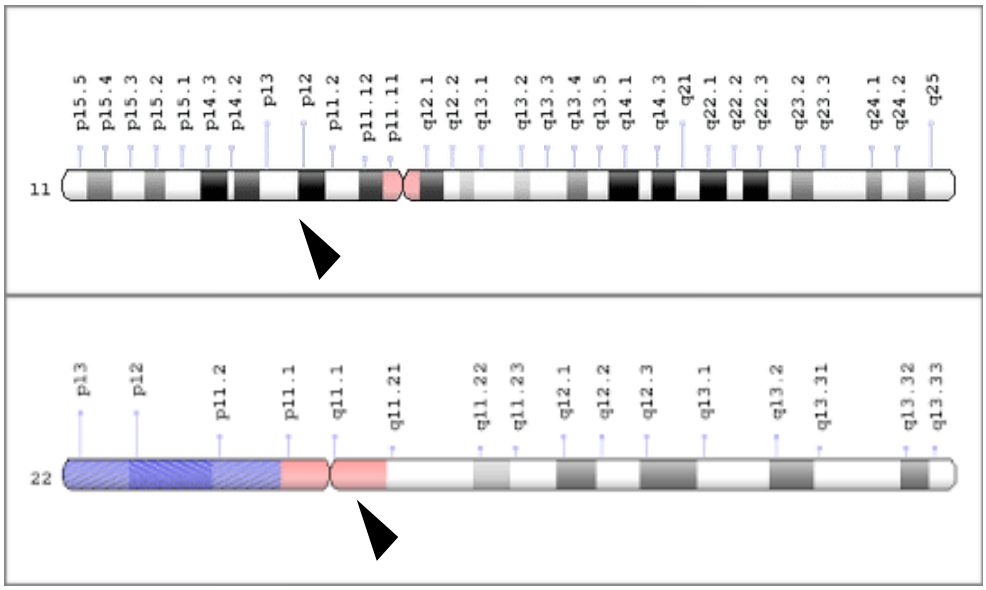
EMANUEL SYNDROME INFORMATION

Emanuel Syndrome

All chromosomal syndromes are caused by deletions (duplications, trisomies) of one chromosome. The only exception is Emanuel syndrome (ES), caused by the cumulative action of partial trisomies for two chromosomes: the distal segment of chromosome 11q and the proximal segment of chromosome 22q.



Most non-Robertsonian translocations are unique. Translocation t(11;22) is an exception. It is the most common non-Robertsonian translocation in humans. The structural similarity of the 22q11.2 segment and the 11q23 segment facilitates the exchange between these areas with formation of t(11;22)(q23; q11.2). As a result of the segregation 3:1 which is almost constant in this translocation[1] the patient will have an additional chromosome der(22) which includes part of chromosome 22 (short arm, centromere and proximal segment of 11q [up to 22q11.2]) and the distal part of chromosome 11 (from 11q23 to the end of the long arm).

This syndrome is usually called Emanuel syndrome after Beverly Emanuel who studied this condition for many years[2]. There is no doubt that several patients described in the early cytogenetic literature as persons with “trisomy 22” actually had ES. Sometimes the term “supernumerary der(22)t(11;22)” syndrome is used to describe this disorder[3].

ES is a relatively common pathology. At least 400 patients have been reported so far.

The clinical manifestations of the syndrome include severe developmental delay, defects of the face, heart, kidneys and other systems.

Most patients have prenatal hypoplasia and their physical parameters (weight, height) are much below those of their healthy peers. Microcephaly is reported in ~25% of patients, more commonly in adolescents or adults. Facial abnormalities include hypertelorism, flattened nose, deep-set eyes, prominent upper lip, hypoplastic mandible (micrognathia). Preauricular pits are found in ~75% of patients, and at least one third have preauricular tags. Cleft palate is very common (~50% of patients have this defect). An association of the micrognathia and cleft palate produces the so-called Pierre Robin sequence (~35%) which in some cases is the first symptom leading to the cytogenetic examination of a newborn baby.

