

Deletions of 10p

Various deletions of the short arm of chromosome 10 have been reported in ~150 patients, including ~55 patients who had associations of partial monosomy 10p with partial trisomies (or — rarely — with deletions) of other chromosomal segments. 95 patients with “pure” deletions of 10p will be the object of further analysis.

Approximately 20 of these patients had proximal deletions (10p11p12) or deletions of the distal end of 10p (10p15.3). Clinical manifestations in these patients do not allow delineating any syndrome associated either with proximal or with very distal 10p deletions. It should be noted, however, that 4 patients with small interstitial deletions 10p12.1 had holoprosencephaly. Several more patients with deletions involving 10p12 had arhinencephaly (absence of olfactory bulbs without defects of brain cleavage), which may be considered as a mild manifestation of the same defect. Therefore, this part of 10p12.1 has to contain a gene involved in formation of the forebrain.

Other patients, most of whom have deletions involving both 10p13 and 10p14, have a complex of clinical abnormalities involving two separate syndromes – DiGeorge syndrome type II and the so-called HDR syndrome (Hypoparathyroidism, Deafness, Renal abnormalities).

DiGeorge syndrome (DGS) is an association of hypoplastic thymus with T-cell deficiency, hypocalcemia (caused by hypoparathyroidism), conotruncal heart defects, facial abnormalities and (sometimes) delay in psycho-motor development. In the vast majority of patients, DGS (or DiGeorge complex) is caused by the deletion of the 22q11.2 area. However, some manifestations of DGS, including hypoplastic thymus with a deficiency of T-lymphocytes, hypoparathyroidism, facial abnormalities and some heart defects were repeatedly found in a group of patients with deletions of 10p. That allowed a suggestion of the so-called DiGeorge syndrome, type II, caused by deletions within 10p13. However, patients with DGS-II usually have relatively mild heart defects, mostly atrial septal defects (ASD) or ventricular septal defects (VSD). Not a single patient had interrupted aortic arch (typical for DGS-I), only one patient had truncus arteriosus and one had tetralogy of Fallot. Moreover, special studies showed that a locus responsible for ASD (on 10p14) seems to be separate from the locus on 10p13, which is responsible for hypoplastic thymus and hypoparathyroidism. The gene BRUNOL3 may be the causative factor for ASD, which is found in patients with DGS-II, but this should be confirmed by further investigations.

Most patients with deletions 10p also have manifestations of the HDR syndrome. This condition, which is a separate entity, is caused by the deletion of the GATA3 gene also located at 10p14, but a little bit closer to the centromere. The full form of this syndrome consists of hypoparathyroidism, hearing loss (deafness) and dysplastic changes of kidneys (renal dysplasia). Defects of the kidneys include the absence of one kidney, polycystic kidneys, hypoplastic kidneys, vesico-ureteral reflux. The whole triad of the main symptoms is uncommon. It was found only in 5 out of 49 patients (however, the level of parathyroid hormones was not tested in some patients). Hearing loss (23/49) and kidney defects (20/49) occur approximately with the same frequency.

Because most patients have simultaneous deletions of the DGS-II critical region and HDR critical region (GATA3 gene), the clinical manifestation usually reflects a mixture of both of

these conditions. Although several patients had short neck, hypospadias, and polytelia (the presence of additional nipples), neither of these manifestations may be considered as typical for del 10p. At least 3 patients with deletions 10p14pter had pyloric stenosis.

Due to the complex clinical picture of del 10p13p14, the patients may need a cardiologic examination, a urologic examination (to exclude renal problems), hearing testing and a special examination for hypoparathyroidism.

Almost all interstitial deletions of 10p are sporadic. Terminal deletions may be the result of familial translocations. Most patients with familial rearrangements also will have trisomies for a segment of chromosome 10q (in families with inversions) for a segment of another chromosome (due to translocations).

