

Angelman syndrome

a case report

MUDr. Klára Drábová, Ph.D.

Angelman syndrome

- Mother - healthy
- Father - healthy, smokes 20/day

They tried together for a concept for over 2 years, then there was a consultation in the center of assisted reproduction and in vitro fertilization, IVF – the 1st embryo-transfer was successful.

Our proband is from the 1st pregnancy, after the embryo-transfer the mother had hyperstimulation syndrome, she was in the ICU for 14 days. Prenatal screenings in pregnancy were normal, mother began to give birth prematurely, maturation of lungs was completed, delivery at 34th week of pregnancy, a boy was born, 2180g/44cm, Apgar Score 9-9-10, 2 weeks in an incubator for immaturity, worse sucking, neonatal jaundice with phototherapy for 2 days, then they started with developmental rehabilitation.

Angelman syndrome

In the next course he gain weight, has slower psychomotor development.

At the age of 2 months - was operated for incarcerated inguinal hernia.

Then he was monitorated for pes abductovalgus on the right leg, it was recommended intensive rehabilitation.

He was examined by neurologist – diagnosis: cerebral palsy, spastic paraparesis of lower limbs, microcephaly, stigmatization, MRI of the brain was normal.

At the age of 3 years he had his first epileptic seizures.

Angelman syndrome

Epileptic seizures recurred, once he was hospitalized on Department of Anesthesiology and Resuscitation for status epilepticus, then on paediatric ICU.

Psychomotor development – from the age of 5 months he started to turn, up to 1 year of age no progress, at 1,5 year of age he began to sit, independent walk started at age of 3,5 years, walking was unsteady, swaying, later ataxic. At the age of 5 months he was not speaking, just made sounds, smiling, significantly salivating, wearing diapers.

Our patient:

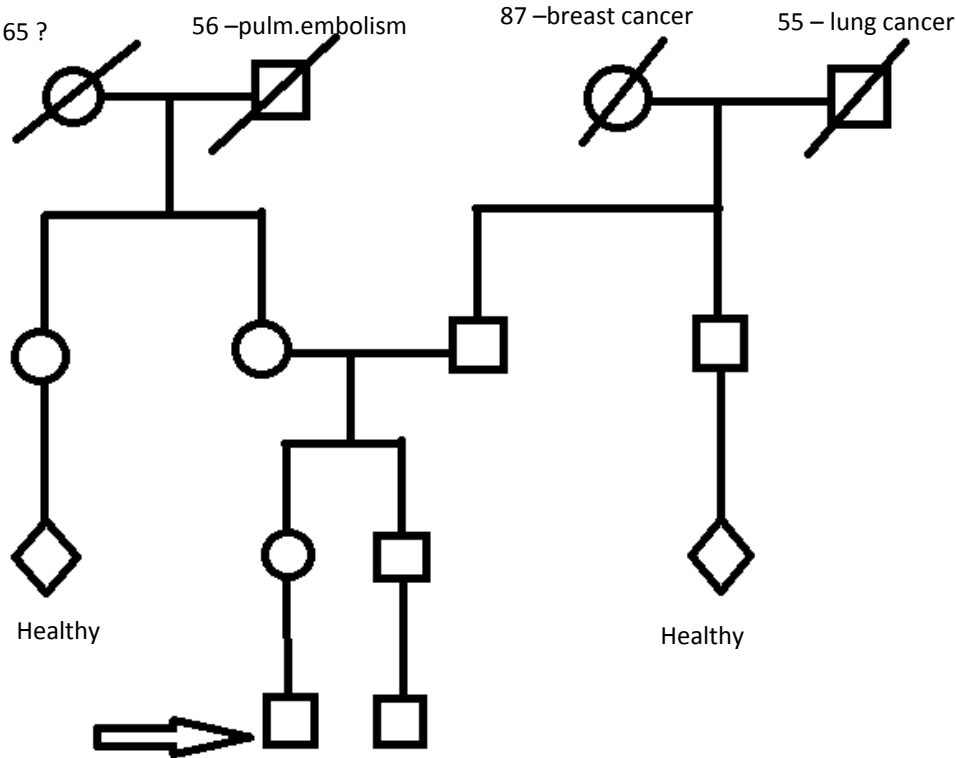


height 105cm (below the 3rd percentile),
weight 16kg (below the 3rd percentile),
head circumference 47cm (significantly below the 3rd percentile),

