Mosaic 2q37 deletion detected in a neonate with IUGR and brain malformations

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BACKGROUND

The hallmark features of 2q37 deletion syndrome are 1) mild to moderate developmental delay v2) brachymetaphalangism or other skeletal anomalies of the extremities, and 3) dysmorphic facial features.

Additional variable features of 2q37 deletion syndrome include congenital heart defects, autistic behavior and other behavioral disorders, hypotonia, seizures, structural brain abnormalities, gastrointestinal/genitourinary abnormalities and increased risk for Wilms tumor.

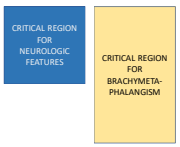
Critical regions for brachymetaphalangism and neurologic features of 2q37 deletion syndrome have been mapped to two overlapping regions of 2q37.3.

Ten percent of 2q37 deletion syndrome cases exhibit variable structural brain abnormalities, including corpus callosum agenesis, Dandy Walker malformation, Chiari malformation, cerebral atrophy and holoprosencephaly.

Variable expressivity has complicated genotype-phenotype correlation in this syndrome. While over 100 individuals with 2q37 deletion syndrome have been described to date, to our knowledge, none have been reported to carry a mosaic deletion.

13 OMIM / Morbid genes fall within this patient's deletion

- *ACKR3*
- *COL6A3*
- *MLPH*
- *PER2*
- *TRAF31P1*
- *TWIST2*
- *HDAC4*
- *NDUFA10*
- *CAPN10*
- *KIF1A*
- *AGXT*
- *D2HGDH*
- *PDCD1*



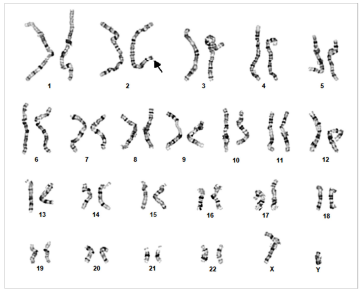
RESULTS

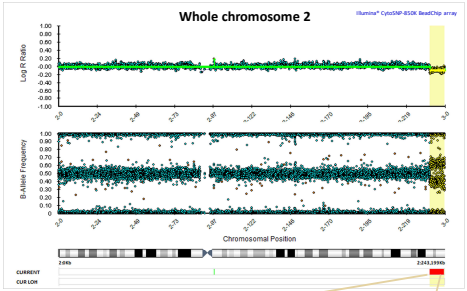
Prenatal ultrasound revealed absent septum pellucidum, left-sided polymicrogyria (PMG) and intrauterine growth restriction (IUGR). The patient was born at 34-36 weeks gestation to a G4P4 with Apgar scores of 6,8. Of note, meconium was positive for cocaine.

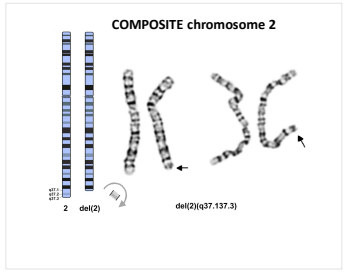
The patient was small for estimated gestational age at 1.86 kg (-1.3 SD if 34 weeks, -2.4 SD if 36 weeks per WHO statistics). Physical exam did not reveal any dysmorphic facial or skeletal features. Newborn screening and hearing tests were normal, and a postnatal brain MRI confirmed the prenatal findings. Family history was notable for a sibling with learning difficulties, seizures from ages 2-5 and a normal brain MRI.

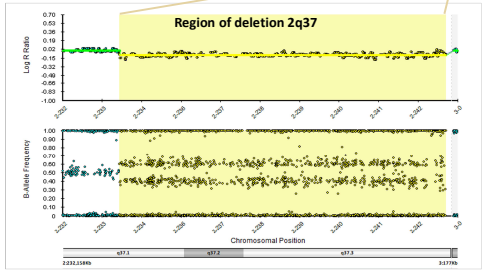
Chromosome analysis of peripheral blood revealed of a karyotype of mos 46,XY,del(2)(q37.1)[2]/46,XY[3], and chromosomal microarray showed a 9.3 Mb mosaic loss in 2q37.1→qter(chr2:233,780,186-243,048,760) estimated to be present in 35-40% of cells. A follow-up analysis of a buccal sample showed the same mosaic loss in 2q37.1→qter, also estimated to be present in 35-40% of cells. This region encompasses 115 genes, of which 13 have been linked to disease.

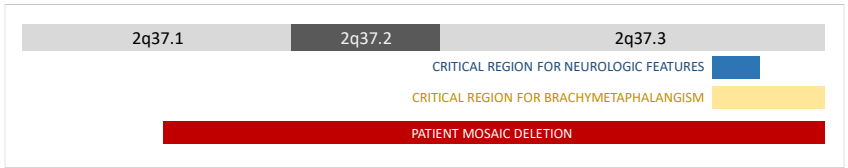
mos 46,XY,del(2)(q37.1)[2]/46,XY[3].arr[hg19] 2q37.1q37.3(233780186_243048760)x1~2











CONCLUSIONS

We report a mosaic 2q37 deletion in a neonate with IUGR and brain malformations but no dysmorphic facial features or skeletal anomalies such as brachymetaphalangism.

This case may represent the first report of PMG in 2q37 deletion syndrome, offering a potential novel genetic mechanism for PMG. IUGR, a presenting feature in this patient, has not been reported in 2q37 deletion syndrome. Prenatal exposure to cocaine cannot be excluded as an explanation for this finding.

Although the deletion observed in this case is larger than most described in the literature on 2q37 deletion syndrome, the patient's phenotype appears to be comparatively mild. The mosaic state of this deletion may have mitigated the severity of its impact. Clinical follow-up for this patient will be necessary for optimal genotype-phenotype correlation of this mosaic 2q37 deletion.

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