BLK-MAX
Super Speciality Hospital

Interesting mimickers of cerebral palsy

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Cerebral palsy

Cerebral palsy (CP) describes a group of permanent disorders of movement and posture, causing activity limitation, that are attributed to nonprogressive disturbances that occurred in the developing fetal or immature brain (BAX 2005)

Accompanied with

-disturbances of sensation, perception
-cognition, communication
-behavior
-epilepsy
-secondary musculoskeletal problems

CASE 1

6-year-old child

-Delayed attainment of milestones

-Difficulty in walking with progressive decline over 8 months

Birth details: Non- consanguineous marriage, G3P2A1, Elder sib, 9 year old is a girl child, alive and healthy. Second G was spontaneous abortion

Natal: FT, 2 Kg, IUGR, cried immediately

Symptomatic neonatal hypoglycemia documented once at 12 hours of life

NICU stay: 8 days

Case details

Development:

- Global developmental delay
- Toe walking 2 years
- Speaking 3 years
- At 6 years:
- Walks independent, partially dependent for ADL
- SQ 75%

Spasticity:

- Only present in lower limb
- Upper limb and trunk normal
- No diurnal variation

Development

Global developmental delay

Motor: Sitting at 12 months, walking with support on toes at 18 months, independent walking at 2 years

Fine motor: Spoon and cup handing by 2 years

Socio cognitive: Responding to name after a year, following one step command at 18 months, pretend play by 3 years

Language: One word with meaning 18 month, two word sentence at 3 year

Current status (6years):

walks independently with toe walking and scissoring

Speaks in sentences

Partially dependent for ADL

Below average intelligence with a SQ of 75%

Hyperactivity and inattention

Gait and spasticity

- Stiffness of both lower lower limbs noted during second year of life
- Upper limbs and trunk were normal, he can independently get up and down the bed.
- No diurnal variation
- No history of seizures

Last 8 months: child had been progressive stiffness and frequent falls

Family: None affected

Examination

- Weight: 14 kgs (<3rd centile)
- Height: 103 cm (<3rd centile)
- Head circumference: 46.5 cm (< 3rd centile)

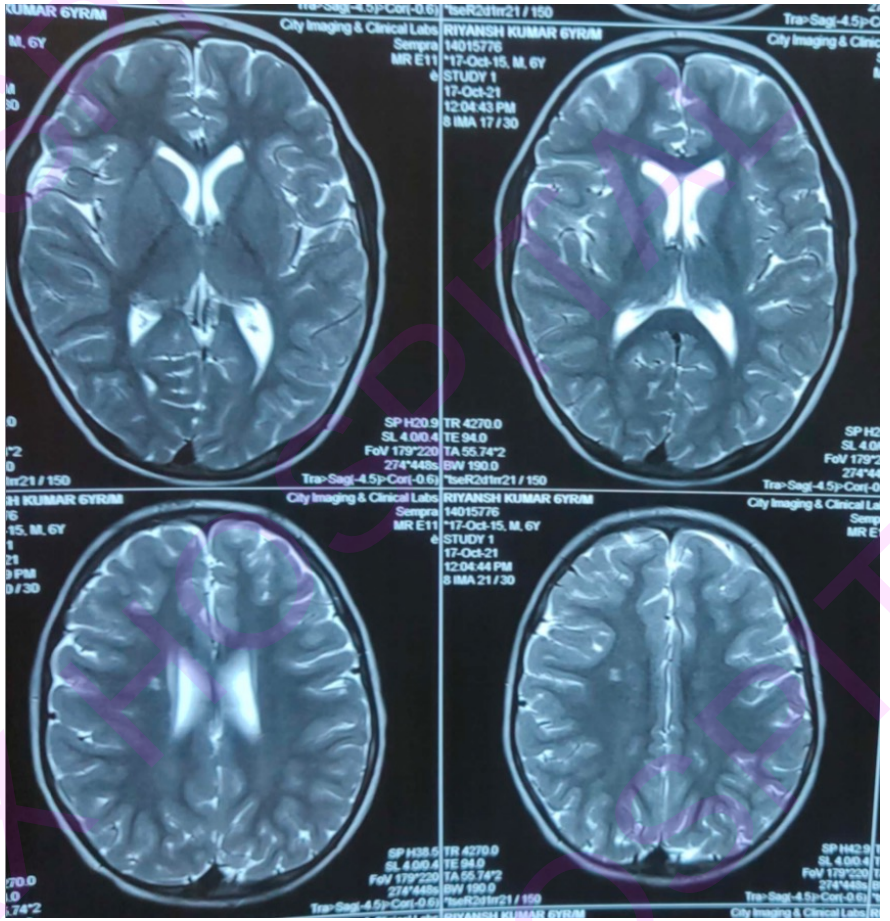
- Bilateral calf hypertrophy
- Gower signs was negative
- Spasticity in both lower limbs with brisk DTRS
- Clonus on right ankle, Left ankle had contracture

Examination

Investigations

- MRI brain: No specific shadows in right frontal region
- MRI spine: Normal

- Total CPK: 326
- SGPT: 184



Case summary

- Progressive spastic paraparesis
- Motor delay with progression
- Intellectual disability
- Microcephaly
- Calf hypertrophy
- Non-specific MRI brain changes

Differentials

Disorders	Points in favour	Points against
Cerebral palsy	Global delay Spastic paraparesis	Progressive MRI brain not suggestive
Muscle dystrophy (DMD/ BMD)	Motor delay with calf hypertrophy	CPK is not very high Other muscle hypertrophy not seen
Metabolic disorder: Hyperargininemia	Spastic paraparesis which is progressive	No aversion to protein rich food No seizures
Genetic: a. Primary dystonia (Segawa disease) b. Hereditary spastic paraparesis	Progressive spastic paraparesis	No diurnal variation

Metabolic Investigations

Blood lactate: 28.9 mg/dl (4.5-19.8)
Blood ammonia: 155 mcg/dl (18.7-102)

Result:

TMS Screening of this baby revealed.

