Case study

A Unusual case of Congenital Hypothyroidism

ABSTRACT

Congenital Hypothyroidism (CH)is a common preventable cause of mental retardation.The incidence of CH is 1 in 2500 to 1 in 3000 newborns.Most common causes are thyroid dysgenesis and dyshormonogenesis. Some disorder like maternal autoantibodies, maternal intake of anti thyroid medication, iodine deficiency or iodine excess can result in transient CH.

Common symptoms include decreased activity and increased sleep, feeding difficulty, constipation, and prolonged jaundice. On examination, common signs include myxedematous facies, large fontanels, macroglossia, a distended abdomen with umbilical hernia, and hypotonia.

Thyroid dysgenesis accounts for 85% of permanent, primary CH, while inborn errors of thyroid hormone biosynthesis (dyshormonogeneses) account for 10-15% of cases. Secondary or central CH may occur with isolated TSH deficiency, but more commonly it is associated with congenital hypopitiutarism. Transient CH most commonly occurs in preterm infants born

CASE REPORT

A 3 day old baby was admitted to SNCU with chief complain of yellowish discoloration upto abdomen and respiratory distress. The baby was born to 2nd Gravida with history of one abortion at 2 month which was spontaneous and the mother was on antithyroid medication for last 6 month before the delivery. The baby was born at 38 weeks 2days with birth weight 1.75kgs with birth history uneventful. Baby was fed within one hour of life and passed stool within 24hrs and urine within 48hrs.

General physical examination revealed a well alert and active baby with tachypnea and mild retraction and icteric upto abdomen with facial dysmorphism , Quebec score-4.

On Examination,there was open posterior fontanelle with facial dysmorphism upslanting palpebral fissure, depressed nasal bridge, low set ears, no skeletal deformity, no umbilical hernia. Assymetrical IUGR (ponderal index - 1.9). Respiratory examination shows tachypnea with mild intercoastal retraction and mild subcoastal retraction.

So, the baby was put on oxygen support and single surface phototherapy for 2days for neonatal jaundice.

And on 6th day of admissionthere was anepisode of regurgitation of the feed and feed intolerance was seen so drop domperidone and drop ranitidine was given followed by burping after half feed and were no sign of constipation.

Investigation shows normal blood picture , sepsis profile positive, USG neck shows both thyroid lobes were normal, TORCH- rubella IgG- 104 IU/ml and CMV-93 IU/ml , blood culture and sensitivity shows MRCONS, CSF analysis was in normal limits, Urine culture and sensitivity was positive for entercoccus , Mother anti TPO antibody 0.84IU/ml which was in normal limit,

Serum TSH 10.6, freeT41 ng/dl , and free T3 2.2 pg/dl

Dried blood spot test revealed urea cycle defect to be presumptive positive with abnormal amino acid metabolism and decrease in citrulline levels

In view of TSH 10.6. Tab Levothyroxine was started and the patient was discharged after a hospital stay of 17 days on the attendant's persistent request on Tab Levothyroxine.

A provisional diagnosis of Term/VD/ Assymetrical IUGR/Neonatal Jaundice/ Late onset neonatal sepsis/ Dysmorphic facies/ Urosepsis / Congenital Hypothyroidism/ Quebec score- 4

DISCUSSION(expand discussion)

(Reframe the sentence)In greater than 95% of newborn infants with CH, there are no symptoms or signs of CH when the diagnosis is suspected by newborn screening.

Congential Hypothyroidism with citrullinemia is one of urea cycle defects and is caused by argininosuccinic acid synthetase deficiency which includes a failure to synthesize urea, resulting in the accumulation of ammonium, glutamine, and citrulline. The neonatal form presents the most severe onset and a fatal course with vomiting, failure to feeding, irritability, apnea, convulsion,lethargy, stupor and coma with respiratory arrest.Although citrullinemia is reported as a rare urea cycle.

CONCLUSION (reduce conclusion in precise manner)

The deficiency of thyroid hormones in the neonate has been known since antiquity.Though still a prevalent nutritional disease worldwide, iodine deficiency rarely causes congenital hypothyroidism (CH) in western countries. Permanent neurodevelopmental deficits were known to occur when CH was not recognized and adequately treated by 2 to 3 months of postnatal age. Since the advent of newborn screening for CH in 1973, intellectual disability as a consequence of CH has been virtually eradicated among affected infants detected by screening within the first 2-3 weeks of age. The incidence is approximately 1:4,000 in iodine sufficient populations. The etiology in 70 to 80% of the non-familial cases is unknown. Maternal hypothyroidism may adversely affect the fetus to rarely cause findings of CH, or to be associated with mildly decreased IQ outcomes when maternal hypothyroidism occurs during the first half of pregnancy despite normal fetal and neonatal thyroid function. So neonatal screening for thyroid function should be done after 72 hours of life and should repeat Thyroid function test on 15th day of life.

