Alström Syndrome- a rare disease presenting with cardiomyopathy and blindness

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Summary

Alström Syndrome (AS) is a rare, autosomal recessive single gene disorder with varying clinical features including blindness/ early nystagmus, dilative cardiomyopathy, hearing loss, obesity, Type 2 diabetes mellitus, hepatic dysfunction and renal failure. Diagnosis can be confirmed by analysis of mutations in the ALMS1 gene on chromosome 2p13. Only symptomatic therapy is available.
We report on two pediatric cases, both of them presenting with cardiomyopathy and vision impairment. In both patients diagnosis was confirmed by genetic analysis.

Case 1

- boy, 13 years old, presenting with syncope
- medical history:
  - 4 months: nystagmus, photphobia, followed by subsequent deterioration of visus und finally blindness
  - 6 months: hearing impairment, ad the time of admission compensated with hearing aid.
  - 2 years: cardiomyopathy, ventricular function normalized under medical treatment, cardiologic follow-up ended at the age of four years.
- on admission:
- Adiposity (Height: 160cm/P75, Weight 80kg/P>>97)
- Type II Diabetes mellitus
- parents report reduced exercise tolerance for approx. 2 weeks.
- LV-EF 20 %
- cardiopulmonary resuscitation after admission, followed by multi organ failure, exitus
- on autopsy: fatty liver

Genetics
- 2 mutations in the ALMS 1 gene found at the index patient (Exon 16 and 8, compound heterozygosis)
- Detection of corresponding mutations in the parents of this boy (Exon 16 in mother, Exon 8 in father)
- Healthy brother, probability of 2/3 heterozygous for this mutation
- Parental repeating risk: 25%

Case 2

- girl, 2 years old, presenting with multiple VSD for corrective surgery after pulmonary artery banding
- medical history:
  - 6 days: cardiopulmonary resucitation (pH 6,85, BE -21), biventricular function seriosly reduced. Intermittent renal failure.
  - Pulmonary artery banding after stabilization at the age of 3 weeks
  - Nystagmus documented in records after birth
- on admission:
- Adiposity: Height 83cm (P15), Weight 14,9kg (P95)
- Photophobia (Sunglasses!), Hyperopia (+7 dpt)
- LV-EF in the normal range
- Uneventful surgery with debanding and VSD Patch

Genetics:
- homozygous mutation in ALMS 1 gene, Exon 8
- consanguinity of parents, genetic analysis pending
- first child of healthy parents, repeating risk: 25%

Alström Syndrome

- First description in 1959 by CH Alström (2)
- rare, probably underdiagnosed syndrome, approx. 450 cases in the literature until now (1)
- autosomal recessive inheritance, mutations in the ALMS 1 gene on chromosome 2p13, function of this gene remains unclear, possible connection to ciliar function (1); very variable phenotype, low genotype- phenotype- correlation (1)
- main criteria:
  - mutation in at least 1 allele of the ALMS 1 gene (mostly mutations in Exon 16,10,8)
  - vision impairment (photophobia, nystagmus)
- secondary criteria:
  - type II diabetes mellitus, adiposity
  - cardiomoypathy (espacially in early childhood!)
  - progressive hearing- loss
  - hepatic dysfunktion, renal failure
  - reduced height/ accelerated bone age
  - male: hypogonadism, female: irregular menses, hyperandrogenism

References

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