- Normal level of acylcarnitines
- Elevation of arginine. (see below table).

Possible Differential Diagnosis:

- Urea cycle disorder (UCD).

Tyrosine	39.58	18.9 - 166
Citrulline	46.37	3.31 - 51.5
Ornithine	24.39	23.0 - 216
Arginine	245.72	2.00 - 54.1
Glycine	180.68	102 - 662
Alanine	197.14	72.5 - 619

: SAN0088700 SSDPL : HSP0059003

[redacted] Registered Dt : 01-Dec-2021

GE / GENDER : 6 Y(s) / Male Reported Dt : 06-Dec-2021

Ref Dr. : DR.RAJNI FARMANIA Ref.Institute : BLK Hospitals (Max Healthcare Institute Limited)

Specimen Type : Urine Collected Dt : 29-Nov-2021

Urine Organic Acids (GC/MS)

Clinical History:
Microcephaly, hyperactivity, spasticity, spastic paraparesis.

Method:
Gas Chromatography /Mass spectrometry (GC/MS) - Semi quantitative analysis(1,2).

Urine Organic Acids - Compound Table

S.no	Compound Name	Relative Peak Area of Compound with respect to Internal Standard - Margaric acid			
		Result	Cut-off	Reference Range	Fold Elevation
1	Uracil-2	19.87%	19.65%	0.00-7.00 %	2.84
2	Orotic-3	66.63%	2.50%	0-1.50 %	44.42

Result:
Urinary organic acidogram shows mild to moderate elevation of (For fold elevations see compound table)

- **Uracil, orotic acid**

Interpretation:
Significant increase in orotic acid along with uracil is observed in ornithine transcarbamylase (OTC) deficiency. Increase in orotic acid (50±several 100 fold) is observed in orotic aciduria and also in Argininemia, citrullinemia, argininosuccinic aciduria. Normal to mildly elevated level (3- 50 fold) of orotic is also observed in Hyperornithinemia Hyperammonemia & homocitrullinuria (HHH) syndrome and in Lysinuric protein intolerance.(LPI) (3, 4).

In this sample there is moderate elevation of orotic acid and mild elevation of uracil.

Impression:
- **Urea Cycle Disorders (UCD).**

Urea cycle defect

Table 2

Urea cycle disorders and expected investigation results

Urea cycle disorder	Gene	Inheritance	Plasma amino acids	Urine organic acids
Carbamoylphosphate synthetase I deficiency	CPS1	Autosomal recessive	↓ Arginine ↓ Citrulline	↓/Normal urinary orotic acid
Ornithine transcarbamylase deficiency	OTC	X linked	↓ Arginine ↓ Citrulline	↑ Urinary orotic acid
Argininosuccinic acid synthase deficiency or citrullineamia type I	ASS1	Autosomal recessive	↑ Arginine ↑ Citrulline	
Argininosuccinase acid lyase deficiency or argininosucciniaciduria	ASL	Autosomal recessive	↑ Arginine ↑ Citrulline	
Arginase deficiency	ARG1	Autosomal recessive	↑↑ Arginine	
N-acetylglutamate synthase deficiency	NAGS	Autosomal recessive	↓ Arginine ↓ Citrulline	↓/Normal urinary orotic acid

- Plasma amino acid and urinary organic acid levels indicated as being low (↓) or high (↑) relative to the reference range.

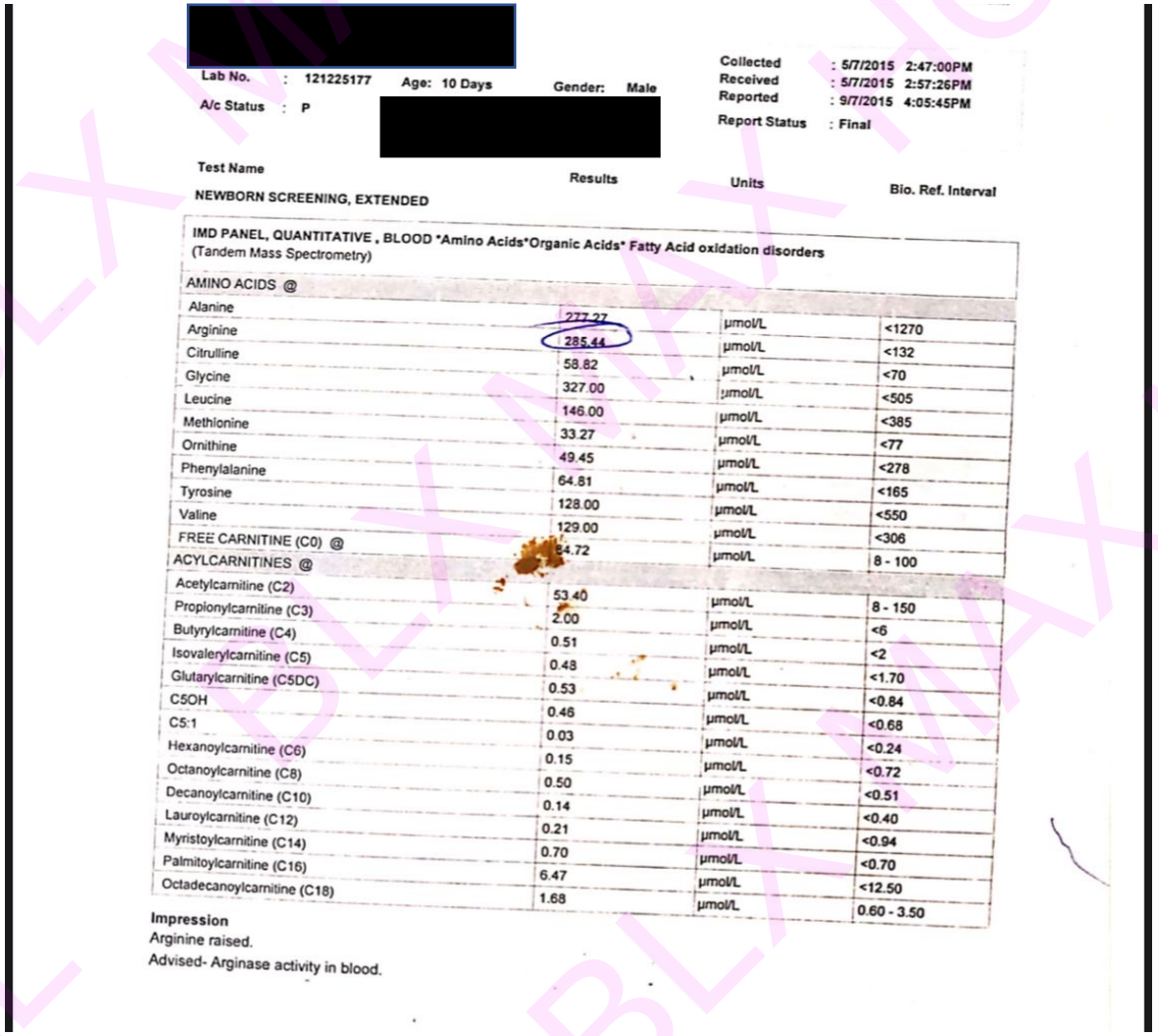
Differentiating different urea cycle defect

