Congenital limb defects

Congenital defects of the limbs (***dysmelia***) are congenital deformities resulting from the intervention of teratogen during the morphogenesis of the locomotor apparatus (critical period: Weeks 4-7) or based on genetic defect[1][2].

We divide deviations in the sense of plus (hyperplasia) and minus (aplasia, agenesis)[3].

We distinguish between **atypical** defects (Ombrédan's disease, arthrogryposis multiplex congenita), **atrophic** (aplasia radii congenita, synostosis radioulnaris congenita , Madelung deformity, aplasia femoris congenita, pseudoarthrosis tibiae congenita etc.), **hypertrophic** (affecting fingers, part of a limb or the whole limb), **numerical** (supernumerary bones), **sprains** (torticollis muscularis congenita) and **dislocations** (developmental hip dysplasia)[3].

Etiology

90% of congenital defects have a genetic origin[1](typical congenital defects – e.g. chondrodystrophy) – familial occurrence, hereditary, arising from a direct disorder of the germinal tissue.

- **AD** (autosomal dominant inheritance) – one parent equally affected → 50% of offspring affected.
- **AR** (autosomal recessive inheritance) – an affected individual has offspring with a heterozygous partner who is also a carrier of the recessive gene.
- **GR** (gonosomal recessive inheritance) – affection linked to sex chromosome X, males affected, females carriers[2].

External causes (atypical birth defects) are applied in 10%[1] - maternal infection, the effect of drugs and other internal and external teratogens, mechanical influences.

- **poisons**, penetrating from the mother to the fetus, e.g. some drugs (thalidomide, drug poisoning);
- **lack of oxygen**, arising exogenously and endogenously (anemia of the mother, nidation disorder);
- **mother's age** (age under 20 + over 40);
- effect of **deficiency** of certain substances (vitamins);
- **ionizing radiation**, which also affects the fetus directly;
- **infectious diseases**, especially viral (rubella, measles, lues, toxoplasmosis);
- **diabetes mellitus**;
- **mechanical noxy** - intrauterine amniotic strips;
- mental **stress** of the mother, **alcoholism** atd[1][3][2].

Embryology

Limbs begin to form at the end of the 4th week of pregnancy from the **limb bar** (mesodermal buds of the embryo, covered by a layer of ectodermu). They are formed in the proximodistal direction. Proliferation of the mesoderm is dependent on the vascular supply.

- The bones of the girdles and proximal segments (humerus, femur - **stylopodium**) are formed from mesoderm directly, other parts (forearm, lower leg - **zeukopodium** and arm, leg - **autopodium**) are formed from the mesoderm under the action of the apical ectodermal ridge (AER, regulates the external growth of the limbs);
- **growth factors**: FGF 1–8, NGF;
- at the distal end of the limb buds **zone of polarization activity (ZPA)** - determines the anterior-posterior orientation of the limbs (induced by the Shh signaling gene - a decrease in activity causes the absence of ulnar or fibular fingers, an increase leads to duplication of fingers).

Muscles - developing separately from myotomes, originating from the middle part of the mesoderm of the somites (primary segments of the embryo). Back muscles (unlike limb muscles) retain their segmental arrangement.

- In the 6th week of pregnancy, flattening of the distal parts of the limbs (hand and foot plates);
- in the 7th week, the rotation of the limbs into the correct position;
- in the 8th week in the AER gene-induced apoptosis leading to the separation of individual fingers;
- at 12 weeks ossification centers in all long bones;
- development of the lower limbs is delayed by about 1 week compared to the upper limbs.

Basic **limb morphogenesis** is therefore **completed in the embryonic period** and most of the influencing factors must apply in this period. An important factor is the ingrowth of blood vessels into the growth zone of undifferentiated mesoderm cells – the disorder leads to a reduction of mesodermal cells; resulting in transverse limb defects (symbrachydactyly)[1].

Genetic regulation of limb development

- **Signal molecules** (acts between cells): Shh ("sonic hedgehog", most important, development of various tissues), Ihh ("indian hedgehog", cartilage differentiation), FGF (fibroblast growth factors, overall limb growth), BMP (bone morphogenetic protein, stimulates osteogenesis).
- **Transcription factors** (acting inside the cell): homeobox genes (Hox A and D), Pax[1] genes.

Classification and examples

1st classification was introduced by **Saint-Hilaire** (1832, outdated nomenclature of birth defects based on Greek): e.g. the terms amelia (absence of the entire limb), peromelia (mutilation of the peripheral part of the limb), phocomelia (failure to develop the proximal segments of the limb) etc[1].

Classification according to **Frantz and O'Rahilly** (1961): terminal and intercalary defects[1].

