The 3q13.31 Microdeletion syndrome: A new patient molecularly characterised using array-CGH

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INTRODUCTION

Microdeletions in 3q13.31 have been reported in only relatively few patients to date and only a subset of cases have been characterised at molecular resolution. The deletion size for most patients is larger than 5 Mb, some smaller deletions allowed previously to define a smallest region of overlap (SRO) (Molin et al. 2012).
Apart from intellectual disability / developmental delay (ID/DD) of varying degrees, which is common to all reported patients, the clinical spectrum comprises speech delay, muscular hypotonia, skull malformations, ocular malformations, skeletal malformations and dysmorphic features.
Here, we report a female patient with a 3.4-Mb *de novo* deletion of 3q13.31.

CASE REPORTE

The patient was born at 38 week of gestation, birth weight 3940g (10th perc.), birth height 51cm (+0,5SD), occipiofrontal circumference (OFC) 37cm (+2,5 SD). Her clinical presentation at the age of 20 month includes: weight 9560g, height 82cm, OFC 50cm, mild DD, severe muscular hypotonia, macrocephaly, strabismus, hypermetropia and dysmorphic signs including hypertelorisme, anti-mongoloid slanted eyes, everted upper lip with a ``tented'' appearance and retrognathia.

Conventional cytogenetic analysis showed a normal female karyotype.

Array-CGH revealed a 3.4 Mb deletion in 3q: arr 3q12.3q13.31(112.144.025-115.514.432) **(Figure 1)**. The deletion was showen to be *de novo* using FISH **(Figure 2)**.

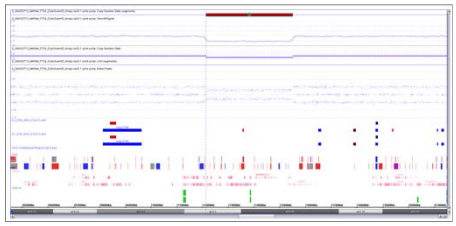

Figure 1: Array-CGH result using a CYTOSCAN HD [AFFYMETRIX] reveals a 3q deletion of 3,4 Mb. The deleted segment of chromosome 3 (chr3:112.144.025-115.514.432) (hg19) contains 24 RefSeq genes and comprises the previously defined SRO.

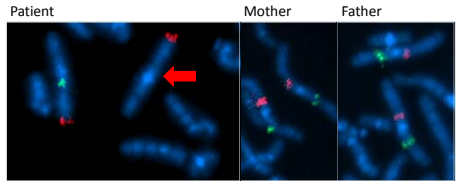

Figure 2: FISH analysis using the probe BAC RP11-271C24 (green signal) confirmed the deletion in the patient (arrow). FISH results in the parents were normal. Chromosome 3 control probes (red signals).

PHENOTYPE and GENOTYPE

Figure 3: Patient at the age of 20 months. Note macrocephaly, strabismus, antimongoloid slanted eyes and tented upper lip.

Literature phenotype	Patient phenotype
Developmental delay	+
Postnatal overgrowth	Macrocephaly
Speech delay	+
Muscular hypotonia	+
Brain malformation	Normal
Skull malformation	-
Broad prominent forehead	+
Tented upper lips	+
Antimongoloid slanted eyes	+
Hypertelorisme	+
	Strabismus internus,
Occular malformations	Hypermetropia
Skeletal malformation	Kyphosis
Abnormal genitalia	Hypolastic labia

Table 1: Comparison of the patients phenotype and clinical features reported in the literature.

Table 2: Deleted genes from 3q12.3q13.31

Name	Location	Description
BTLA	3:112182815-112218408	B and T lymphocyte associated
ATG3	3:112251356-112280893	autophagy related 3
SLC35A5	3:112280556-112304424	solute carrier family 35, member A5
CCDC80	3:112323407-112368377	coiled-coil domain containing 80
CD200R1L	3:112534556-112565703	CD200 receptor 1-like
CD200R1	3:112640056-112693969	CD200 receptor 1
GTPBP8	3:112709765-112733907	GTP-binding protein 8 (putative)
C3orf17	3:112721287-112738708	chromosome 3 open reading frame 17
BOC	3:112929850-113006303	Boc homolog (mouse)
WDR52	3:113005777-113160457	WD repeat domain 52
SPICE1	3:113161565-113234034	spindle and centriole associated protein 1
SIDT1	3:113251143-113348425	SID1 transmembrane family, member 1
KIAA2018	3:113367232-113415493	KIAA2018
NAA50	3:113437841-113465147	N(alpha)-acetyltransferase 50, NatE catalytic subunit
ATP6V1A	3:113465866-113530903	ATPase, H+ transporting, lysosomal 70kDa, V1 subunit A
GRAMD1C	3:113547029-113666021	GRAM domain containing 1C
ZDHHC23	3:113666748-113684248	zinc finger, DHHC-type containing 23
KIAA1407	3:113682984-113775460	KIAA1407
QTRTD1	3:113724680-113807269	queuine tRNA-ribosyltransferase domain containing 1
DRD3	3:113847498-113918254	dopamine receptor D3
ZNF80	3:113953483-113956425	zinc finger protein 80
TIGIT	3:113995760-114029135	T cell immunoreceptor with Ig and ITIM domains
ZBTB20	3:114056941-114866118	zinc finger and BTB domain containing 20
GAP43	3:115342171-115440337	growth associated protein 43

In total 24 RefSeq genes are located within the patients deletion. Genes from the SRO of the 3q13.31 deletion syndrome are given in red.

CONCLUSION / REFERENCES

Our patient with a relatively small deletion of 3.4-Mb confirms the pertinence of the previously delineated SRO and helps to identify the core phenotype of the 3q13.31 microdeletion syndrome.

REFERENCES: AM Molin et al. A novel microdeletion syndrome at 3q13.31 characterised by developmental delay, postnatal overgrowth, hypoplastic male genitals, and characteristic facial features. *J Med Genet* 2012;**49**:104-109.