

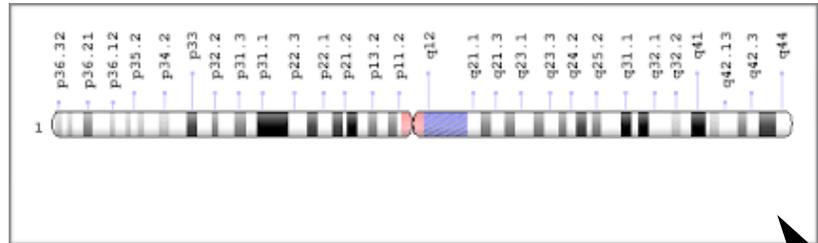


# 1Q43-Q44 DELETION INFORMATION

## 1q43-q44 Deletion Syndrome

Chromosome 1q44 is a 6 Mb long terminal segment of the long arm of chromosome 1<sup>1</sup>. The more proximal segment 1q43 is approximately the same size. There are at least 230 reports on patients having isolated deletions 1q43q44 (or 1q44) and more than 130 reports when deletions of this area were accompanied by an additional imbalance (mostly due to familial translocations or inversions). This condition is usually reported as 1q43q44 deletion syndrome, but is it obvious that the loss of genes in 1q44 is the main factor causing the clinical manifestations<sup>1-3</sup>.

Although prenatal hypoplasia is relatively mild the postnatal growth of patients is significantly delayed. Most children have dysmorphic features (sparse fine hair, round face, epicanthus, low set ears, short broad nose with flat bridge, downturned corners of the mouth, small chin). Half of patients have small hands with tapering fingers or short curved 5<sup>th</sup> fingers.



Defects of the brain and the clinical consequences of these defects are the most characteristic and most serious features of this condition. Microcephaly is found in ~90% of patients and causes significant delay in psycho-motor development. Seizures (sometimes drug-resistant) are found in ~75% of patients. Other consequences of abnormal brain development are floppiness (hypotonia), dysphagia (leading to difficulties in feeding) or autonomic dysfunction [disturbance in the function of the cardiac muscle, smooth muscles and different glands]. In 90% of examined patients, an MRI of the brain shows an absence or hypoplasia of the corpus callosum [part of the brain, connecting cerebral hemispheres]. There are also several reports of hypoplastic cerebellar vermis, Dandy-Walker malformation and occipital encephalocele.

Contemporary research<sup>2</sup> shows that the loss of the AKT3 gene is the main factor leading to microcephaly, the loss of the HNRNPU gene determines the degree of intellectual disability, and a mutated ZBTB18 gene is the leading cause of the corpus callosum abnormalities. However other genes in this area may also participate in development of microcephaly and epilepsy; and the cumulative action of several genes may be more important than a deletion or malfunction of any single gene<sup>3</sup>.

Some children have small pits or additional skin tags in front of their ear. Hearing impairment was reported in ~15% of examined patients. Cleft palate or bifid uvula is relatively common (~15%). Several children had a hypoplastic thyroid gland, and the exclusion of hypothyroidism should be a part of any clinical examination.

Heart defects (usually not life threatening) are the most common abnormality of the internal organs. They are found in ~30% of the patients. Some boys have hypospadias.

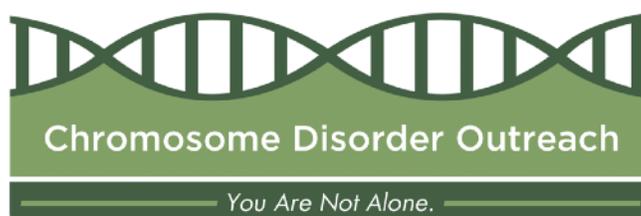
A significant number of terminal deletions may be the result of parental translocations: an examination of parental chromosomes is a prerequisite for further decisions. The risk for further affected children of a couple is very low if the parental karyotypes are normal.

#### REFERENCES

<sup>1</sup> Caliebe A. et al. Four patients with speech delay, seizures and variable corpus callosum thickness sharing a 0.440 Mb deletion in region 1q44 containing the HNRNPU gene. *Europ. J. Med. Genet.* 2010, v. 53, 179-185.

<sup>2</sup> Depienne C. et al. Genetic and phenotypic dissection of 1q43q44 microdeletion syndrome and neurodevelopmental phenotypes associated with mutations in *ZBTB18* and *HNRNPU*. *Hum. Genet.* 2017, v. 136, 463-479.

<sup>3</sup> Raun N. et al. Quantitative phenotypic and network analysis of 1q44 microdeletion for microcephaly. *Amer. J. Med. Genet.* 2017, v. 173, 972-977.



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