Inherited duplication (X) (p11.4) associated with obesity, autoaggressive behaviour and delayed speech development

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Background

Obesity is a major feature in several syndromes. In patients with early-onset severe obesity, 7 % harbour a single locus mutation (Farooqui S. et al., Genetics of Obesity in Humans, Endocrine Reviews (2006)).

Comparative genomic hybridization arrays can be used to identify subtle chromosomal rearrangements that cannot be identified by conventional karyotyping.

Patient

We report a 3.11 year old male patient with early onset obesity (BMI 29,9 kg/m^2 >> P97), ongoing excessive weight gain, autoaggressive behaviour, and delayed speech development. No growth retardation or further dysmorphic signs. Early postnatal feeding difficulties required tube feeding.

Hyperphagia began at the age of 6 months resulting in excessive weight gain.
Delayed speech development, currently babbling without specific words and autoaggressive behaviour occurred.

Laboratory examination showed insulin resistance with elevated HOMA-index of 10.5.
Prader-Willi-Syndrome was suspected. Non-consanguineous parents of Turkish origin, obesity of the father and the sister, otherwise unremarkable family history.

Method

Molecular genetic testing for PWS was performed, subsequently an array CGH analysis.

Results

Unremarkable Prader-Willi genetic results on chromosome 15. In the array CGH analysis, a duplication was found at Xp11.4 (arr[hg19] Xp11.4 (40,380,579 – 40,487,209)x3).

Within this region the *ATP6AP2*-gene is located. Point mutations in this gene are associated with X-linked mental retardation and obesity.

A gene duplication of *ATP6AP2* has not been reported so far, however, we assume that this may cause of the patient's clinical symptoms. Genetic analysis of the mother has been performed demonstrating maternal X-linked inheritance.

Conclusions

Early onset and rapidly progressive obesity in early childhood should raise the suspicion of a genetic/syndromic origin, especially if there are further associated clinical symptoms such as developmental delay.

Array CGH revealed a duplication of Xp11.4 in a patient with Prader-Willi-like phenotype which is suspected to be the cause the syndromic disease.

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