Deletions of 10q

Deletions of 10q11.2 and Cockayne Syndrome

Cockayne syndrome (CS) is a very rare recessive disorder characterized by post-natal growth failure, hypersensitivity to sunlight, premature senile appearance, psycho-motor retardation, and retinal pigmentations. Mutations of the ERCC6 and ERCC8 genes are responsible for this syndrome. In 1991, Fryns et al. described a patient with CS and the deletion 10q11.2q21.2. No other report of CS in patients with proximal 10q deletions has been published for almost 20 years. In 2010, Jain et al. presented a girl with CS and a 5 Mb deletion of 10q11.2, which was inherited from a healthy father. Molecular study showed that this girl also had frame-shift mutation of the ERCC6 gene. Absence of the paternal allele in association with the mutation of the maternal allele explained the occurrence of CS in that child. Although the vast majority of patients with del 10q11.2 do not have any signs of CS, cytogenetic examination should be recommended for children with CS who do not have two mutations in the ERCC6 gene.

Deletion of 10q11.2 and Hirschsprung's Disease

Aganglionic megacolon, or Hirschsprung's disease (HD), is a disorder characterized by the absence of parasympathetic ganglion cells in the submucosal and myenteric plexuses of the gut. HD belongs to the group of disorders connected to the development and migration of neurons. The clinical consequences of this condition are constipation, abdominal distension and failure to thrive. Resection of the affected segment of the gut remains the best treatment.

There are several genes involved in the development of HD. One of these genes lies on 10q11.2. There are 4–5 reports of patients with HD and deletions involving 10q11.2. Approximately 15 other patients with this deletion did not have any signs of HD. Most likely, participation of other genetic (or non-genetic) factors is necessary for development of HD in patients with del 10q11.2.

Deletion of 10q23 and Syndromes with Polyposis

Historically there are two overlapping syndromes, which include the association of intestinal polyposis, macrocephaly, multiple lipomas and cutaneous lesions. One of these conditions is called Bannayan–Riley–Ruvalcaba syndrome (BRRS); another is called Cowden syndrome.

Both of these conditions are caused by the mutations of the tumor-suppressor gene PTEN, located at 10q23. In both of these syndromes, intestinal polyposis is important, but it is not a leading clinical symptom. Several patients having BRRS or Cowden syndrome had a small deletion involving 10q23.

Juvenile polyposis syndrome is a much more serious condition, where multiple hamartomatous polyps of the gastro-intestinal tract lead to intestinal bleeding, diarrhea and exudative enteropathy. These polyps may become malignant. Juvenile polyposis may be caused by the mutation of another tumor suppressing gene, BMPR1A, which is also located at 10q23.

There are ~10 reports of patients with juvenile polyposis and deletions involving 10q23 (the minimal overlapping segment is 10q23.2q23.31). These deletions involve both the PTEN gene and the BMPR1A gene. Simultaneous deletion of two contiguous tumor-suppressor genes may increase the severity of the disease.

Almost all patients with a confirmed deletion of both of these genes had juvenile polyposis, usually in association with macrocephaly, delayed psycho-motor development and some dysmorphic features (epicanthus, hypoplastic nasal bones, small ears, etc). However, at least 1/3 of patients showed normal psycho-motor status.

At least 6 of 16 known patients had mild heart defects, including four patients with VSD and 3 patients with ASD (some patients had both VSD and ASD). Other defects (cleft palate, hypospadias, vesico-ureteral reflux) have been reported in several patients, but these abnormalities are not typical for the syndrome that is caused by the deletion of 10q23. Although all patients with juvenile polyposis had deletions of both PTEN and BMPR1A genes, absence of these genes does not guarantee the development of this condition: there are patients with deletions encompassing both genes, but with a relatively mild phenotype. To date, all reported deletions causing intestinal polyposis were sporadic.

