Prevalence of copy number variations (CNVs) in a cohort of SGA children with persistent short stature associated with additional clinical features.

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Background

Multiple factors may affect intrauterine growth leading to birth of children small for gestational age (SGA). The impact of subtle genetic alterations on both pre and post-natal growth is still largely unknown.

Objective and hypotheses: The aim of this study was to investigate the prevalence of CNVs in a cohort of SGA children with persistent short stature.

Methods

26 SGA children (9.5 ± 1.2 yrs, 10F/16M) with short stature associated with dysmorphic features and/or developmental delay underwent array-CGH (aCGH) analysis.

Results

aCGH analysis showed CNVs in 50% (n=13) of short SGA children. Specifically, six patients had a microdeletion involving the following regions: 22q11.2, 8p21.2-8p12, 3q24q25.1, 19q13.11, 20q11.21q12, 15q26. In three females the same microdeletion involving 17p13.3 was found. In two patients the detected anomaly consisted of microduplication involving 10q21.3 and Xp11.3 region. In a female patient a compound microduplication was found (11q12.2 inherited from mother and Xq27.1 from father). In a boy the presence of both a microdeletion of 12p13.33 and a microduplication of 19q13.43 was observed.

Patient	Gender	BW (sds)	BL (sds)	Height (sds)	GH therapy	Genetic anomalies
1	F	- 2.33	n.a.	- 2.7	yes	microdupl Xp11.3
2	M	- 2.9	- 2.7	- 2.5	yes	microdupl of 10q21.3
3	F	- 1.84	-2	- 2.7	yes	microdel 17p13.3
4	F	- 2.44	n.a.	- 3.4	yes	microdel of 17p13.3
5	F	- 3	- 2.4	- 3.1	yes	microdel 17p13.3
6	F	- 1.65	- 2.5	- 4.5	yes	microdel 8p21.2-8p12
7	M	- 1.5	- 2.1	-2	no	microdel 22q11.2
8	F	- 2.57	n.a.	- 2	no	microdel 3q24q25.1
9	M	- 2.8	- 3.3	- 2.2	no	microdel 19q13.11
10	F	- 2	- 1.9	- 2.5	no	microdeletion 20q11.21q12
11	M	- 2.5	n.a.	- 2.2	yes	microdel 15q26
12	F	- 2.5	- 3	- 4.5	yes	microdupl 11q12.2 and microdupl Xq27.1
13	M	- 3.3	- 3.5	- 3.3	yes	microdel 12p13.33 and microdupl 19q13.43

Conclusions

These results show that CNVs can be detected by aCGH analysis in a large proportion of SGA children with short stature associated with additional clinical features. Interestingly, the involvement of 17p13.3 region occurs with a relative high frequency, suggesting that genes located in this region play a key role in pre and post-natal growth.