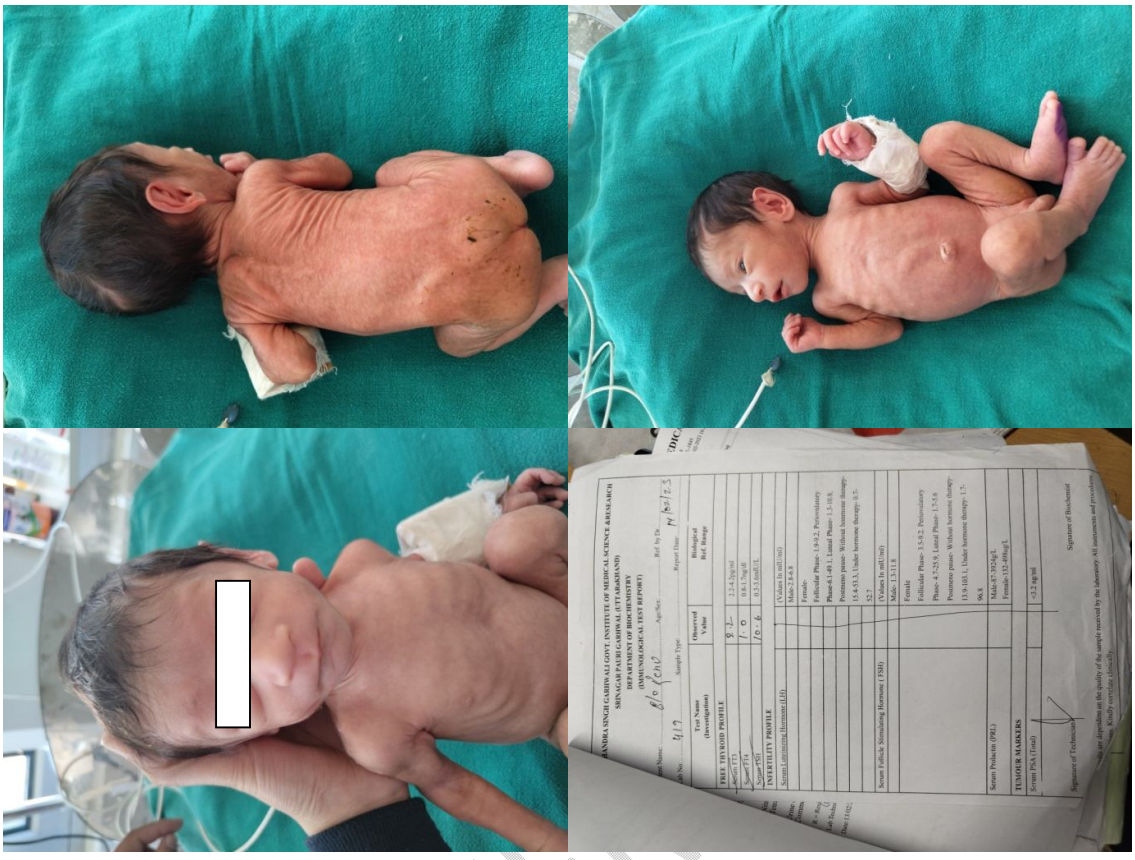
REFERENCE (number the references maintain Vancouver style)

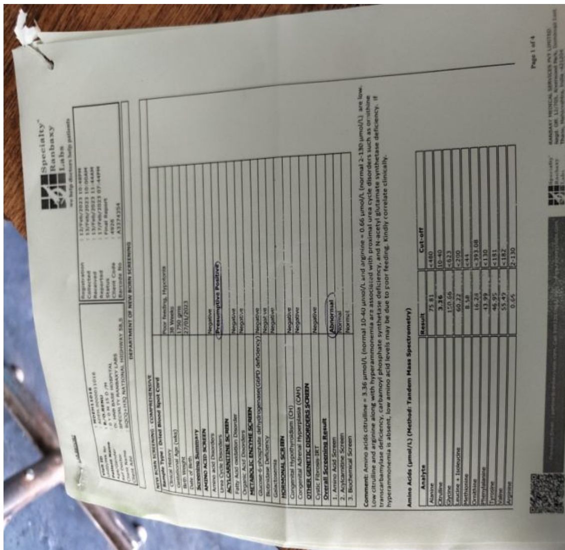
- American Academy of Pediatrics, Rose SR, Section on Endocrinology and Committee on Genetics, et al: Update of newborn screening and therapy for congenital hypothyroidism, Pediatrics 117:2290–2303, 2006.