Swanson's Classification (1964)[1]:

- faulty development,
- wrong differentiation and separation,
- duplication,
- excessive growth (gigantism),
- insufficient growth (hypoplasia),
- congenital constrictions (amniotic bands),
- generalized skeletal defects[2].

The new classification created at **IPSO** (1973) distinguishes transverse and longitudinal defects[2].

Transverse defects
They include so-called congenital amputations (similar to surgical amputations at different levels of the limb). The plane of congenital amputation is indicated by the name of the limb segment (e.g. arm, thigh, lower leg), the length of the stump is indicated in thirds (proximal, middle, distal)[2].
Where a segment of a limb is completely missing, we will use the name "complete".

Longitudinal defects
This includes other defects that do not belong to transverse defects.
We list all the bones or their parts that are missing.

We indicate the missing length of the bone in thirds.

Where the entire bone is missing, we use the word "complete"[2].

Incorrect positioning of limb parts (limb defects, formation disorders)

Defects are divided into terminal and intercalary defects, as well as transverse and paraaxial defects. Other names used (based on Saint-Hilaire's original classification):

- according to the severity of the impairment (so-called teratological series): hypoplasia, partial aplasia, complete aplasia;
- amelia (complete absence of a limb), hemimelia (impairment of one of the paired bones of the forearm and lower leg) - complete (complete absence of a bone) / incomplete (only a part of the bone is missing)[1].

Transverse limb defects

Part of the limb is missing in its entire cross-section[1].

Terminal defects

- **Amelie** - missing entire limb;
- **hemimelia** - the terminal part of the limb is missing at different heights;
  - complete – defect at elbow or knee level;
  - incomplete – defect below elbow or knee level[1].

Intercalary defects

- **Phocomelia** - some of the central parts of the limb are missing;
  - complete – hand or foot goes on the girdle;
  - incomplete – the hand or foot fits on the reduced part of the limb[1].

Symbrachydactyly

In German literature, this term refers to rudimentary fingers mounted on the stump of a limb. In Anglo-Saxon literature 4 groups:

- **shortening of fingers** (in Poland's syndrome);
- **missing central fingers** (cleft hand);

- **monodactyly** (only the thumb is present);
- **peromelia** (deformed stump of hand without fingers, adactyly)[1].

Paraxial limb defects

They damage one part of the limb in the sagittal plane (preaxial, central, postaxial part) distal to the elbow (or knee).

Terminal hemimelia

Intercalary hemimelia

Oligodactyly

Also *partial adactyly*. It is a reduced number of fingers, sometimes founded only as rudiments.

- Preaxial (missing thumb and 2nd finger);
- postaxial (4th finger and little finger missing).

These two types are often associated with aplasia or hypoplasia of the respective bone of the forearm or lower leg.

- Cleft hand (lobster claw - missing central fingers, others preserved).

Errors in differentiation and separation of limb parts

They are caused by **apoptosis disorder**. They are formed between the 7th and 8th week of embryonic development and can be combined with other defects (Poland's syndrome, Apert's syndrome, cleft foot, polydactyly, congenital constriction band syndrome). Typical representatives are synostoses of various parts of the limbs:

Radioulnar synostosis

Tarsal Coalition

Syndactyly

It is the most common congenital limb defect (1:2000), 15-40% AD. According to the length of the connection we distinguish syndactyly:

- ***complete*** (fingers joined in full length),
- ***incomplete'*** *(only parts of the fingers are connected, proximal or (rarely) distal = fenestrated syndactyly, acrosyndactyly).*

According to the nature of the connection, we distinguish syndactyly:

- ***simple*** (membranous - fingers connected by skin),
- ***complex*** (bone connection).


Syndactyly

By brachysyndactyly we mean the shortening of the joined fingers. According to Flatt, the 3rd and 4th toes, 4th and 5th toes are most often connected. In ½ children, the disability is bilateral[1].

Therapy is as follows:

- separation of adjacent fingers with multiple Z-plasty, creation of an interdigital space, covering of the resulting defects with free skin grafts;
- method of separation: when several fingers are connected, only 2 marginal ones are separated at one time, the others no earlier than in 6 months;
- indication: up to 1 year of age, only fingers of unequal length are separated (4th and 5th finger / thumb and 2nd finger), fingers of equal length are separated later (after 18 months - better planning of incisions, the interdigital fold does not tend to migrate distally), but it is always necessary to separate the fingers in preschool age;
- on the feet, the toes are separated quite exceptionally for cosmetic reasons[1].

Duplication of limb parts

These are defects due to the **splitting of embryonic tissues**, leading to the development of supernumerary segments (peripheral or even central)[1].