Deficiency	Disorder	Clinical Feature
N-Acetylglutamate synthase	Hyperammonemia that may be accompanied by high plasma concentrations of alanine and glutamine	Lethargy; persistent vomiting; poor feeding; hyperventilation; enlarged liver; seizures
Carbamoyl phosphate synthetase	Hyperammonemia; citrullinemia; respiratory alkalosis	Lethargy; coma; seizures; vomiting; poor feeding; hyperventilation; hepatomegaly
Ornithine transcarbamylase	Hyperammonemia; respiratory alkalosis; elevated orotic acid in urine	Seizures; vomiting; poor feeding; hyperventilation; hepatomegaly
Arginosuccinate synthetase	Citrullinemia	Lethargy; coma; seizures; vomiting; poor feeding; hepatomegaly
Arginosuccinate lyase	Elevated arginosuccinic acid in urine	Lethargy; seizures; vomiting; poor feeding; hyperventilation; hepatomegaly
Arginase	Markedly elevated plasma arginine, lactate, and CSF glutamine, and modestly elevated blood ammonia	Delayed development; protein intolerance; spasticity; loss of muscle control; seizures; irritability

CSF indicates cerebrospinal fluid.

Vangala, Subrahmanyam & Tonelli, Alfred. (2007). Biomarkers, metabonomics, and drug development: Can inborn errors of metabolism help in understanding drug toxicity?. The AAPS journal. 9. E284-97.

Final diagnosis



[redacted]

Lab No. : 121225177 Age: 10 Days Gender: Male

A/c Status : P

[redacted]

Collected : 5/7/2015 2:47:00PM
Received : 5/7/2015 2:57:26PM
Reported : 9/7/2015 4:05:45PM
Report Status : Final

NEWBORN SCREENING, EXTENDED

IMD PANEL, QUANTITATIVE , BLOOD *Amino Acids*Organic Acids* Fatty Acid oxidation disorders (Tandem Mass Spectrometry)

Test Name	Results	Units	Bio. Ref. Interval
AMINO ACIDS @			
Alanine	277.27	µmol/L	<1270
Arginine	285.44	µmol/L	<132
Citrulline	58.82	µmol/L	<70
Glycine	327.00	µmol/L	<505
Leucine	146.00	µmol/L	<385
Methionine	33.27	µmol/L	<77
Ornithine	49.45	µmol/L	<278
Phenylalanine	64.81	µmol/L	<165
Tyrosine	128.00	µmol/L	<550
Valine	129.00	µmol/L	<306
FREE CARNITINE (C0) @	54.72	µmol/L	8 - 100
ACYLCARNITINES @			
Acetylcarnitine (C2)	53.40	µmol/L	8 - 150
Propionylcarnitine (C3)	2.00	µmol/L	<6
Butyrylcarnitine (C4)	0.51	µmol/L	<2
Isovalerylcarnitine (C5)	0.48	µmol/L	<1.70
Glutarylcarnitine (C5DC)	0.53	µmol/L	<0.84
C5OH	0.46	µmol/L	<0.68
C5:1	0.03	µmol/L	<0.24
Hexanoylcarnitine (C6)	0.15	µmol/L	<0.72
Octanoylcarnitine (C8)	0.50	µmol/L	<0.51
Decanoylcarnitine (C10)	0.14	µmol/L	<0.40
Lauroylcarnitine (C12)	0.21	µmol/L	<0.94
Myristoylcarnitine (C14)	0.70	µmol/L	<0.70
Palmitoylcarnitine (C16)	6.47	µmol/L	<12.50
Octadecanoylcarnitine (C18)	1.68	µmol/L	0.60 - 3.50

Impression
Arginine raised.
Advised- Arginase activity in blood.

MedGenome Labs Ltd.
3rd Floor, Narayana Nethralaya Building, Narayana Health City,
#258/A, Bommasandra, Hosur Road, Bangalore - 560 099, India.
Tel : +91 (0)80 67154989 / 990, Web: www.medgenome.com

MEDGENOME

DNA TEST REPORT - MEDGENOME LABORATORIES

[redacted]

Gender:	Male	Order ID/Sample ID:	**356099/7386780**
Date of Birth / Age:	6 years	Sample Type:	Blood
Referring Clinician:	Dr. Rajni Farmania, Max Healthcare Institute Limited, New Delhi	Date of Sample Collection:	30th November 2021
		Date of Sample Receipt:	30th November 2021
		Date of Order Booking:	30th November 2021
		Date of Report:	29th December 2021
Test Requested:	**Whole Exome Sequencing**		

CLINICAL DIAGNOSIS / SYMPTOMS / HISTORY

Baby *Riyansh Kumar*, born of a non-consanguineous marriage, presented with clinical indications of microcephaly, spasticity, global developmental delay, calf hypertrophy, and hypoglycemia. Laboratory investigation showed elevated CPK levels. His brain and spine MRI were normal. He is suspected to be affected with Hereditary spastic paraplegia and has been evaluated for pathogenic variations.