- Maestri NE, Clissold DB, Brusilow SW. Long-term survival of patients with argininosuccinate synthetase deficiency. J Pediatr 1995; 127:929-35.
- Tokatlı A, Çokun T, Özalp . Citrullinemia. Clinical experience with 23 cases. Turk J Pediatr 1998; 40:185-193.
- National institute of health

Summer M, Tuchman M. Proceedings of a consensus conference for the management of patients with urea cycle disorders.Pediatr 2001; 138:S6-S10.
Maestri NE, Hayser ER, Bartholomew D, Brusilow SW. Prospective treatment of urea cycle disorders. J Pediatr 1991; 119:923,8.
La Franchi S. Disorders of the Thyroid Gland. In: Behrman RE, Kleiman RM, Jenson HB (ed). Nelson Textbook of Pediatrics. 16thed. Philadelphia: Saunders 2000; 1698-1702.
Summer M. Current strategies for the management of neonatal urea cycle disorders.Pediatr 2001; 138:S30-S39.
Rezvani I. Defects in Metabolism of Amino Acids. In: Behrman RE, Kleiman RM, Jenson HB (ed). Nelson Textbook of Pediatrics.16th ed. Philadelphia: Saunders 2000; 344-377.
Tokatlı A, Çokun T, Özalp . Citrullinemia. Clinical experience with 23 cases. Turk J Pediatr 1998; 40:185-193.
Tokatlı A, Çokun T, Özalp . Fifteen years' experience with 212 hyperammonaemic cases at a metabolic unit. J Inher Metab Dis 1991; 14:698-706.

Fig 1 Congenital Hypothyroidism and pathological report


AMBEDKAR INSTITUTE OF MEDICAL SCIENCE & RESEARCH
SHIVAGAR PAURI GARHWAL (UTTARAKHAND)
DEPARTMENT OF BIOCHEMISTRY
(IMMUNOLOGICAL TEST REPORT)
Test Name (Investigation)
Observed Value
Biological Ref. Range
THYROID PROFILE
Serum FT3
Serum FT4
Serum TSH
INFERTILITY PROFILE
Serum Luteinizing Hormone (LH)
Serum Follicle Stimulating Hormone (FSH)
TUMOUR MARKERS
Serum Prolactin (PRL)
Serum PSA (Total)
Signature of Technician
Signature of Biochemist



NEW BORN SCREENING - COMPREHENSIVE

DEPARTMENT OF NEW BORN SCREENING

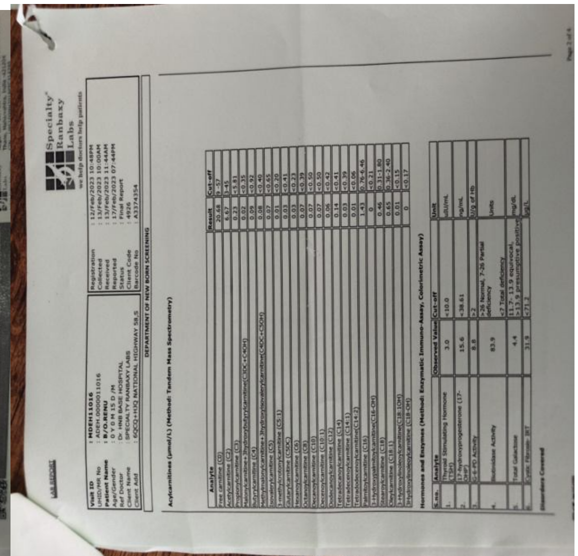
Sample Type : Dried Blood Spot Card	
Clinical History	Poor feeding, Hypotonia
Gestational Age (wks)	38 Weeks
Birth Weight	1750 gms
Date of Birth	27/01/2023
Screening Summary	
AMINO ACID SCREEN	
Amino acid Disorders	Negative
Urea Cycle Disorders	Presumptive Positive
ACYLCARNITINE SCREEN	
Fatty Acid oxidation Disorder	Negative
Organic Acid Disorders	Negative
METABOLIC ENZYME SCREEN	
Glucose-6-phosphate dehydrogenase(G6PD deficiency)	Negative
Biotinidase Deficiency	Negative
Galactosemia	Negative
HORMONAL SCREEN	
Congenital Hypothyroidism (CH)	Negative
Congenital Adrenal Hyperplasia (CAH)	Negative
OTHER GENETIC DISORDERS SCREEN	
Cystic Fibrosis-IRT	Negative
Overall Screening Result	
1. Amino Acid Screen	Abnormal
2. Acylcarnitine Screen	Normal
3. Biochemical Screen	Normal