Polydactyly of hands and feet

Belongs to the most common congenital limb defects (1:3000). They are often associated with other systemic defects (organ impairments).

- Duplication ***preaxial*** (duplication of the thumb, connected to the triphalangeal thumb, note: the axis passes through the 2nd finger) – predominates in the white race (mostly not hereditary);
- ***central*** (duplication of 2nd, 3rd and 4th finger);
- ***postaxial*** (duplication of the little finger) – most common, hl. in the black race (AD).

Therapy:

- in duplicating the thumb, the radially positioned thumb is mainly supported so that the collateral ligament for the grasping function is preserved;
- complex decision-making in central polydactyly;
- in case of ulnar polydactyly, a peripherally positioned finger is tolerated (if it is only a soft-tissue appendage, then it is only tied up - it becomes necrotic)[1].

Duplication of ulna with missing radius (so-called mirror hand)

In addition to the ulna, the ulnar fingers are multiplied[1].

Overdevelopment

It affects the entire limbs or parts of the lower (or possibly upper) limbs, which are disproportionately enlarged. It can affect the skeleton and soft tissues (hypertrophy of fat, lymphangiomay, hemangiomay). The etiology is unknown (hormonal, lack of receptors for growth arrest in embryonic development, excessive influence of nerve mediators), causing cosmetic and functional problems. In localized lesions, the multiplied parts are formed by hamartomas (a mixture of different tissues with a predominant nerve component)[1].

Hemangiomatosis in Klippel-Trénaunay syndrome

It manifests itself as hypertrophy of the entire ½ body[1].

Hypertrophy in other syndromes

These include: Proteus syndrome, multiple enchondromatosis, neurofibromatosis[1].

Gigantism

This is an overall increase in all body proportions, usually associated with hyperplasia of the adenohypophysis[1].

Localized Disability

Macrodactyly:

- pseudomacrodactyly – only soft tissues are enlarged,
- right macrodactyly – also hypertrophic bone.

Therapy is:

- reduction surgery or ablation of hypertrophic parts (often repeatedly during growth);
- for hemihypertrophy, then shortening osteotomy of long bones[1].

Insufficient development

These are defects with reduced limb development:

Whole limbs

Its terminal parts (microdactyly)

Her intercalary parts (hypoplasia)

- **Elbow joint agenesis**,
- **proximal focal femoral deficiency (PFFD)**,
- **hypoplasia of the tibia and fibula**.

It can affect all tissues of the limb or only individual components (skin, blood vessels, nerves, tendons, muscles, bones). Insufficient development is often associated with other limb defects (e.g. deformities of the ankle joint and foot joints)[1].

Amniotic constrictions, congenital constriction band syndrome (Streeter's dysplasia)

It is a non-hereditary defect, classified as a disorder. The etiology is not fully understood, 2 theories[1]:

Defective development of limbs from endogenous causes (Patterson and Streeter)

In certain parts of the body, the mesoderm does not form under the skin, which leads to its strangulation[1].

Exogenous theory

Premature rupture of the amniotic sac leads to the formation of streaks that can cause constriction on the limbs and trunk (restriction of venous drainage → edema → amputation or deep incision) – most often partial amputation of fingers and toes, supramalleolar constriction of the lower leg, several limbs are often affected[1].

Accompanying anomalies include: fenestrated syndactyly, brachydactyly, pes equinovarus, cleft lip and palate.

Syndrome occurs around the 6th week of development, it can occur in mothers with oligohydramnios, premature contractions and amniotic fluid leakage.

Classification according to Patterson:

- simple constriction;
- constriction with deformity of the distal parts of the limb caused by lymphedema, cyanosis and swelling;
- constriction associated with syndactyly;
- intrauterine amputation.

Therapy[3]:

- simple constitution – multiple Z-plasties of the skin;
- more complex constrictions – often complex reconstructive procedures on hands and feet[1].

Congenital limb defects associated with other anomalies (generalized abnormalities and syndromes)

This includes congenital defects, mainly of the upper limbs (mainly the humerus), which are often combined with other congenital anomalies. For most of them, I know the genetic background and heredity.

Every child with a congenital limb defect should be examined for involvement of: craniofacial region, heart, gastrointestinal, urogenital, skin and nervous system, hematopoietic system. Some of these syndromes are caused by mutations in FGF[1] coding regions.

Poland Syndrome

- Unilateral agenesis of the pectoralis minor muscle and the sternal part of the pectoralis major muscle + abnormalities of the unilateral hand (hypoplasia of the hand and fingers, syndactyly, brachydactyly, oligodactyly);
- the affected limb grows more slowly;
- can be combined with kidney impairment;
- in left-sided involvement (10%) associated with dextrocardia;
- etiology: disorder of the vascular supply in the embryonic stage of development due to obstruction of the subclavian artery[1].

