Slide Seminar
Congenital tumours and pseudo tumors
(10th of September)

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Clinical data

Premature female baby, born at 34 wg

- Intrauterine growth retardation
- Bilateral polydactyly
- Urogenital malformations
- Necrotizing enterocolitis
- Death at D14 (36 GW corrected term)
Autopsy findings

Hypertelorism
Palate cleft

Hypoplastic hallux and overlapping toes

Bilateral post-axial hexadactyly
Right syndactyly

Necrotizing enterocolitis

Hydrocolpos
Vaginal atresia

Hydronephrosis

Utérus
Bladder
Brain weight: 283 g

< 5th pc at 36 wg

- Bilobed mass located in the area of infundibulum and mamillary bodies and developed in front of the ventral part of mesencephalon.
The lesion was not detected on US.

US data were further analyzed and demonstrated the lesion.
On coronal sections
Cortex

Nodules mainly made up of immature cells
Small tiny weakly myelinated fascicles
In addition, Anoxo-ischemic encephalopathy → Diffuse and focal white matter lesions → Ponto-subicular necrosis

Differentiated neurons
Hypothalamic Hamartoblastoma

PALLISTER-HALL SYNDROME
Hypothalamic Hamartomas (OMIM 241800)

- Rare, benign, congenital lesions: malformations rather than “true” tumours
- Variable in size as well as in their relationship to hypothalamus

- Hamartomas isolated in most cases, in children/adolescents
  - intractable epilepsy, gelastic seizures,
  - cognitive deficits
  - various endocrinal disturbances

- Hamartomas precociously identified in fetuses or neonates
  - various visceral and/or skeletal malformations
  - part of different syndromes
  - Hamartoblastoma (predominant immature component)
5% of Hypothalamic Hamartomas : Pallister-Hall syndrome (OMIM : 146510)

- In addition to HHb, **Pallister-Hall syndrome** includes
  
  ➔ Post-axial polydactyly

  ➔ Uro-genital malformations
  ▷ hypospadias, in male
  ▷ vaginal atresia in female

  ➔ Imperforate anus

  ➔ Inconstantly, cleft palate, cardiac defects…
Conditions demonstrating clinical overlapping features

- Smith-Lemli-Opitz syndrome (OMIM 270400)
- Holoprosencephaly-Polydactyly syndrome (OMIM 264480)
- Oro-Facio-Digital syndrome type VI (OMIM 277170)
- Hydrolethalus syndrome (OMIM 236680)
- McKusick-Kaufman syndrome (OMIM 236700)
PALLISTER-HALL syndrome

autosomal dominant disorder

- Heterozygous mutations of *GLI3* gene (7p14)
  - *GLI3*: zinc-finger transcription factor
    - SHH signalling pathway
Mutations of GLI3

↓

GREIG CephaloPolysyndactyly Syndrome (GCPS)

• Some overlapping features with Pallister-Hall syndrome
  → Both: cranio-facial anomalies and polysyndactyly with an autosomal dominant mode of inheritance
  → GCPS: pre axial polysyndactyly, no hamartoma

• Genotype/phenotype correlations
  → GPCS: various anomalies translocations, large deletions, exonic duplications, different mutations
  → Pallister-Hall: frameshift/non sense and splicing mutations
Our case fulfils the clinical criteria of **PALLISTER-HALL SYNDROME**

- Hypothalamic Hamartoblastoma
- Bilateral post-axial polysyndactyly
- Hydronephrosis
- Vaginal atresia – hydrocolpos
- Cleft palate

**Heterozygous in the GLI3 gene for a sequence Variant C 3485G>A**

⇒ not reported previously
⇒ expected to be pathogenic
Thank you!