Comment: Amino acids citrulline = 3.36 µmol/L (normal 10-40 µmol/L) and arginine = 0.66 µmol/L (normal 2-130 µmol/L) are low. Low citrulline and arginine along with hyperammonemia are associated with proximal urea cycle disorders such as ornithine transcarbamylase deficiency, carbamoyl phosphate synthetase deficiency, and N-acetyl glutamate synthetase deficiency. If hyperammonemia is absent, low amino acid levels may be due to poor feeding. Kindly correlate clinically.

Amino Acids (µmol/L) (Method: Tandem Mass Spectrometry)

Analyte	Result	Cut-off
Alanine	75.81	<480
Citrulline	3.36	10-40
Glycine	150.66	<623
Leucine + Isoleucine	60.22	<200
Methionine	8.58	<44
Ornithine	16.24	<393.08
Phenylalanine	43.99	<130
Tyrosine	46.95	<181
Valine	55.49	<182
Arginine	0.66	2-130

Page 1 of 4



Client Name : SPECIALTY RANBAXY LABS
Client Add : 6QCQ+HJQ NATIONAL HIGHWAY 58,5
Client Code : 4926
Barcode No : A33743354

DEPARTMENT OF NEW BORN SCREENING

Acylcarnitines (µmol/L) (Method: Tandem Mass Spectrometry)

Analyte	Result	Cut-off
Free carnitine (C0)	20.68	9 -57
Acetylcarnitine (C2)	6.67	3-45
Propionylcarnitine (C3)	0.23	<5.81
Malonylcarnitine+3hydroxybutyrylcarnitine(C3DC+C4OH)	0.02	<0.35
Butyrylcarnitine (C4)	0.09	<0.92
Methylmalonylcarnitine+3hydroxyisovalerylcarnitine(C4DC+C5OH)	0.08	<0.40
Isovalerylcarnitine (C5)	0.07	<0.65
3-methylcrotonylcarnitine (C5:1)	0.01	<0.20
Glutarylcarnitine (C5DC)	0.03	<0.41
Hexanoylcarnitine (C6)	0.03	<0.23
Octanoylcarnitine (C8)	0.07	<0.39
Decanoylcarnitine (C10)	0.07	<0.50
Decenoylcarnitine (C10:1)	0.07	<0.50
Dodecanoylcarnitine (C12)	0.06	<0.42
Tetradecanoylcarnitine (C14)	0.14	<0.41
Tetradecenoylcarnitine (C14:1)	0.03	<0.39
Tetradodecenoylcarnitine(C14:2)	0.01	<0.06
Palmitoylcarnitine (C16)	1.43	0.76-6.46
3-Hydroxypalmitoylcarnitine(C16-OH)	0	<0.21
Stearoylcarnitine (C18)	0.46	0.31-1.80
Oleylcarnitine (C18:1)	0.65	0.36-2.40
3-Hydroxylinoleoylcarnitine(C18:1OH)	0.01	<0.15
3Hydroxylinoleoylcarnitine (C18-OH)	0	<0.17

Hormones and Enzymes (Method: Enzymatic Immuno-Assay, Colorimetric Assay)

S.no.	Analyte	Observed Value	Cut-off	Unit
1.	Thyroid Stimulating Hormone (TSH)	3.0	<10.0	uIU/mL
2.	17-hydroxyprogesterone (17-OHP)	15.6	<38.61	ng/mL
3.	G-6-PD Activity	8.8	>2	U/g of Hb
4.	Biotinidase Activity	83.9	>26 Normal, 7-26 Partial deficiency <7 Total deficiency	Units
5.	Total Galactose	4.4	11.7- 13.9 equivocal, >13.9 presumptive positive	mg/dL
6.	Cystic Fibrosis- IRT	31.9	<71.2	µg/L

Disorders Covered