RESULTS

PATHOGENIC VARIANT CAUSATIVE OF THE REPORTED PHENOTYPE WAS DETECTED

Gene# (Transcript)	Location	Variant	Zygosity	Disease (OMIM)	Inheritance	Classification
ARG1 **(+)** (ENST00000356962.2)	Intron 4	c.490-2A>G **(3' Splice site)**	Homozygous	Argininemia	Autosomal recessive	Pathogenic

$Genetic test results are reported based on the recommendations of American College of Medical Genetics [1].

ADDITIONAL FINDINGS: NO VARIANT(S) OF UNCERTAIN SIGNIFICANCE (VUS) DETECTED

All the genes covered in the whole exome assay have been screened for the given clinical indications. To view the coverage of all genes *Click here*

Literature review

Arginase deficiency

- Hyperargininemia is a rare AR metabolic disorder caused by the deficiency of the enzyme arginase I.
- Incidence of 1 in 2 million live births.
- The common phenotype is quite distinct from that of other urea cycle disorders
- Hyperammonemic encephalopathy is uncommon.
- Manifest with insidious onset of spastic paraplegia, cognitive deficiency, and epilepsy during childhood.
- Because of the slow progression of signs, the typical presentation of hyperargininemia can be mistaken for cerebral palsy

Clinical Features and Neurologic Progression of Hyperargininemia. Pediatric Neurology 46 (2012).

Pathophysiology

- Majority of neurotoxicity of arginase deficiency is suspected to result from alternative conversion of arginine that leads to activation of Nitric oxide synthase.
- Increased levels of Nitric oxide and causing oxidative damage, and guanidino compounds including guanidine and guanidinosuccinic acid.
- Correlated with epileptogenic effects and cognitive decline due to disruptions in the GABA neurotransmission

Pediatric Neurology 46 (2012) 369–374

Contents lists available at ScienceDirect

PEDIATRIC NEUROLOGY

Table 2. Neurodevelopmental features, neurologic presentation, and progression of disease in 16 patients with hyperargininemia

Patient Number	Age at Diagnosis (yr)	Age at Acquisition of Gait (mo)	First Neurologic Sign	Onset of LLS/Age at Loss of Gait (yr)	Spasticity of the Upper Limbs	Other Neurologic Features	Spoken Language*	Worsening of Language Function	Sphincter Control (yr)	Urinary Incontinence or Urgency	Cognitive Skills/Mental Retardation
1	10	12	36 mo, LLS	5	Severe		Sentence	Loss of spoken language, 7 yr	2	I, 5 yr	F/severe
2	12	17, abnormal	17 mo, LLS	4	Severe	Choreic movements	Sentence	Loss of spoken language, 10 yr	2-3	I, 12 yr	F/severe
3	7	11	21 mo, LLS	3	Moderate		No		No		F/severe
4	7	11	22 mo, LLS	3	Mild		No		No		F/severe
5	12	13	15 mo, LLS	5	Mild		No		<2		F/severe
6	14	13	16 mo, LLS	6	No		Sentence	Decrease of vocabulary	<2		S, F/moderate
7	15	12	33 mo, seizure	4/13	Mild		Sentence	No	2-3		S, F/moderate
8	6	30, abnormal	3 mo, seizure	2.5/No	No		Sentence	No	2-3		S, F/moderate
9	14	17	4 yr, LLS	9	No		Sentence	Decrease of vocabulary	2-3		S, F/moderate
10	5	16	36 mo, LLS	6	No		Sentence	Decrease of vocabulary	No		S, F/moderate
11	6	16	18 mo, LLS	7	No		Sentence	No	2-3		S, F/moderate
12	6	14, abnormal	14 mo, LLS	13	No	Hyperactivity, ataxia	Sentence	No	2-3	U, 10 yr	S, F/moderate
13	18	12	24 mo, upper limb tremor	10/14	No	Ataxia	Narrative	Decrease of vocabulary	<2	U, 22 yr	R, S, F/mild
14	21	8	4 yr, seizure	5/16	Mild		Narrative	Decrease of vocabulary	2-3		R,S,F/ mild
15	21	12	10 yr, LLS	13	No	Involuntary tremor of upper limbs	Narrative	No	2-3		R, S, F/mild
16	27	28	7 yr, LLS	27	No		Narrative	No	2-3 yr		R, S, F/mild

Abstract

Arginase deficiency is a rare autosomal recessive urea cycle disorder (UCD) caused by mutations in the *ARG1* gene encoding arginase that catalyses the hydrolysis of arginine to ornithine and urea. Patients have hyperargininaemia and progressive neurological impairment but generally suffer fewer metabolic decompensations compared to other UCDs. The objective is to describe the clinical features, biochemical profile, neuroradiological findings and experience of managing children with arginase deficiency. Twenty-year retrospective review of patient medical records at a single metabolic centre was performed. Six patients from three unrelated families were identified. Mean age at first symptom was 3.3 (1.5–9.0) years, while mean age at diagnosis was 8.8 (0.16–15.92) years. Four patients developed spastic diplegia and two of six with spastic quadriplegia with classical features including hyperreflexia, clonus and toe walking. This resulted in gait abnormalities that have been monitored using the GAITRite system and required Achilles tendon release in five children. Generalised tonic-clonic seizures and/or absences were present in three of six children and were controlled with anticonvulsants. All patients had moderate learning difficulties. Neuroimaging showed cerebral/cerebellar atrophy in four patients and basal ganglia abnormalities in two. Arginine levels were universally elevated throughout follow-up despite protein restriction, essential amino acid supplementation and ammonia scavengers, and neurological outcome was generally poor. Two patients died following severe metabolic decompensation in adolescence. Children with arginase deficiency continue to present a management challenge of what appears to be an inexorable course of neurocognitive impairment. Further insight into disease mechanisms may provide insight into novel treatment strategies.

