	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10	Case 11	Case 12	Case 13	Case 14	Case 15	Case 16	Case 17	Case 18	Case 19	Case 20
***SLC19A3* DNA Variant**[a]	c.1264A>G (homozygous)	c.1264A>G (homozygous)	c.1264A>G (homozygous)	c.1264A>G (homozygous)	c.1264A>G (homozygous)	c.1264A>G (homozygous)	c.1264A>G (homozygous)	c.1264A>G (homozygous)	c.1264A>G (homozygous)	c.1264A>G (homozygous)	c.1264A>G (homozygous)	c.1264A>G (homozygous)	c.1264A>G (homozygous)	c.1264A>G (homozygous)	c.1264A>G (homozygous)	c.1264A>G (homozygous)	c.1264A>G (homozygous)	c.1264A>G (homozygous)	c.1264A>G (homozygous)	c.1264A>G (homozygous)
***SLC19A3* Protein Variant**	p.Thr422Ala	p.Thr422Ala	p.Thr422Ala	p.Thr422Ala	p.Thr422Ala	p.Thr422Ala	p.Thr422Ala	p.Ala318Thr	p.Thr422Ala	p.Thr422Ala	p.Thr422Ala	p.Thr422Ala	p.Thr422Ala	p.Trp59Arg	p.Thr422Ala	p.Thr422Ala	p.Thr422Ala	p.Thr422Ala	p.Thr422Ala	p.Thr422Ala
Novel Variant	No	No	No	No	No	No	No	Yes	No	No	No	No	No	Yes	No	No	No	No	No	No
Age at diagnosis	32 years	20 years	2.5 years	3 years	5 years	2 years	2 years 2 months	3 years	4.5 years	2 years	3 years	1 year (by screening)	3 years	2.5 years	2.5 years, (by screening)	1.5 years	2 years 11 months	3 years	2 years	At birth, by screening)
Current age	36 years	25 years	23 years	18 years	17 years	15 years	12 years	10 years	10 years	9 years	9 years	8 years	8 years	8 years	6 years	5years	4 years	3 years	2.5 years	2 years
Gender	Male	Male	Female	Male	Male	Female	Female	Female	Male	Female	Female	Male	Male	Female	Male	Female	Male	Male	Female	Female
Nationality	Kuwaiti	Non-Kuwaiti	Kuwaiti	Kuwaiti	Kuwaiti	Kuwaiti	Kuwaiti	Kuwaiti	Kuwaiti	Kuwaiti	Kuwaiti	Kuwaiti	Kuwaiti	Jordanian	Kuwaiti	Kuwaiti	Kuwaiti	Kuwaiti	Kuwaiti	Kuwaiti
Consanguinity	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Family history	-2 affected cousins **(Case 2 &16)** -Leigh disease -Type 1 diabetes mellitus -Mitochondrial dysfunction	-2 affected cousins **(case 1 & 16)** -Cousin with Leigh disease **(Case 1)**	-Affected sibling **(Case 4)** and niece **(Case 19)**	-Affected sibling **(Case 3)** and niece **(Case 19)**	-Unremarkable	- Affected sibling **(Case 7)** - 2 paternal cousins with Leigh's disease	- Affected sibling **(Case 6)**	-Unremarkable	-Affected sibling **(Case 15)**	-2 affected siblings **(Case 12&20)**	-A relative with metabolic disease	-2 affected siblings **(Case 10&20)**	-Unremarkable	-Infant deaths in cousins	-Affected sibling **(Case 9)**	- 2 affected cousins **(case 1&2)**	-Unremarkable	-3 early miscarriages -Hypothyroidism -Absence seizure on Depakene	-Affected maternal uncle & aunt **(Case 3&4)**	-2 affected siblings **(Case 10&12)**
GDD/ID	+	-	+	+	+	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-
Dysmorphic features	Hypertelorism, telecanthus, bilateral epicanthic fold synophy, prominent nasal bridge, anteverted nostril, high arched palate, interdigital webbing, long fingers, wide space between the first and second toes and shawl scrotum	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Long eyelashes	-	-
Skeletal findings	-	-	Scoliosis	-	Scoliosis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Drowsiness/ irritability/ lethargy	+	+	+	-	+	-	-	-	+	+	+	-	+	+	-	-	-	+	-	-
Convulsions	+	+	-	+	+	+	-	+	-	-	-	-	-	+	-	-	-	-	-	-
