Deletion 2q24

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Abstract
Deletion of 2q24, i.e. the loss of a small but specific region of the long arm of chromosome 2 forms a clinically recognizable syndrome. Twenty-three cases are known from the literature. Several symptoms are commonly seen in patients with chromosome aberrations, such as low birth weight, growth retardation, mental retardation, and low and malformed ears. However, the eye anomalies (coloboma, cataract and microphthalmia), anomalies of hands and feet (flexion deformities) and the congenital heart defects are more specific features, and are especially important in recognizing the clinical phenotype.

Key words
chromosome 2q23q24, interstitial deletion, camptodactyly, eye anomalies, cardiac defects

Disease name and synonyms
Deletion of chromosome band 2q24
Monosomy 2q24

Excluded diseases
All the other chromosome anomalies associated with low birth weight, growth retardation, mental retardation and facial dysmorphism.

Diagnosis criteria/definition
The diagnosis is made when chromosome analysis shows a deletion of a specific part (band q24) of the long arm of chromosome 2. Because many of the clinical symptoms are non-specific the clinical symptoms are not part of the diagnostic criteria. However, the combination of low birth weight, growth retardation, mental retardation, facial dysmorphism together with eye anomalies, flexion deformities of the hand and feet and/or heart defects seem to be more specific for this deletion.

Differential diagnosis
If the cytogenetic anomaly is detected, no differential diagnosis is needed. If no microdeletion at 2q24 can be found the clinical features may point to a vast array of other chromosome anomalies of monogenic entities.

Prevalence
To our knowledge there are twenty-three reported cases (in detail) with a deletion involving chromosome band 2q24. There are no exact data about the prevalence of this chromosome aberration.
Clinical description
The most frequent abnormalities are growth retardation, poor neurological development (mental retardation, hypotonia, seizures), microcephaly, malformed and low-set eyes with large upper lids, ear anomalies (ptosis, coloboma, cataract), depressed nasal bridge with a small upturned nasal tip, micrognathia, flexion deformities of the fingers, sandal gap, and congenital heart defects. The association of growth retardation and poor neurological development together with multiple minor facial anomalies is a common denominator to many deletion syndromes. The eye anomalies (one or more in ten of the patients), digital flexion deformities (fourteen patients) and congenital heart defects (eight patients) are more specific features.

Neurologic symptoms
Microcephaly, abnormal head shape (sagittal synostosis, craniosynostosis, cranial suture irregularities and scaphocephaly), occipital meningomyelocele and internal hydrocephalus, occipital encephalocoele and ventricular enlargement and seizures were prominent findings in most of the patients. This made authors to suggest that some of the many genes, which have significant impact on brain development, and function may be located in the q22.3 through q31 region of chromosome 2.

Eye involvement
Eye anomalies are reported in half of the patients. Different eye anomalies are described. Ptosis is reported in 7 patients. Microphthalmia is only reported in 2 patients. Cataract is mentioned in 3 cases. These three patients have a common deleted segment in q23.3q24.2. However, two other patients in whom ophthalmologic examination did not show cataract also have this segment deleted, and in another case with again deletion of this segment cloudy corneas were found, which attributed to ocular immaturity. In another patient with a deletion of the 2q23.3q24.3 segment no ophthalmic examination was performed. Therefore it is unlikely that band q23.3q24.2 is a critical region for cataract. Colobomas were reported in 5 patients.

Acral defects
Bilateral digital anomalies are often found, and have included camptodactyly, also of the thumbs, clinodactyly of the fifth fingers, short feet with broad halluces, absent second digits, hypoplastic third, fourth and fifth digits, syndactyly of the 2nd or 3rd to 5th toe, and a clefting between the halluces and the other digits, best described as a split foot.

Flexion deformities of the fingers have been reported in most cases. A common deleted segment in all these cases is q24.3, except in one case, who has joint contractures of several fingers, who had a deletion of the 2q21q23.2 segment.

Apparently both the 2q24.3 region and the 2q31.1 region are responsible for limb defects. The present data suggest that deletions of the 2q24.3 region are more often associated with finger flexion deformities. Except for a sandal gap between the first and second toe no other feet anomalies were described in patients with deletions in this region, providing that they did not have in addition a deletion in the 2q31.1 region. Data suggest furthermore that the more distal the deletion is located, the more severe the reported hand and feet anomalies are. Split feet may represent the extreme end of the spectrum of digital anomalies associated with deletions in this region.

Heart anomalies
Different congenital heart defects have been present in 8 patients. Ventricular septal defects were described in 4 patients, atrial septal defect in three patients, aortic coarctation in two patients, a truncus arteriosus was described in 2 patients and a patent ductus arteriosus in 3 patients. Segment 2q24.2 is deleted in 4 of the 8 patients but is also deleted in one case in which ECG and auscultation were normal.

Management including treatment
Management of the growth retardation and mental retardation should be taken care of similar to the care for any other child with these features. The other clinical features caused by the deletion, like the camptodactyly or cardiac defects, should be treated in a similar way.

Etiology
This syndrome is the result of a deletion of an interstitial part of the long arm of chromosome 2. In almost all the cases the deletion will arise spontaneously, probably due to a disturbance of the first meiotic division in either parent. An increasing number of genes are mapped to the region 2q24 (OMIM). No single gene seems to be able to explain all symptoms, making the deletion 2q24 probably a continuous genes syndrome. Genes in this region involved in the phenotype of patients with a 2q24 deletion may be several neuronal voltage dependant sodium channel genes (SCN1A, 2A1, 2A2 and 3a). Mutations in the SCN1A gene are for example associated with generalized epilepsy with febrile seizures and are described as a major cause of severe myoclonic epilepsy of infancy. No
candidate genes for the congenital defects of brain, eyes and limbs are known.

**Diagnostic methods**
One should look for a deletion of chromosome 2q24 if the clinical symptoms are suggestive. A deletion of chromosome 2q24 is usually visible on a standard karyotype if suspicion for this anomaly is expressed due to the clinical features. FISH studies may be indicated.

**Genetic counselling**
If a deletion of chromosome 2q24 is found in a child chromosome analysis should be performed in the parents and other family members should be counselled according to the cytogenetic results.

**Antenatal diagnosis**
If the chromosome anomaly is caused by a translocation present in one of the parents, antenatal diagnosis may be offered because of a recurrence risk. If parental karyotypes are both normal the recurrence risk is very low, and depending on the presence of absence of germ line mosaicism in one of the parents. Antenatal diagnosis in a next pregnancy may still be offered, for psychosocial reasons.

**Unresolved questions**
Most of the gene(s) that are causative for the different parts of this microdeletion syndrome are still unknown.

**References**


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