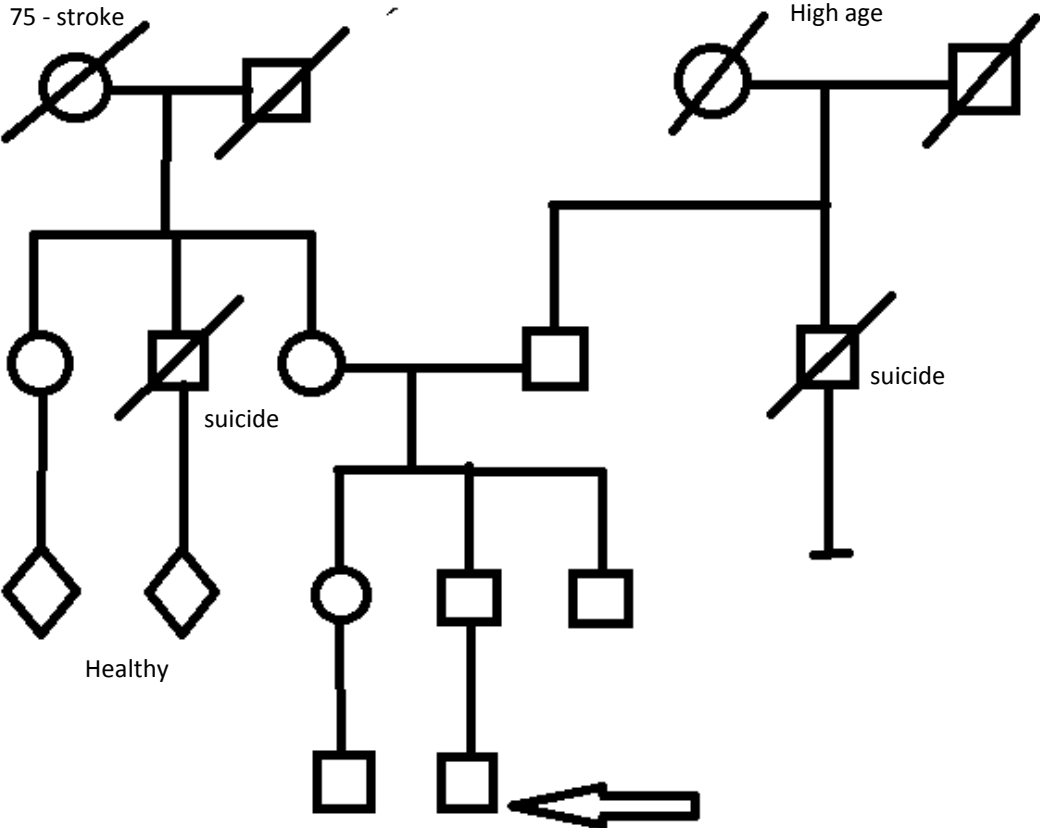
brachycephaly, flat occiput, lower hairline, red hair, face – narrow eye slits, epicanthus, pronounced nose, thin upper lip, the oral cavity – high palatum, teeth missing after extraction because of dental caries, excessive drooling, normal neck, thorax without deformity, limbs symmetric, spastic paraparesis, genua valga, flat feet, upper limbs – short fingers, transverse groove on the right palm, he was smiling, friendly, very active, fascinated with water

Angelman syndrome - pedigree

Mother's pedigree



Father's pedigree



Angelman syndrome – genetic examination

1) Karyotype:

46, XY normal male

2) Array-CGH:

It was found microdeletion of the region 15q11.2-q13.1 about the size approximately 5,74 Mb.

Microdeletion of the region 15q11.2-q13.1 is described as a causal for Angelman and Prader-Willi syndrome.

The result was verified by the MLPA method. This change was not found in either parent.

Angelman syndrome – genetics

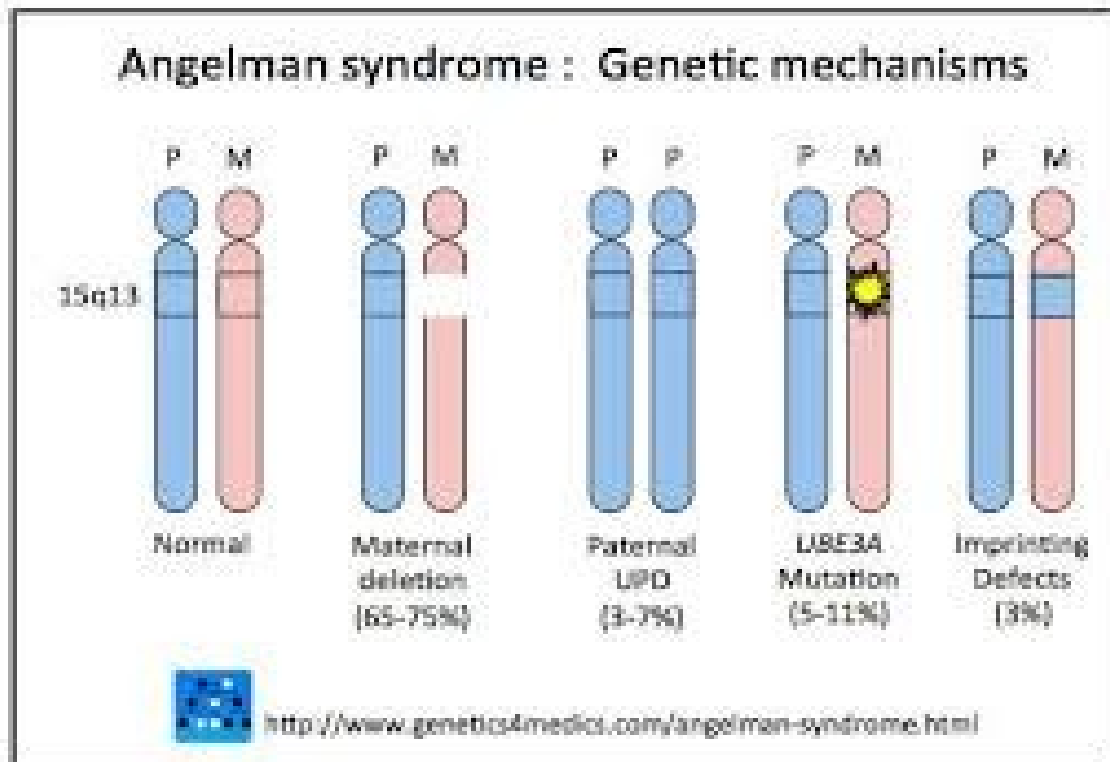
Angelman syndrome (AS, *Happy puppet syndrome*) is a microdeletion syndrome, most often caused by a deletion of the region 15q11-13 on the **maternal** chromosome or a uniparental disomy of the paternal chromosome.