Distal Deletions of 10q

Deletions involving distal segments of 10q are relatively common. There are at least 135 reports of patients with monosomy for these areas as a sole anomaly. At least 100 more patients had an association of monosomy 10q and partial trisomies for other chromosomal segments. Only the patients with "pure" deletions will be the object of this analysis. There is no typical breakpoint which could be considered characteristic for this deletion. Almost every patient had his/her own unique breakpoints. At least 24 patients had interstitial deletions without the loss of the most distal segments of 10q26.3. The actual frequency of interstitial deletions cannot be determined because the methods used before the invention of "molecular cytogenetics" were not sufficient enough to distinguish between terminal and interstitial deletions. 30 patients had deletions involving both the 10q25 and 10q26 segments; in other patients, the loss of genetic material was limited to the 10q26 segment.

The main manifestations of the distal deletion of 10q are delay in psycho-motor development, cranio-facial dysmorphism, hearing loss, heart defects, urinary (or genitor-urinary) defects and behavioral problems. Almost all known patients had a different degree of delay in psycho-motor development, mostly mild or moderate. Low birth weight is typical. Cranio-facial abnormalities are very common: they include small head circumference, prominent

forehead, broad nasal bridge, prominent nose, strabismus, thin upper lip, low-set dysplastic ears. However, these defects may be found in many other forms of autosomal deletions (or partial trisomies).

Sensori-neural hearing loss, which was mentioned at least in 20 patients is related to the loss of the material from 10q26.13: all patients with more distal deletions had normal hearing. The genes HMX2 and HMX3 are proposed as the candidates to explain the reduced hearing function.

Heart defects are relatively common. They were reported in ~30% of patients. Most of these defects were relatively mild (patent ductus arteriosus, ASD, etc), but at least 5 patients had tetralogy of Fallot and several others had arterial trunk, atrio-ventricular communication, double outlet right ventricle.

Defects of the urinary tract are also common. At least 11 patients had hydronephrosis, 11 — vesico-ureteral reflux, 5 — megalobladder [giant urinary bladder]. The last defect is very uncommon in other conditions, which is caused by a chromosomal imbalance. The gene behind these abnormalities is still unknown, but the critical segment for this kind of defect is 10q26.2q26.3. Urologic study should be a component of examination in each patient with distal 10q deletion.

Seven patients (mostly with deletions involving 10q25) had atresia ani. Other defects of the gastro-intestinal system are very uncommon.

There is a small sub-group of patients with severe genital abnormalities: from completely female genitalia in 46,XY patients to different kinds of genital ambiguity. The critical region for these defects seems to be within 10q25.3 and 10q26.11.

Structural defects of the brain are uncommon for the patients with deletions of 10q25-q26 (the more proximal segment 10q24.32 may contain, however, a gene related to microcephaly and holoprosencephaly, but deletions of this area are very uncommon). Although cleft lip and/or palate is relatively uncommon, some data suggest that the segment 10q26.11-q26.12 may harbor a gene, which (when deleted) may lead to the formation of cleft lip.

A considerable number of patients may reveal hyperactivity, aggression, and sometimes self-damaging behavior. There is no strong correlation between the level of intellectual defect and the frequency of behavioral problems.

From the genetic point of view, part of the deletions (especially very small deletions, recognizable only by molecular methods) may be inherited from one of the parents. Usually the “unbalanced” carriers have mild intellectual defects (some type of learning disability), but most of them have neither facial dysmorphism nor congenital abnormalities.

Ring Chromosome 10

Ring chromosome 10 is highly uncommon. There are only 16 reports on patients with this abnormality. One of these patients also had a translocation of the part of the deleted material onto another chromosome. Only four out of 16 patients did not have any morphologic

abnormalities.

The most common defects in patients with r(10) are abnormalities of the eyes and kidneys. Abnormalities of eyes included microphthalmia (2), cataracts (2), partial atrophy of choroid (2), hypoplastic macula and coloboma. The high prevalence of eye defects seems unusual. Neither patients with distal deletions of 10p nor patients with distal deletions of 10q have this kind of pathology. Different kidney abnormalities were reported in 10 patients. Most of them had abnormalities of ureters (megaureter, hydroureter, and ureteral valves) leading to hydronephrosis. Hypoplastic kidneys were found in two patients. This spectrum of defects was caused most likely by the deletion of the terminal segment of 10q26.