KEYWORDS

arginase deficiency, hyperammonaemia, metabolic decompensation, trial end points, urea cycle disorder

JIMD REPORTS SSIEM WILEY

d management of a
e deficiency

. Alderson[2,3] |
eeney[1] | Marjorie Dixon[5] |
os[1]

Dietary restriction of protein

Providing essential aminoacids

Preventing metabolic decompensations of hyperammonemia with scavengers

Learning points: Case 1

- Spastic paraplegia has many differentials other than cerebral palsy
- History and MRI will give the clue that it’s a mimic
- Metabolic disorders though rare, are worth suspecting and investigating
- Appropriate management since early age might improve the disease course.

Case 2

- A 9-month-old boy presented with:

-Delayed attainment of motor milestones

-Normal socio-cognitive milestones

-No history of seizures

Birth details: Non- consanguineous marriage, G6 P2 A4

Antenatal- gestational diabetes mellitus, hypothyroid, PIH

Natal: PT36 week, 2.4Kg, cried immediately, NNJ not requiring phototherapy.

Case 2

Family: First sib, 11-year-old girl, alive and healthy

Four 1st TM miscarriages

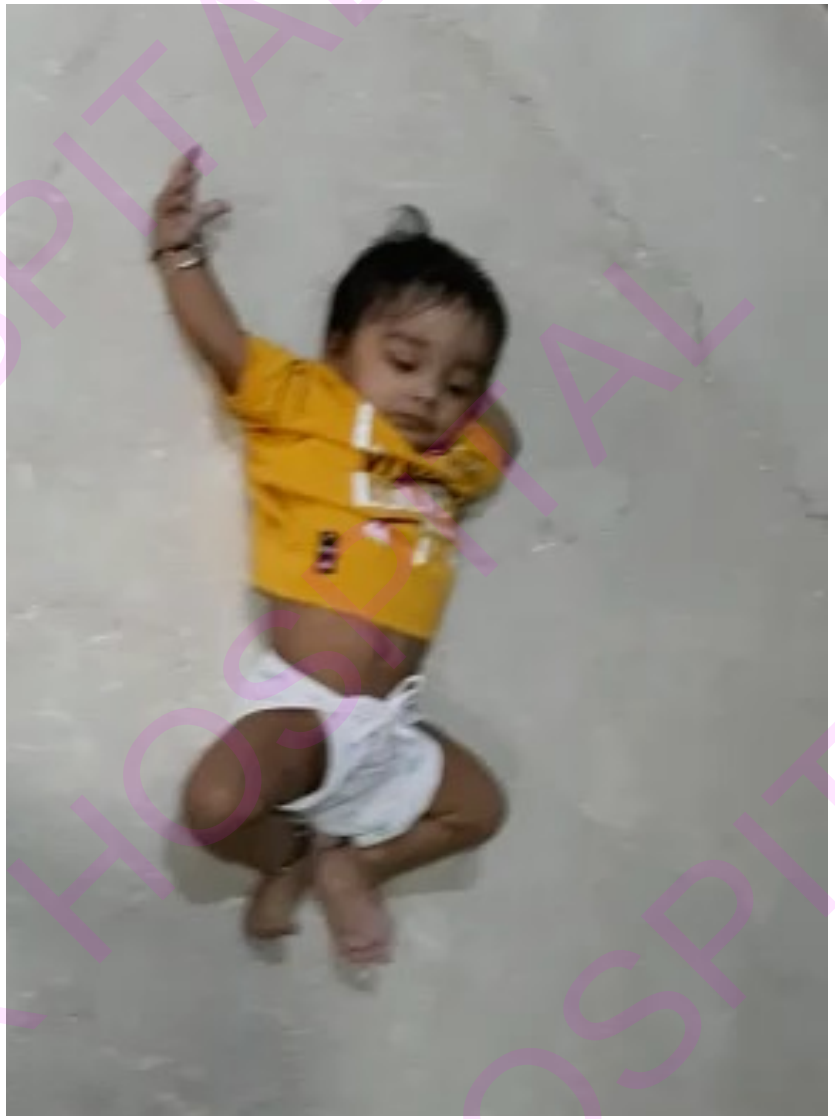
Distant cousin, the girl had a history of neuro regression from the age of 4 years and expired at 11 years of age

Development: Predominant motor delay

- Motor: able to hold head partially, not able to roll over (dev age around 4 months)
- Socio cognitive: Response to name present, stranger anxiety present (around 8 months)
- Language: babbling present
- Vision and hearing: normal

Clinical video:

Alert, active
Abnormal hand movement
Rigidity



Differentials:

- Dyskinetic cerebral palsy
- Metabolic disorder: Glutaric aciduria, Mitochondrial (Leigh's disease)
- Other genetic disorder

Investigations:

MRI brain: Normal

Blood: Normal complete blood count,
Thyroid profile, Vitamin B12

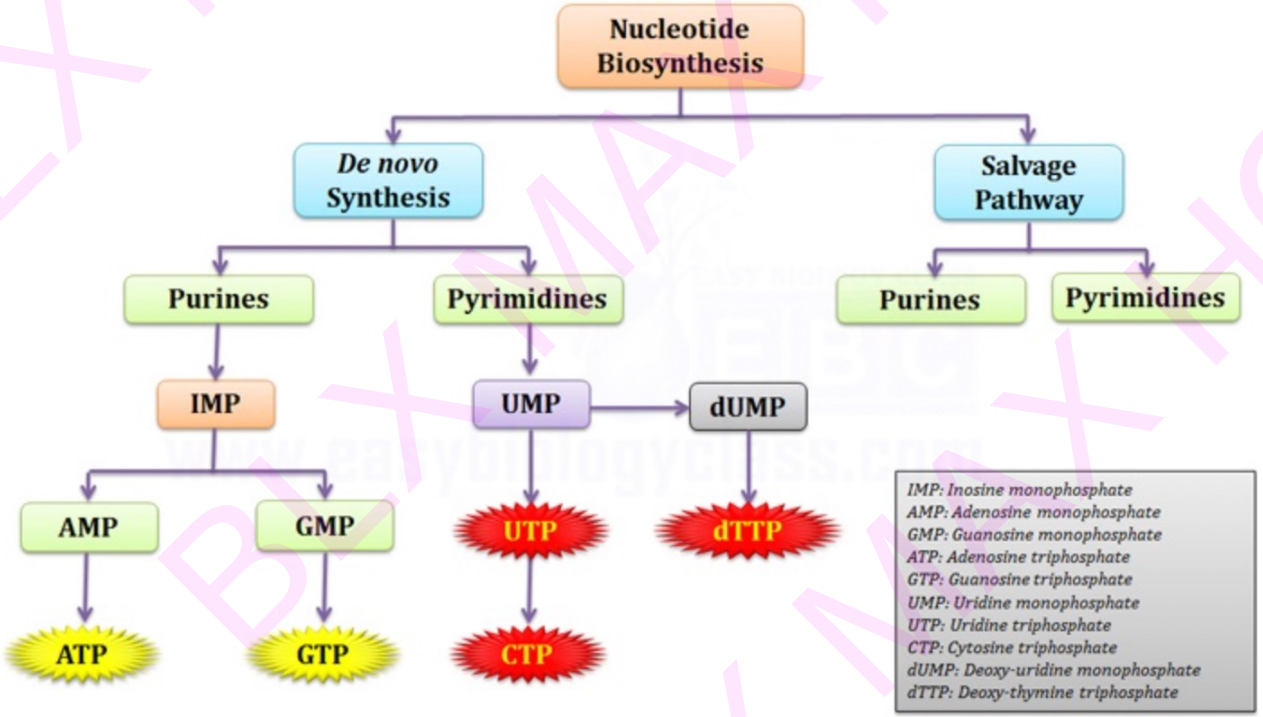
High uric acid (8 mg/dl)

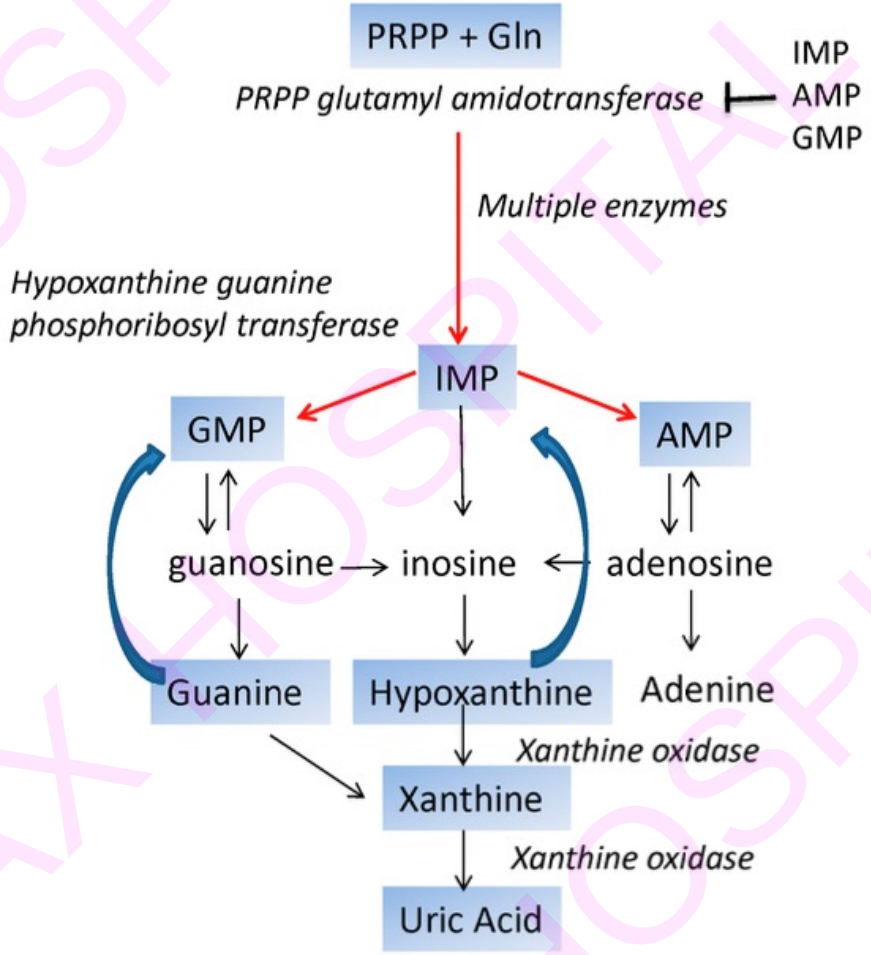
Differentials for uric acid abnormality

	Disorder	Symptoms	Serum uric acid	Excretion of uric acid in urine (uric acid/creat ratio)
1	Xanthine oxidase deficiency	Hematuria and calculus in bladder	Low uric acid	Low excretion
2	Molybdenum cofactor deficiency	Severe neurodevelopmental delay with seizures	Low uric acid	Low uric acid excretion Increased excretion of xanthine, hypoxanthine and sulfocysteine
3	Hereditary renal hypouricemia	Hematuria and calculus	Low	Increased
4	Lesch Nyhan syndrome	Motor delay Dystonia Renal calculus and failure Self mutilation	Increased	Increased