The incidence of that syndrome is about 1 / 16,000.

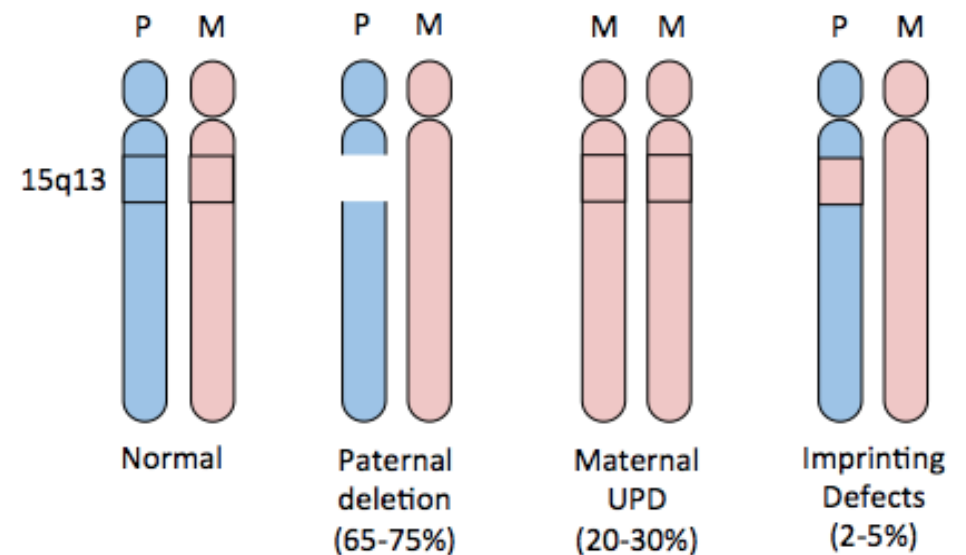
Prader–Willi syndrome (PWS) is a microdeletion syndrome 15q11-13 on the **paternal** chromosome or a uniparental disomy of the maternal chromosome.

The incidence of that syndrome is about 1 / 10,000-30,000.

Angelman / Prader-Willi syndrome



Prader-Willi syndrome : Genetic mechanisms



Angelman syndrome - symptoms

- Developmental delay, including no crawling or babbling at age of 6 to 12 months
- Intellectual disability
- No speech or minimal speech
- Difficulty walking, moving or balancing well
- Frequent smiling and laughter
- Happy, excitable personality
- Trouble going to sleep and staying asleep
- Seizures, usually beginning between 2 and 3 years of age
- Stiff or jerky movements
- Small head size, with flatness in the back of the head
- Tongue thrusting
- Hair, skin and eyes that are light in color
- Unusual behaviors, such as hand flapping and arms uplifted while walking
- Sleep problems

Prader-Willi syndrome - symptoms

Newborns and infants

- Hypotonia, craniofacial dysmorphism – almond shaped eyes, strabismus, a narrow forehead at the temples, a thin upper lip and a downturned mouth, small hands and feet
- feeding difficulties and underweight until the age of 1 year
- Fatigue, poor response to stimulation, weak crying

Toddlers and children

- the child will start to show an increased interest in food, ask for extra food and behave badly to get extra food. This behaviour increases during childhood and is seen in all children with Prader-Willi syndrome.
- hypogonadotropic hypogonadism – reduced production of sex hormones and reduced fertility
- Short stature (about 150 cm), **obesity**, scoliosis, short arms and legs
- Learning difficulties, delay in development, behavioural problems, sleep problems

Angelman syndrome – conclusion

Angelman syndrome (and Prader-Willi too) is one of the microdeletion syndromes.

The presented case report shows the characteristic phenotype of Angelman syndrome.

Our patient is monitored multidisciplinarily.