

Supplementary Table S1

Plasma amino acids and urine organic acids alterations in our case at the age of 23 months.

	This case	Normal value
Plasma amino acids		
Alanine	520 umol/l	167-389
Valine	381.33 umol/l	140-302
Isoleucine	100.26 umol/l	31-88
Urine organic acids		
Lactate	235 umol/mmol	< 50
Pyruvate	305 µmol/mmol	< 20
Ethylmalonic acid	39 µmol/mmol	< 20
Succinic acid	98 µmol/mmol	< 20
Fumaric acid	118 µmol/mmol	< 10
Glutaric acid	202 µmol/mmol	< 10
2-OH-glutaric acid	165 µmol/mmol	< 20
Ketoglutaric acid	1200 µmol/mmol	< 120

Supplementary Table S2

In silico pathogenicity predictions for *COX11* mutation c.739C>A (p.P247T)

<i>In silico</i> tool	Predictions
CADD	deleterious (26.1)
MetaRNN	damaging (0.8927)
REVEL	pathogenic (0.5889)
PolyPhen-2	probably damaging (0.999)
SIFT	damaging (0.003)
MutationTaster	disease causing (1)
EIGEN	pathogenic (0.8179)

CADD (<http://cadd.gs.washington.edu/>); MetaRNN (<http://www.liulab.science/metarnn.html>)

REVEL (<https://sites.google.com/site/revelgenomics/>); PolyPhen-2

(<http://genetics.bwh.harvard.edu/pph2>); SIFT (<https://sift.bii.a-star.edu.sg/index.html>); Mutation

Taster (<http://www.mutationtaster.org>); EIGEN (<http://www.columbia.edu/~ii2135/eigen.html>).

Supplementary Table S3

Spectrophotometric determination of RC activities in patient skeletal muscle

Enzyme	Activity	Normal Range
NADH:ubiquinone oxidoreductase (Complex I)	25.06 (2.01)	27.5-39.5 (1.56-2.60)
Succinate dehydrogenase (Complex II)	1.82 (0.15)	1.2-2.0 (0.05-0.105)
NADH cytochrome c oxidoreductase (Complexes I+III)	2.14 (0.17)	0.65-1.50 (0.11-0.25)
Succinate cytochrome c reductase (Complexes II+III)	0.56 (0.04)	0.45-0.90 (0.05-0.08)
Cytochrome c oxidase (Complex IV)	2.89 (0.23)	1.80-2.45 (0.17-0.28)
Citrate synthase (CS)	12.44	8.91-15.00

Activities are expressed in nmol/min/gr tissue. In brackets the values normalized to the activity of CS