Thrombocytopenia-absent-radius syndrome (TAR)

- Thrombocytopenia (with bleeding manifestations) + unilateral / bilateral aplasia / hypoplasia of the radius (with typical radial deviation of the hand), deformity / absence of the thumb, hypoplasia of the ulna.
- Associated anomalies: shorter stature, strabismus, congenital heart defect, other defects of the upper limbs (hypoplasia of the shoulder girdle and humerus) or lower limbs (hip dislocation, pes equinovarus, etc.)[1].

Fanconi-pancytopenia syndrome

- Variable limb involvement: hypoplasia / aplasia of the thumb, hypoplasia of the radius, DDH + pancytopenia (bleeding manifestations – hematomas, pallor, repeated infections);
- the child is born smaller with limb defects and irregular areas of brown colored skin;
- manifestations of pancytopenia appear between the 5th and 10th a year;
- associated anomalies: involvement of the heart, urogenital tract, vision[1].

Holt-Oram Syndrome (Hand-Heart Syndrome)

- The whole range of deformities: deformity of the forearm and hand (hypoplasia / aplasia of the thumb, hypoplasia / aplasia of the radius);
- elbow dysfunction and severe forearm hypoplasia;
- defects of the humerus, clavicle, shoulder blades and sternum;
- associated defects: cardiac impairment (atrial/ventricular septal defect, tetralogy of Fallot), spinal impairment (scoliosis, pectus excavatum);

- involvement usually bilateral but asymmetrical[1].

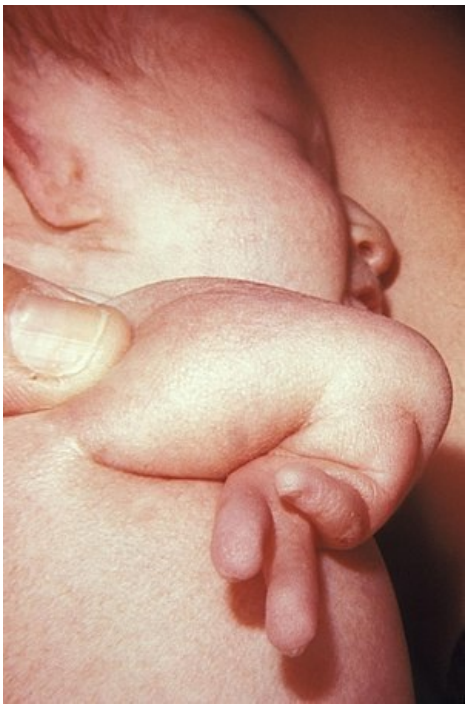
VATER syndrome

1. vertebral defects (V);
2. imperforate anus (A);
3. tracheoesophageal fistula (T) – see Congenital developmental defects of the respiratory system;
4. esophageal atresia (E);
5. radial and renal dysplasia (R)[1].

VACTERL syndrome

Sporadic defect with unknown cause, more common in children of mothers with diabetes mellitus, additionally includes:

1. cardiac impairment (C),
2. other limb development abnormalities (L)[1].


VACTERL syndrome

Tibial hemimelia

- AD hereditary,
- hemimelia more often associated with radial ray duplication and heart defect[1].

Femoral hypoplasia syndrome and unusual faces

- Hypoplasia / aplasia of the femur and fibula, (affecting the humerus and the lower part of the spine and pelvis) + on the face, a short nose and small nostrils, long philtrum, narrow upper lip, gothic palate, slanting eye slits< ref name="Dungl"/>.

Ulnar Femoral Syndrome

- Combination of femur and ulna involvement[1].

Therapy of congenital limb defects

It is individual according to the type of defect, anatomical area and impaired function. The aim is to correct the axis of the lower limbs and their stability for walking + the upper limbs to ensure self-care for food and hygiene[1].

An integral part is the effort to correct the position using orthoses and replace the function of missing parts of the limbs with various types of prostheses[1].

Links

Related Articles

- Congenital developmental defects
- DDH
- Ombrédann's disease
- Arthrogryposis multiplex congenita
- Phocomelia
- Aplasia radii congenita
- Talipomanus
- Synostosis radioulnaris congenita
- Madelung's deformity
- Congenital shin splints
- PFFD
- Aplasia fibulae congenita
- Torticollis muscularis congenita
- Dog equinovarus congenitus

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3. KOUDELA, K., et al. *Orthopedics.* 1. edition. Prague : Karolinum, 2004. ISBN 80-246-0654-2.

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