Hypertonia / contractures Dystonia / Choreoathetosis	-	+	+	+	+	-	-	+	-	+	-	-	+	+	-	-	-	+	+	-
Tremor	-	+	-	-	-	-	-	-	+	-	-	-	+	-	-	+	-	-	-	-
Hypotonia	+	+	-	+	-	-	-	-	-	+	-	-	+	+	-	-	-	-	-	-
Poor head control	-	+	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Limping/unsteady/ataxic gait	-	+	+	+	-	+	+	+	+	+	+	-	+	-	-	-	+	+	+	-
Dysarthria/ drooling/ nasal speech	-	+	+	+	-	-	-	+	-	+	-	-	-	-	-	+	-	-	-	-
Nystagmus / strabismus / abnormal gaze	-	-	+	-	-	+	-	-	-	-	-	-	-	+	-	-	-	+	+	-
Drooling	-	+	-	-	+	-	-	+	-	-	-	-	-	-	-	-	-		+	-
Chronic constipation	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
PICU admission	-	-	-	-	-	-	-	-	-	-	-	-	+, For irritability and acute encephalopathy	+, For apnea, desaturation and respiratory acidosis and MRSA in throat swab	-	-	-	-	-	-
Neonatal history	FT, NVD	FT, CS, Bwt 2.5kg	Not reported	FT, NVD, Bwt 2.5 kg	FT, NVD, Bwt 3.5kg	FT, NVD, Bwt 3 kg	FT, NVD, Bwt 3.5 kg	FT, NVD	PO 28, NVD, Bwt 800kg	FT, NVD, Bwt 3.5kg	FT, NVD, Bwt 3.1kg	FT, NVD, Bwt >4kg	FT, NVD, Bwt 2.9kg	FT, NVD, Bwt 3kg	FT, NVD, Bwt 1kg	FT, NVD, Bwt 3kg	FT,NVD, Bwt 3kg	FT, NVD, Bwt 2.7kg	FT, NVD	FT, NVD, Bwt 3.5 kg
Perinatal history	Gestational HTN on treatment &	Gestational HTN on methyldopa	Not reported	-	-	-	-	-	NICU admission for LBW	IEM	-	-	-	PFO, tiny closing PDA	ASD	-	-	Maternal hypothyroidism & 3 early	-	-

	maternal IDA on iron injections, Child NNJ & RD																	miscarries after this child Maternal aunt with childhood absence seizure controlled with Depakene		
Other	-	-	-	-	-	-	-	-	-	-	-	-	-	Mild elevated lactate level in blood and CSF	-	-	-	-	-	-
Brain MRI	Bilateral signal alteration in lentiform nucleus; f/u: subacute necrotizing encephalopathy	Bilateral corpus striatum signal alteration with lentiform dystrophic calcification associated with normal brain parenchyma; f/u: reduction in size with some atrophic changes	Bilateral corpus striatum signal alteration with central necrosis at the head of caudate nuclei, restricted diffusion at the outer aspect of lentiform nuclei and central dysmorphic calcifications	Bilateral swelling and diffuse hyperintensity of putamen. Follow up MRI revealed corpus striatum atrophy with multiple hyperintense foci of necrosis.	Bilateral symmetrical involvement of the basal ganglia and thalamus.	Acute diffuse gray matter metabolic disease involving deep gray matter and basal ganglia suggestive of mitochondrial disease	Initially normal, then at age of 6 years it progressed to develop bilateral putamen mild cystic changes	Cortical and subcortical hyperintensities at both cerebellar hemispheres and cerebral parenchyma as well as bilateral caudate and putamen.	Symmetrical bilateral basal ganglia involvement affecting the lentiform nuclei as well as the medial portion of the thalamic nuclei	Bilateral symmetrical hyperintensity with diffused restriction and swelling in caudate nuclei and putamen, sparing the globus pallidus	Bilateral symmetrical central necrosis of basal ganglia	Not done	Symmetrical diffusely swollen lentiform and caudate nuclei with lentiform fork sign; f/u: showed regression course with reduction of lentiform and caudate nuclei size bilaterally associated with abnormal signals representing old insults	Symmetrical