hyperpigmentation of the skin and mucosal surfaces associated with fatigue and weight loss are the most specific signs(1)
- The commonest causes of Addison's disease are autoimmune and tuberculous adrenalitis. Others are fungal infection, metastatic neoplasia, haemochromatosis and congenital adrenal hyperplasia-adrenoleukodystrophy. (1)Adrenal calcification seen on abdominal CT are important signs of adrenal tuberculosis. Calcification of the left adrenal gland was observed in our patient.(3)
- Often, there is a delay in diagnosis due to lack of suspicion on account of the subtle nature of the signs and symptoms in many cases as was with our case (recurrent-hypoglycemia) . Contributory factor could be lack of awareness amongst physicians too leading to increased morbidity and mortality. A survey of patients with Addison's disease who are members of the National Adrenal Disease Foundation revealed that 60% had sought medical attention from two or more physicians before the correct diagnosis was ever considered. Thus, physicians should keep a high index of suspicion for adrenal insufficiency in unexplained illness.(4)

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