Jasinge *et al. BMC Res Notes (2017) 10:454*
DOI 10.1186/s13104-017-2795-2

Purine metabolism





DNA TEST REPORT - MEDGENOME LABORATORIES

[redacted]

Gender:	Male	Order ID/Sample ID:	**206914/442509**
Date of Birth / Age:	10 months	Sample Type:	Blood
Referring Clinician:	Dr. Rajni Farmania, Blk Super Speciality Hospital, New Delhi	Date of Sample Collection:	15th September 2020
		Date of Sample Receipt:	17th September 2020
		Date of Order Booking:	17th September 2020
		Date of Report:	12th October 2020
Test Requested:	**Clinical Exome**		

CLINICAL DIAGNOSIS / SYMPTOMS / HISTORY

Baby *Mehan Rustagi*, born of a non-consanguineous marriage, presented with clinical indications of motor delay, speech and socio-cognitive delay, extrapyramidal signs in the form of rigidity and dystonia. His MRI and TMS were normal and laboratory investigations showed elevated ammonia, lactate, prolactin and uric acid. His mother has history of four missed abortions. There is a history of neuroregression in two children in the extended family who expired at the age of 11 years. Baby *Mehan Rustagi* is suspected to be affected with Lesch-Nyhan syndrome or neurotransmitter defect and has been evaluated for pathogenic variations.

RESULTS

PATHOGENIC VARIANT CAUSATIVE OF THE REPORTED PHENOTYPE WAS DETECTED

Gene (Transcript) #	Location	Variant	Zygosity	Disease (OMIM)	Inheritance	Classification
HPRT1 **(+)** (ENST00000298556.8)	Intron 5	c.403-2A>G **(Splice variant)**	Hemizygous	Lesch-Nyhan syndrome	X-linked recessive	Pathogenic

Pathophysiology of neurological dysfunction

Relative deficiency of GTP lead to decreased dopamine receptor activation is the probable mechanism

Areas of high dopamine concentration: Caudate, putamen, Nu. accumbens are most affected

Neurological features in Lesch Nyhan Syndrome

- Hypotonia, developmental delay
- Extrapyramidal features (action dystonia) after 8 months
- Choreoathetoid movements and ballismus in first few years
- Self mutilation after 2-3 years

Case Reports > Pediatr Nephrol. 2008 Jan;23(1):155-8. doi: 10.1007/s00467-007-0588-x. Epub 2007 Aug 16.

Lesch-Nyhan syndrome presenting with acute renal failure in a 3-day-old newborn

Ivana Pela [1], Maria Alice Donati, Elena Procopio, Patrizio Fiorini

Affiliations + expand

PMID: 17701224 DOI: 10.1007/s00467-007-0588-x

Abstract

Acute renal failure developed during the first 3 days after birth in a newborn subsequently diagnosed with hypoxanthine-guanine-phosphoribosyl-transferase (HPRT) deficiency. Fluid infusion and allopurinol therapy normalised renal function and serum uric acid levels. Only a few cases of acute renal failure due to acute hyperuricemic nephropathy related to HPRT deficiency have previously been reported in infants, and there are no reported cases in newborns as young as 3 days old.

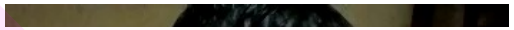
topnaceous gout are unusual presenting features of this rare condition. This child also had transient neonatal hypothyroidism, which is not a recognized manifestation of the syndrome.

Learning points: Case 2

- Normal MRI brain in a child with the developmental delay with pyramidal or extrapyramidal signs must be investigated

- Uric acid is an important and simple screening test in cases of developmental delay.

Case 3



CLINICAL INFORMATION/HISTORY

Shivani is a 3 years old girl, who presented with global developmental delay, features of autism, socio-cognitive delay, motor delay, prefer right hand over left, do not recognize parents and able to walk did not climb stairs. She has been evaluated for the gene variation related to the phenotype.

RESULT SUMMARY

Pathogenic variant causative of the reported phenotype was identified

*Correlation with clinical profile and family history is required

FINDINGS RELATED TO PHENOTYPE

Gene & Transcript	Variant	Location	Zygosity	Disorder (OMIM)	Inheritance	Classification
MECP2 NM_001110792.2	c.353G>A (p.Arg118Gln)	Exon 2	Heterozygous	Rett syndrome (312750)	X-linked Dominant	Pathogenic

All children with motor delay with abnormal tone are non cerebral palsy

Clinical pointers for CP Mimics

- Absent history of any perinatal risk factor for brain injury
- Family history of a sibling with similar neurological symptoms
- Motor symptom onset after an initial period of normal development
- Developmental regression
- Progressive neurological symptoms
- Paroxysmal motor symptoms or marked fluctuation of motor symptoms
- Clinical exacerbation in the setting of a catabolic state (e.g., febrile illness)
- Isolated generalized hypotonia
- Prominent ataxia
- Signs of peripheral neuromuscular disease (reduced or absent reflexes, sensory loss)
- Eye movement abnormalities (e.g., oculogyria, oculomotor apraxia, or paroxysmal saccadic eye-head movements)

Pearson TS, Pons R, Ghaoui R, Sue CM. Genetic mimics of cerebral palsy. Mov Disord. 2019 May;34(5):625-636