Congenital heart defects (a relatively common manifestation of patients with an autosomal imbalance) were found only in two patients with ring chromosome 10. Several patients had microcephaly, dysgenesis of the cerebellar vermis, cleft palate, rhizomelic shortness of limbs, and Hirschsprung disease. One patient developed cancer of the thyroid.

Direct transmission of ring chromosome 10 from a parent to a child is not known.

Partial Trisomies of Chromosome 10

Trisomies of 10p

There are more than 250 reports on patients with trisomies for different segments of the short arm of chromosome 10, including ~100 patients who did not have any additional imbalance, except trisomy 10p. These patients will be the object of further analysis.

From the practical point of view, all of these patients may be divided into three groups — patients with trisomy for the whole (or almost whole) 10p, patients with trisomies for the distal half of 10p (10p13–pter), and patients with small trisomies for the most distal segment of 10p — 10p15.3.

Trisomy for the whole (or almost whole) 10p

There are ~40 patients who may be placed to this group. Usually, these patients have a recognizable pattern of cranio–facial dysmorphies and congenital anomalies. Usually, this complex is reported as “10p trisomy syndrome”.

Most characteristic manifestations of the syndrome include growth retardation, a moderate delay in psycho–motor development, muscular hypotonia, high and bulky forehead, an upswept frontal hair pattern, mongoloid slanting of palpebral fissures, epicanthus, hypertelorism, broad nasal bridge, micrognathia, and low set ears. Three patients had preauricular skin tags, and three others had hearing impairment. Cleft lip was found in 10 of 40 patients, and four more children had a cleft palate. Short neck was reported in six of 40 patients.

Abnormalities of the loco–motor system are generally relatively mild. They include brachydactyly, camptodactyly, contractures, hip dysplasia, knee dislocation, pectus excavatum, cervical ribs, or joint laxity.

Abnormalities of the brain and internal organs are also common. Brain defects include agenesis of the corpus callosum (3), megacysterna magna (3), and hypoplastic cerebellar vermis. Coloboma of the optic nerve was reported in two children, and one had atrophy of the optic nerve. Microphthalmia, microcornea, cataract, and myopia were found in one patient, each. Endocrine defects include diabetes in two patients and hypothyroidism (1).

The most common internal defects are heart defects, reported in 14 patients. Almost all defects were not life-threatening (ventricular septal defect, patent foramen ovale, pulmonary stenosis). One patient had tetralogy of Fallot.

From the clinical point of view, defects of the kidneys are much more significant. Polycystic kidneys were reported in seven patients. Three patients had unilateral kidney agenesis, and one more had hypoplastic kidneys. Such kidney abnormalities may lead to renal insufficiency with grave consequences. Other abnormalities involve defects of the collecting system (hydronephrosis, dilated kidney pelvis and ureters, ureteral atresia, and megaureter). Two infants had an abnormal lung lobation, where the right lung had only two lobes (instead of the usual three). Sporadic defects of the gastro-intestinal system (agenesis of the gallbladder, atresia ani, and rectal prolapse) cannot be considered as characteristic for the syndrome.

The most likely duplication of 10p12 is critical for the occurrence of cleft lip and palate and most visceral defects, because patients with more distal duplications (10p13-pter) do not have these abnormalities.

Duplications 10p13pter (or 10p13p15)

There are less than 20 patients with “pure” trisomy for the distal half of 10p. Most patients reveal a delay in psycho-motor development, but they do not have typical manifestations of the “10p trisomy syndrome”. Most patients do not have any morphological abnormalities, although there are reports of the absence of the external ear, cleft palate, kyphosis, contractures, camptodactyly, tetralogy of Fallot, and even XY-gonadal dysgenesis. Because all of these defects were reported only once each, it is unclear whether these abnormalities are causally related to distal trisomy 10p.