Heart defects are very common. They may be found in ~60% of patients[1]. Defects of the atrial septum are the most common type of abnormality (~45%). Other defects are less common. Severe defects like tetralogy of Fallot or endocardial cushion defects are rarely reported. Surgical correction may be necessary in ~30% of patients having heart defects.

Kidney abnormalities are also common (at least 30%) and include unilateral kidney agenesis, hypoplastic kidneys, cystic kidneys, and duplication of the collecting system[1]. In some patients kidney defects are the main factor determining the vital prognosis. Genital abnormalities (mostly in boys) include cryptorchidism and hypoplastic penis.

Anal atresia (stenosis) or ventral ectopia ani is the most common defect of the gastro-intestinal tract (~15% of patients). Constipation is a very common manifestation.

Morphological defects of the brain are not so common, although ~15% of patients have hypoplastic corpus callosum and ~10% have hydrocephalus. A significant number of recently reported patients have Dandy-Walker malformation (hypoplastic cerebellar vermis with dilatation of the posterior fossa)[4] but it may reflect the common phenomenon that when any syndrome is well known only the persons having unusual manifestations are preferentially reported. The same may be true regarding diaphragmatic hernia which may be found in ~10% patients.

Defects of the locomotor system include dislocation or subluxation of the hips (up to 50%), scoliosis, kyphosis or joint contractures. Defects of the immune system are very common. Almost all patients have recurrent infections of the ears, respiratory organs or urinary tract.

Global developmental delay is actually an obligate symptom. The patients reveal gross motor delay and achieve supported walking at 5 years (on the average). Most patients are non-verbal, and those who are verbal use only single words or short phrases. Most patients need help

dressing or undressing, and only a third can use a spoon or a fork. If not home-schooled they attend classes for disabled individuals. At least 10% of patients have seizures.

The vital prognosis depends on the presence and type of heart and kidney defects and diaphragmatic hernia. There are numerous reports of adult patients with ES.

Recent examinations show that the additional marker chromosome includes ~3.5 Mb of 22q and ~18 Mb of 11q[5]. At the same time the relative role of excessive genes from 11q and from 22q is not known. Congenital heart defects are common both for isolated duplications 22q11 and for isolated distal trisomy 11q. Anal defects are common for tetrasomy 22q11 (cat eye syndrome), but patients with this syndrome have colobomas (highly uncommon for ES) and satisfactory intellectual development.

In almost all cases ES is caused by a parental translocation t(11;22)(q23;q11.2) and in 90% of patients this translocation is found in the mothers. The recurrence risk of ES for women with such a translocation is about 9%, the recurrence risk for males with the same translocation in only 2-3%. In any case prenatal cytogenetic examination (even by "standard" methods) can show the karyotype of the fetus. Ultrasonography is not so reliable, because ultrasonographically recognizable defects of the fetus may be missing.

REFERENCES

[1] Carter MT, St.Pierre SA, Zackai EH, Emanuel BS, Boycott KM. Phenotypic delineation of Emanuel syndrome (supernumerary derivative 22 syndrome): clinical features of 63 individuals. Am J Med Genet Part A 2009, v. 149A, 1712-1721.

[2] Yosunkaya Ferenci E, Guven GS, Kuru D, Yilmaz S, Tarkan-Argüden Y et al. Supernumerary chromosome der(22)t(11;22): Emanuel syndrome associates with novel features. Genet Counseling 2007, v. 18, 401-408.

[3] Choudhary MG, Babaji P, Sharma N, Dhamankar D, Naregal G et al. Derivative 11;22 (Emanuel) syndrome: a case report and review. Case Rep Pediatr 2013: 237935.

[4] Walfisch A, Mills KE, Chodirker BN, Berger H. Prenatal screening characteristics in Emanuel syndrome: a case series and review of the literature. Arch Gynecol Obstet 2012, v. 286, 299-302.

[5] Zou P-S, Li H-F, Chen L-S, Ma M, Chen X-H et al. A rare case of trisomy 11q23.3-q25 and trisomy 22q11.1-22q11.21. Genet Molec Res 2016, v. 15: 15028140.

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