Two Cousins with the Allan-Herndon-Dudley Syndrome Caused by a Novel MCT8 Mutation

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Background

- **MCT8 (monocarboxylate transporter 8)** is an active and specific thyroid hormone transporter encoded by a gene located on the X chromosome.
- MCT8 mutations in males cause a rare X-linked disorder known as the **Allan-Herndon-Dudley syndrome (AHDS),**
- It is characterized by severe psychomotor retardation and abnormal thyroid parameters (*high T3, low T4 and normal/high TSH*).

Case -1: 4-year and 9-month old boy

- On L-T4 treatment for hypothyroidism
- Congenital hydrocephaly, cerebral palsy and epilepsy.
- Severe neuromotor retardation
- Complete blindness
- The parents were non-consanguineous.
- Family history: similar neuromotor deficits and epilepsy at his uncle and cousin.
- Physical examination revealed severe central hypotonia
- Exaggerated deep tendon reflexes.
- Weight: 18.7 kg (P50),
- Height: 106 cm (P10-25),
- Head circumference: 47 cm (P3-10, -1.29 SDS).
- No goiter
- Unilateral cryptorchidism

Case-2: 2-year and 9-month old boy

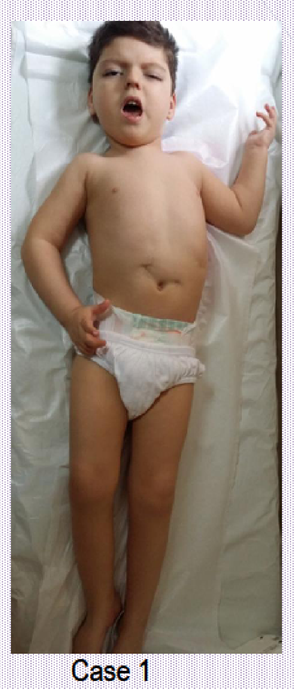
- Cousin of first case
- Severe neuromotor retardation
- Complete blindness
- Weight 9,5 kg (-3,1 SDS)
- Head circumference 87,5 cm (10p)
- BMI: 12,4 kg/m2 (-3,4 SDS)
- Blood pressure: 118/75 mmhg
- Strabismus
- No goiter
- Central hypotonia
- External genitourinary system was normal

Laboratory tests

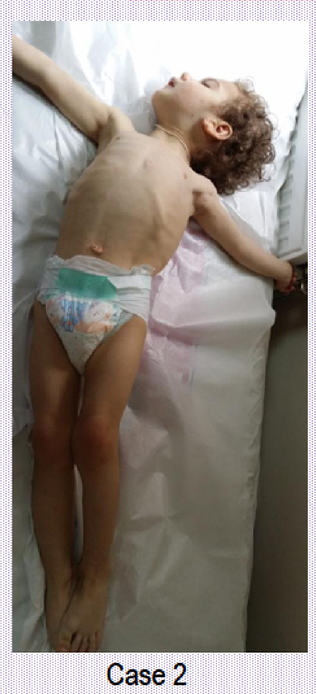
	Case -1	Case -2	Normal level
Free T4 (ng/dl)	0,62	0,7	0.8-2.2
Free T3 (pg/ml)	5.76	5,4	1.7-3.7
TSH (uIU/ml)	0,75	5,5	0.7-6.4
SHBG (nmol/L)	248	>250	11.2-78.1

100 mcg/d L-thyroxine

Peripheral hyperthyroidism



Case 1



Case 2

- Hemizygous 1-nucleotide deletion in exon 6 of MCT8 (c.1683delC, p.P561fs566X) in both cousins.
- Their mothers (sisters) were heterozygous for the mutation.

Conclusion

In boys with low FT4 levels in association with severe neurologic findings, serum (F)T3 should be measured. The finding of a low (F)T3 level is highly suggestive for a MCT8 mutation.

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Pituitary

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