There are reports of the direct transmission of this duplication from minimally affected parents. Therefore, cytogenetic examination of the parents is necessary for having further offspring.

Duplications 10p15.3

There is a relatively large group of patients with an isolated trisomy for the most distal segment of 10p — 10p15.3. Most patients have a tiny duplication (0.43 Mb), but several patients have duplications of a significantly larger size. Clinical manifestations in such persons are very heterogeneous. Most patients have a mild or moderate delay in psycho-motor development, several had autism, obesity, or seizures. Microcephaly and heart defects are described in 2–3 patients, each. There are single reports of other defects (Dandy-Walker anomaly, craniosynostosis, and agenesis of kidney).

In four families, the duplication was inherited from a clinically normal parent. In that context, this duplication may be considered as the so-called “copy number variant”, predisposing to a wide range of clinical abnormalities.

Trisomies of 10q

Traditionally all trisomies for the long arm of chromosome 10 are divided into two groups: “proximal” trisomies (involving areas from 10q11 (or 10q12) to 10q22) and “distal” trisomies (involving duplications of more distal segments — mostly 10q23 to 10qter). Two new types of trisomy 10q (with very different clinical consequences) have been delineated over the last couple years: small duplications of the proximal segment 10q11.21q11.23 and a tiny duplication within 10q24.32. These forms of trisomy 10q must be presented separately.

Duplication 10q11.21q23

At least 25 persons with this duplication have been presented in the literature. This small duplication may be recognized only using molecular technologies. The size of the duplicated segment in these patients varies from 0.3 Mb to 6 Mb. There are no common breakpoints typical for all carriers of this duplication.

Clinical manifestations in patients with this duplication usually include a delay in psychomotor development and some behavioral problems, usually considered as autistic features or pervasive developmental disorder. Several patients had seizures. Organ defects were reported only once.

It should be noted that in at least eight families, the same duplication was found in one of the healthy parents of the affected individual. In that context, it is still unclear, whether this reflects “incomplete penetrance” of the pathologic duplication or some additional (and yet unknown factors) are necessary to produce a negative outcome for persons with a “benign” duplication.

Sporadic occurrence of the duplication increases the chance considering this aberration as a pathologic one.

Cytogenetic examination of the parents seems to be necessary for counseling regarding further offspring.

“Proximal” Trisomy 10q

There are ~22 patients with pure trisomies for the proximal segments of 10q: 10q11(12) to 10q22. All of these patients have various degrees of delay in psychomotor development. Clinical manifestations include borderline microcephaly, unspecific facial dysmorphism, and defects of the eyes and internal organs.

Microphthalmia was reported in at least eight patients. (Microphthalmia may be found in numerous chromosomal syndromes, but its incidence in proximal trisomy 10q is unusually high). Other eye defects include colobomas of the iris (3), blepharophimosis (3), retinal dysplasia (2), and hypoplastic optic nerve (1).

Many patients had different (but usually mild) abnormalities of the skeleton and extremities: scoliosis (2), camptodactyly (3), partial syndactyly (2), joint laxity (1), bifurcated ribs (1), and preaxial polydactyly (1). Two patients had supernumerary nipples. Cleft palate, ear pits and short neck were reported in one patient each.

The most common internal defects are heart defects (7 patients). However, these defects were typically not life-threatening. Most patients had either atrial septal defect, ventricular septal defect, or patent ductus arteriosus (sometimes, these defects were combined in one patient); one child had coarctation of the aorta.

Three patients with such duplications had anomalies of the anus: anal atresia (2) or ventral ectopia of the anus (leading to a very short perineum). One patient had biliary atresia. Defects of the genitor-urinary system (pyeloectasia, vesico-urinary reflux, and hypospadias) were reported in one patient each.