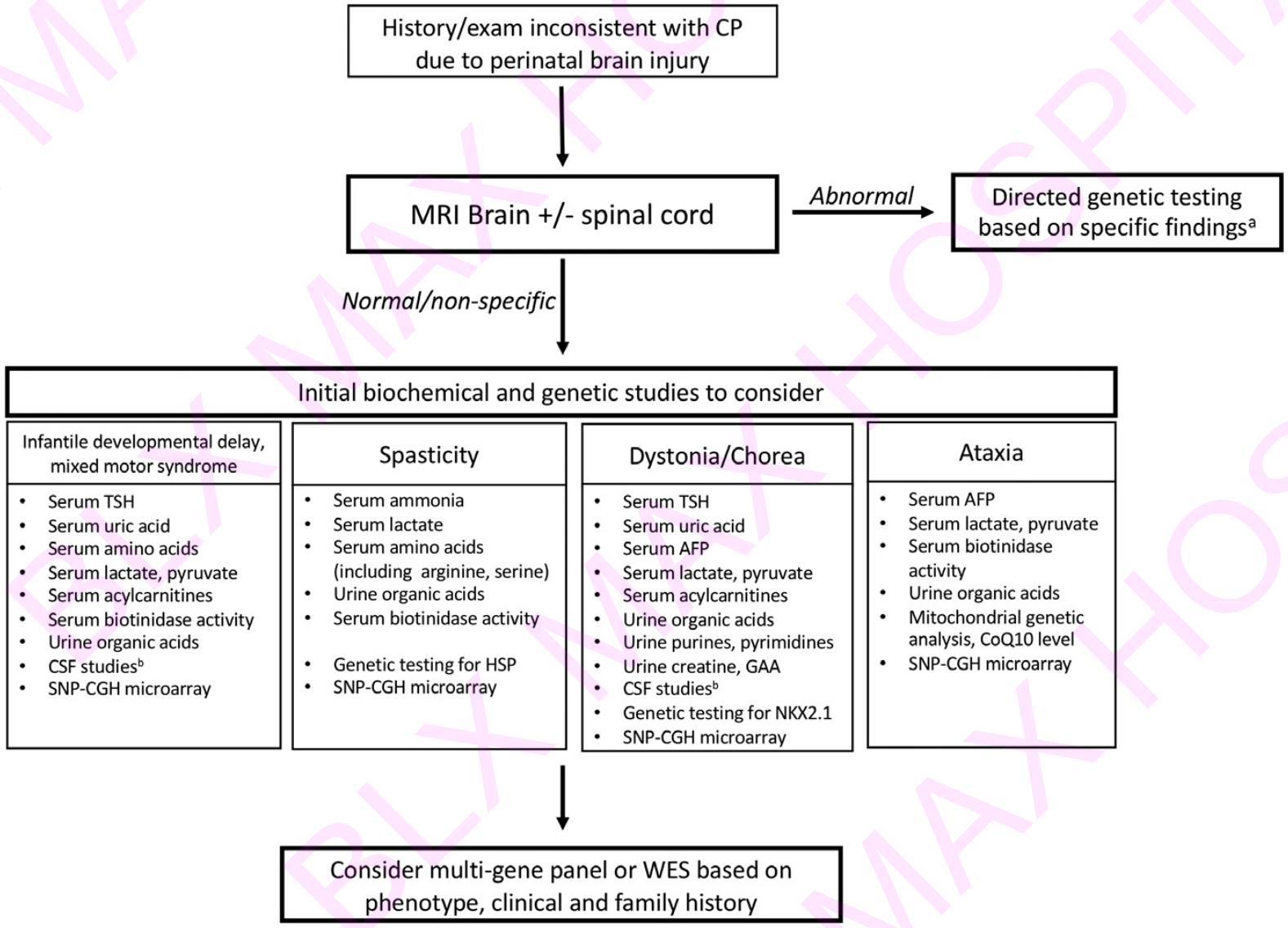
Suspected metabolic genetic disorder by most prominent motor symptoms

Disorders with prominent spasticity	Disorders with prominent dyskinesia	Disorders with prominent ataxia
- Hereditary spastic paraglegias - Arginase deficiency - COL4A1-Related spastic CP - Biotinidase deficiency - Aicardi-Goutières syndrome - Sulfite oxidase deficiency/ Molybdenum cofactor deficiency[22] - Leukodystrophies, such as metachromatic leukodystrophy,[23] adrenoleukodystrophy,[24] Sjorgen Larsson syndrome[25]	- Dopa-responsive dystonia - Sepiapterin reductase deficiency - Glutaric aciduria type 1 - Glucose transporter deficiency type 1 - Neurodegeneration with brain iron accumulation - Cerebral creatine deficiency syndrome - Lesch Nyhan syndrome - Cerebral folate deficiency - ADCY5-related dyskinesia - PCDH12-related dyskinesia[34] - NKX2-1 related ataxic dyskinetic CP[35] - TSEN54 Gene-related pontocerebellar hypoplasia type 2[36]	- Glucose transporter deficiency type 1 - Ataxia telangiectasia - Pelizaeus-Merzbacher disease - Hereditary ataxias - Joubert syndrome - Mitochondrial cytopathies (mainly 8993 mutation)[42] - Pontocerebellar hypoplasia[36] - Cockayne syndrome[43] - Niemann-Pick disease type C[44] - Angelman syndrome[12] - Gangliosidosis type 1 , juvenile and adult forms[45] - Non-ketotic hyperglycinemia[3] - Maple syrup urine disease[3] - NKX2-1 related ataxic dyskinetic CP[35]

CP- cerebral palsy

Hakami WS, Hundallah KJ, Tabarki BM. Metabolic and genetic disorders mimicking cerebral palsy. Neurosciences (Riyadh). 2019 Jul;24(3):155-163

Approach



Pearson TS, Pons R, Ghaoui R, Sue CM. Genetic mimics of cerebral palsy. Mov Disord. 2019 May;34(5):625-636

Key take aways

- All cases of motor delay are not always cerebral palsy
- Investigate cases where history is atypical
- Most prominent type of motor symptoms should be identified
- MRI may give direct clue to diagnosis
- Judiciously investigate cases for metabolic and genetic etiology

THANK YOU