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 (Faroqui 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.

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 of the syndromic disease.

Disclosure statement: nothing to disclose

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