Duplication of the segment 10q22 seems to be responsible for the main manifestations of this condition (microphthalmia, coloboma, and anal atresia). However, it will be too early to consider proximal trisomy 10q as a clinically recognizable syndrome.

Trisomy 10q24.32 and Ectrodactyly

Ectrodactyly, also known as “cleft hand” or “cleft foot” is a serious defect of the extremities, where the patient does not have one or several central digits, but the 1st and 5th digits are usually preserved. Ectrodactyly may involve all four limbs, but it may be limited to only the hands or only the feet. In some patients, it affects only one extremity. More severe forms of this defect may lead to monodactyly (when the hand or foot has only one digit). Ectrodactyly is found in several forms of chromosomal pathology, including deletions 2q31 and 7q21. Examination of several persons with ectrodactyly showed that duplication 10q24.32 may be another cause of this malformation.

Currently, there are ~45 reported patients with ectrodactyly in association with the tiny duplication 10q24.32. In some families re-examination of the patients, which were considered to be the people with autosomal-dominant ectrodactyly, lead to the discovery of a small duplication 10q24.32 in the affected patients.

Most patients have normal intellectual development. Usually, the patients have “typical” ectrodactyly, although there are reports of monodactyly of the hands and feet, femoral duplication, or syndactyly of the fingers or toes as more severe (or more mild) manifestations of the same basic defect.

Although some published reports do not provide clinical details regarding all manifestations in the affected persons, at least nine patients had associated defects of the kidneys (mostly hypoplastic kidneys). Four patients with 10q24.32-related ectrodactyly had hearing impairment, two had epilepsy, and one had cataract.

The mechanism of the defect remains unknown. All affected patients, reveal a very small (~0.5 Mb) duplication of the approximately the same segment (~102.9 Mb – 103.4 Mb). In two families, people with a mosaic duplication did not have any abnormalities. There are numerous reports of patients having much larger distal duplications of 10q, either as a single anomaly (see below) or in association with partial monosomies for other chromosomes, and, for this group of patients, ectrodactyly does not seem to be typical. It was found in five patients with distal trisomy 10q in association with deletions for other chromosomes, mostly with deletions 4p (three patients). Because some patients with “pure” del 4p have ectrodactyly, the role of the associated trisomy 10q in the origin of this defect remained

unclear. Not a single reported person with cytogenetically visible distal duplication 10q had ectrodactyly, although the region 10q24.32 was definitely duplicated in all of these patients. In that context, the duplication of the responsible gene per se does not seem sufficient for the origin of ectrodactyly. Therefore, either a tiny isolated duplication 10q24.32 breaks or somehow disables the control or regulatory element or there are some other factors affecting the expression of the triplicated gene in the patients with ectrodactyly.

Distal Trisomy 10q

Isolated distal trisomy 10q was reported only in 47 patients. At least 200 more patients had this trisomy in association with partial monosomies for different chromosomes, mostly as a result of familial translocations. Distal trisomy 10q is considered to be a well-known and recognizable entity.

In a typical situation, the infants are born with prenatal hypoplasia: their birth weight is less than normal, although most of them are born at term. Typical cranio-facial findings include microcephaly, high forehead, small palpebral fissures, hypertelorism, blepharophimosis, ptosis, round flat face, broad nasal bridge, small upturned nose with prominent philtrum, small mouth (microstomia), malformed low-set and posteriorly rotated ears and small chin (micrognathia).

Characteristic skeletal anomalies include camptodactyly, proximally placed thumbs, pectus excavatum, kyphoscoliosis, and partial syndactyly between the second and third toes. Not a single person with isolated distal 10q duplication had ectrodactyly (although it was mentioned in several patients who had trisomy 10q in association with partial monosomies for other chromosomes).