bilateral lentiform hyperintensity sparing the caudate, with central hypointensity and peripheral hyperintensity, suggestive of edema and query brain insult of glycolysis; f/u: bilateral infarction with symmetrical restricted diffusion reduced in severity suggestive of MELAS, CADASIL or Krabbe	Not Done	Bilateral symmetrical central necrosis of basal ganglia	Bilateral symmetrical central necrosis of basal ganglia	Multiple scattered hyperintensity lesions at the cortical and subcortical cerebral parenchyma as well as bilateral caudate, putamen and medial thalamic nuclei; some of these areas showed diffusion restriction on DWI	Bilateral hyperintensity of putamen with central necrosis.	Not done
Current medications	Valproic acid (Depakene), vitamin B6, thiamine, clonazepam drops (Rivotril), biotin supplement, coenzyme Q10 & carnitine	Vitamin B6, vitamin B complex, L-carnitine syrup, coenzyme Q10, biotin and thiamine supplementation	Biotin and thiamine supplementation	Vitamin B6, vitamin B complex, biotin and thiamine supplementation	Carbamazepine (Tegretol), clonazepam and baclofen, biotin and thiamine supplementation	Coenzyme Q10, L.carnitine, vitamin B6, thiamine, and B complex supplementation	Coenzyme Q10, L.carnitine, vitamin B6, thiamine, and B complex supplementation	Biotin and thiamine supplementation (Not compliant & disadvantage home situation)	Biotin and thiamine supplementation	Biotin and thiamine supplementation	Biotin and thiamine supplementation	Biotin and thiamine supplementation	Biotin and thiamine supplementation	Biotin, thiamine, vitamin B6, vitamin B complex, coenzyme Q10, L-carnitine and ketogenic diet.	Biotin and thiamine supplementation	Biotin and thiamine supplementation	Biotin and thiamine supplementation	Biotin and thiamine supplementation	Biotin and thiamine supplementation	Biotin and thiamine supplementation
Residual neurological deficit	+	+	-	-	+ wheelchair bound	-	-	- but multiple relapses and admissions due to stopping medication by caregiver	-	-	-	-	+	+ MV dependent, NGT feeding, Bed-ridden	-	-	-	-	-	-

Supplementary Table S3: Overview of individuals diagnosed with Biotin Thiamine Responsive Basal Ganglia Disease in Kuwait (n=20).
Abbreviations: ASD, atrial septal defect; BG, basal ganglia; Bwt, birth weight; CADASIL, cerebral autosomal dominant arteriopathy with sub-cortical infarcts and leukoencephalopathy ;CS, cesarian section; CSF, cerebral spinal fluid; CT, computed tomography; DWI, diffusion-weighted images; FT, full-term; f/u, follow up; FLAIR, fluid-attenuated inversion recovery; GDD, global developmental delay; HTN, hypertension; ID, intellectual disability; IDA, iron deficiency anemia; IEM, inborn errors of metabolism; Kg, kilogram; LBW, low birth weight; MELAS, mitochondrial encephalomyopathy lactic acidosis and stroke-like episodes; MRI, magnetic resonance imaging; MRSA, methicillin-resistant Staphylococcus aureus; MV, mechanical ventilator; NA, not applicable; NGT, nasogastric tube; NICU, neonatal intensive care unit; NNJ, neonatal jaundice; NVD, normal vaginal delivery, PDA, patent ductus arteriosus; PFO, patent foramen ovale; PICU, pediatric intensive care unit; PO, product of; RD, respiratory distress;
*** The reference transcript is NM_025243.4**