Angelman syndrome (genetics)

Angelman syndrome (AS, *Happy puppet syndrome*) is a microdeletion syndrome, most often caused by a deletion in section 15q11–13 on the maternal chromosome (i.e. a certain section on the long arm of the 15th chromosome) or by uniparental disomy of the paternal 15th chromosome. The incidence of that syndrome is about 1/16,000.

105830 (https://omim.org/entry/105830)

Etiology

The etiology of Angelman syndrome is closely related to Prader-Willi syndrome. Both syndromes have a different phenotype, but the deletion region is the same in both. Genome imprinting decides which of them the individual will be affected by.

70% microdeletion chromosomeu (15q11–13)mat

- In the deleted section, there are two critical gene sections, which we denote:
  - PWCR
  - ASCR
- Angelman syndrome then arises when both sections are deleted on the maternal fifteenth chromosome, but as a result the ASCR section on the paternal homologous chromosome is methylated, resulting in its inactivation. Thus, only the PWCR section on the paternal chromosome remains active.
- For the sake of completeness, Prader Willi syndrome, on the other hand, arises because the deletion occurred on the father's 15th chromosome, and thus the ASCR section on the mother's was inactivated.

Uniparental disomy of the paternal or maternal chromosome

- In some cases where deletion of 15q11–13 cannot be demonstrated in the affected person, the syndrome is probably caused by uniparental disomy. This means that the individual received both chromosomes 15 from one parent and therefore has two identical copies of one chromosome from one of the parents. Which of the parents he inherited the chromosomes from again influences the manifestation of the respective syndrome. So if:
  - has both chromosomes from the mother – Prader-Willi syndrome occurs, and both sections of the PWCR are inactivated
  - has both chromosomes from the father – Angelman syndrome occurs and both sections of ASCR are methylated

Other Mutations

- other causes of Angelman syndrome, such as
  - mutation of the E6–AP gene (UBE3A), which encodes a ubiquitin-protein ligase or
  - in 7-9% of patients affected by Angelman syndrome, mutations of the imprinting center, which controls the imprinting of other genes and is located in the critical section, were demonstrated.

Clinical picture

The syndrome occurs more often in girls, but it is not the rule. Children need lifelong assistance and about 70% of them can learn to do simple household chores.

Angelman syndrome phenotype

- we observe in all sufferers:
  - poorly developed speech - only a minimum of words, rather non-verbal expression
  - severe mental retardation in the range of debility to imbecility
  - motor problems – ataxic movements, stiff gait (reminiscent of movements of a puppet)
  - unprovoked fits of laughter
- about 80% have:
  - attention deficit disorder
  - hypotonia
  - microcephaly
  - abnormal EEG
- 20-80% may also experience:
  - squinting
  - disorders of the swallowing reflex
  - hypopigmentation
  - flattened header
  - hyperactivity
  - epileptic seizures

Links

Related Articles

- Gene imprinting and human pathologies
- Gene imprinting
- Beckwith-Wiedemann syndrome
- Prader-Willi syndrome
- Uniparental disomy

External links

- OMIM:105830 (Angelman syndrome) (http://omim.org/entry/105830)
- angelman.cz (http://angelman.cz/)
- angelman.org (https://www.angelman.org/)
- Angelman syndrome (anglická wikipedie)

Reference

- KOČÁREK, Eduard – PÁNEK, Martin – NOVOTNÁ, Drahuše. *Klinická cytogenetika I.: úvod do klinické cytogenetiky, vyšetřovací metody v klinické cytogenetice.* 1. edition. Praha : Karolinum, 0000. pp. 120. ISBN 80-246-1069-8.

- ŠTEFÁNEK, Jiří. *https://www.stefajir.cz : Medicína, nemoci, studium na 1. LF UK* [online]. [cit. 15. 2. 2023]. <https://www.stefajir.cz/>.