Beckwith-Wiedemann Syndrome: From mosaicism to a unified management

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Introduction:
- Beckwith-Wiedemann syndrome (BWS) is a paediatric overgrowth disorder involving a predisposition to tumour
- Estimated prevalence of 1 in 10,300 to 13,700, but underestimated because of milder phenotypes (due to mosaicism)
- Hallmark symptoms include macroglossia, macrosomia, hemi hyperplasia, neonatal hypoglycemia, omphalocele, visceromegaly and solid embryonal cell cancers during early childhood: Wilms tumour (52%), hepatoblastoma (14%), neuroblastoma (10%), rhabdomyosarcoma (5%), and adrenal carcinoma (3%)
- Cancer risk is the highest during the first 2 years of life

Case report:
- A 4-week-old male infant addressed to the emergency room for left arm cyanosis
- Physical examination:
  - Hemi-macroglossia associated with left face hypertrophy
  - Umbilical hernia 2x1cm
- Lab workup: increased 24h urinary catecholamine, total plasmatic metanephrines
- Genetic: BWS due to mosaicism of paternal uniparental disomy of chromosome 11p15.5
- Tumour board: suspicion of neuroblastoma of the left adrenal gland associated with BWS
- Follow-up:
  - Adrenal mass: follow-up every month until 3 months of age and ± MIBG scan
  - General screening after the age of 3 months: follow-up with serial abdominal ultrasounds every 3 months + follow-up by an oncologist until 7 years of age

Genetics & uniparental disomy
- The critical BWS genes in the 11p15.5 region include:
  - IGF2: potent foetal growth factor
  - H19 in domain 1: tumour suppressor gene
- Uniparental disomy refers to the situation in which for a given imprinted gene pair, one parental allele is exclusively or preferentially expressed, whereas the other allele is silenced or weakly expressed
- Confirmation test: DNA test from a jugal smear

Radiological findings
- Neck MRI (a): left macroglossia and left face hemi-hypertrophy
- US and abdominal MRI: US (b) as well as T2 Blade (c) and diffusion-weighted (d) images in the axial plane demonstrate a nodular focal enlargement of the posterior arm of the left adrenal gland

Conclusion
- BWS is a genetic disorder that requires an intense oncology follow-up during the first years of life.
- Clinical manifestations may not be obvious at birth and patients may present with variable phenotypes due to mosaicism which may delay diagnosis and patient follow-up.
- Paediatricians should have a high index of suspicion for BWS in infants born with macroglossia.
- Awareness of this condition may enable prompt diagnostic and initiation of cancer screening.

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