Cleft palate is relatively common: it was reported in six out of 47 patients with pure distal trisomy 10q; two more patients had cleft lip and palate or cleft lip. Three patients had hearing impairment. Short neck was mentioned in at least in seven patients.

Most patients have a significant delay in psycho-motor development, although structural defects of the brain (except microcephaly) are not characteristic (hypoplastic corpus callosum and cerebellar hypoplasia were reported in one patient each). The most frequent eye defect — microphthalmia — was described in four patients. There are sporadic reports of coloboma, optic atrophy, and retinal dysplasia.

As usual, congenital heart defects are the most common internal defects; they were reported in ~25% of patients. Two defects: hypoplastic left heart and tetralogy of Fallot were life-threatening. Defects of the kidneys usually affect the collecting system. These defects include hydronephrosis, double ureters, dilated renal pelvis, and hypoplastic urinary bladder. One patient with a mosaic form of distal trisomy 10q, however, had bilateral renal agenesis. There is no characteristic pattern of defects of the lungs, endocrine system, or gastro-intestinal tract. Genital defects are not characteristic, but two adult female patients with distal trisomy 10q had amenorrhea.

Usually, pure distal trisomy 10q is a result of a sporadic mutation (with a negligible risk for future pregnancies), but translocations (especially small) may remain unrecognized without cytogenetic examination of the parents.

Trisomy 10

Trisomy 10 is an exceptionally rare condition. There are only 16 reports of this abnormality, including six reports of full trisomy and ten reports of mosaic trisomy.

Full trisomy 10 is not compatible with life; not a single fetus with full trisomy 10 has been born alive. In all reports, full trisomy 10 was found upon prenatal diagnosis, and all pregnancies were terminated (or fetuses died in utero).

Mosaic trisomy is not so grave, but vital prognosis is very serious. In two families, pregnancies with mosaic trisomy 10 were terminated after prenatal diagnosis. Out of eight children born alive, four died during first year of life and only four were alive. In all (or almost all) cases, trisomy 10 produces very serious defects, including (but not limited to) abnormalities of the brain, heart, kidney and gastro-intestinal tract. Most reported fetuses had severe neck edema; short neck was noted in patients without edema. Usually fetuses (and infants) have cleft lip and palate (6/6 in full trisomy and 2/10 in mosaic trisomy). Facial dysmorphism is common; blepharophimosis was mentioned in four out of eight live-born patients.

Abnormalities of the brain include agenesis of the corpus callosum (3), defects of the cerebellum (2), microcephaly (2), and even meningocele (1). Reported eye defects include microphthalmia (3), coloboma (1), absence of one optic nerve (1), and abnormal pigmentation of ocular fundus (1).

Various heart defects were reported in ten people. Most of these defects were very severe and included interrupted aortic arch (2), transposition of the great arteries (1), monovalvular heart (1), atretic 3-cuspid valve (1) or a combination of more common defects.

Diaphragmatic hernia and unlobated lungs (in a person without a diaphragmatic hernia) are also known in patients with trisomy 10.

Serious kidney abnormalities may be considered as a hallmark of trisomy 10. They were found in five out of six fetuses with complete trisomy 10 and in three people with mosaic trisomy. Agenesis of one kidney was reported in four persons, four had cystic kidneys, two had hypoplastic kidneys (sometimes the absence of one kidney was accompanied by hypoplastic of cystic contralateral kidney). Defects of the kidneys (as well as heart defects) determine grave vital prognosis.

Anal atresia was the most common defect of the gastro-intestinal system; it was reported three times. Other people had intestinal malrotation (2), agenesis of the liver (1), or absent gallbladder (1).

Almost all persons with trisomy 10 have multiple skeletal effects, which include defects of the spinal column (scoliosis, vertebral fusion), contractures, camptodactyly, and structural defects of the digits: syndactyly (4), proximal position of thumbs or great toes (2), preaxial polydactyly (2), or even absent toe on one foot.

All children with mosaic trisomy 10 who survived show significant delay in psycho-motor development.