Chromosome aberration

Deletion 1p36.33-36.31::36.22-21

Patient

A 5 year-old boy with mental retardation and a mitochondrial pyruvate oxidation disorder. He had mild facial dysmorfisms that did not lead to a diagnose. With 250K SNP array two interstitial deletions on the short arm of chromosome one were found.

Background information

Among a large number of terminal deletions, a substantial number of deletions and complex rearrangements on 1p36 have been described. However, uncommon about our patient is the extent of the proximal deletion on 1p36.22 and 1p36.21.
Several clinical features found in our patient such as his dysmorphic facial characteristics, the hypotonia and his developmental delay are common in patients with a 1p36 deletion. Other features such as the disturbed pyruvate oxidation and ATP production have never been described before in a 1p36 deletion patient.

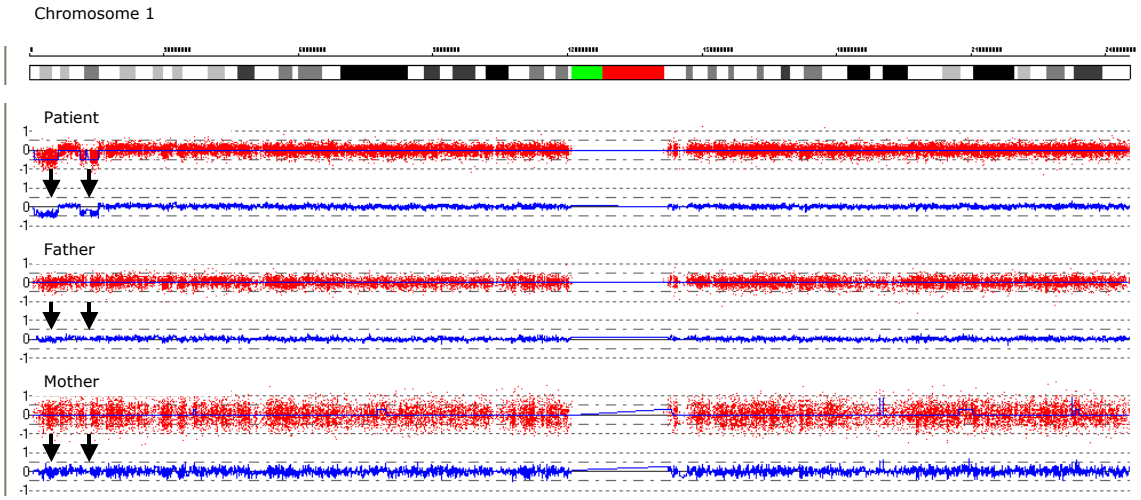
Clinical details

- Last age of examination: 5 years and 9 months.
- Perinatal history: patient was born prematurely at 36 weeks and 3 days. Vacuumextraction was performed after fetal bradycardia. The membranes were prematurely ruptured. Birthweight 2430 grams (normal).
- Congenital anomalies: Microcephaly and hypotonia
- Psychomotor development: He was not able to sit till the age of three years and unable to walk unsupported at the age of 5 years and 9 months. He had not developed speech at that age. Hearing and vision were normal.
- Dysmorphic features at 5 years and 9 months: progressive growth retardation with a length of 104 cm (-3 SD) and an OFC of 44,5 cm (-4,5 SD). His facial dysmorphisms included sparse hair, brachycephaly, a high prominent forehead, a long flat face with bitemporal narrowing, low-set and protruding ears, narrow up slanting palpebral fissures, deep set eyes, a ptosis, midfacial dysplasia, a small flat nose with a wide nasal bridge, small teeth in broad processi alveolari and down turned corners of the mouth. Furthermore, his hands and feet were small and his fifth fingers where obvious short, he had tapering fingers with hypoplastic nails of the fifth fingers and the toes, over-riding second toes, microgenitalism and retractile testis. He showed hyperlaxity of joints and a marked hypotonia, and he showed hypotrophic muscles of the leg, especially below the knee.

- Other investigations: Magnetic resonance imaging of the cerebrum at the age of 1 year and 8 months showed an agenesis of the corpus callosum. The rostrum was absent, the genu was intact. The lateral ventricles were mildly enlarged. Electroencephalography at the age of 4 months showed epileptic activity. From the age of 2 years seizures seemed to be absent, even without anti-epileptic medication.
- Treatment: At 1 year and 9 months he was operated on an inguinal hernia. He attends physiotherapy three times a week.

Cytogenetic details

- These deletions were detected with a 250k Nsp SNP Array and were verified by a 250k Sty array.
- Two deletions were found, one of 4 Mb located at bands 1p36.22-1p36.21 and one distal deletion reaching to 6.4 Mb from pter. As there are only a few SNPs covering the most distal region of chromosome 1p, the array was not informative for the distal subtelomeric area. FISH analysis confirmed that both deletions were interstitial. The eventual deletion sizes are: 1.1Mb-6.4Mb and 11.4 Mb-15.4 Mb. (UCSC genome browser, may 2004 assembly.)
- SNP analysis of parental samples confirmed de novo occurrence of both deletions.



Additional

The 1p36 deletion patient was previous diagnosed with a mitochondrial encephalomyopathy. As he had an uncommon interstitial deletion on 1p36.22-1p36.21 a candidate gene for this feature was located in this region. MFN2 seems to be a good candidate gene as it is involved in mitochondrial transport and is postulated to have role in mitochondrial metabolism.