Beckwith-Wiedemann Syndrome: From mosaicism to a unified management

Department of Women-Child-Teenager, service of Peadiatric[1], service of Peadiatric Radiology[2]
Geneva University Hospital

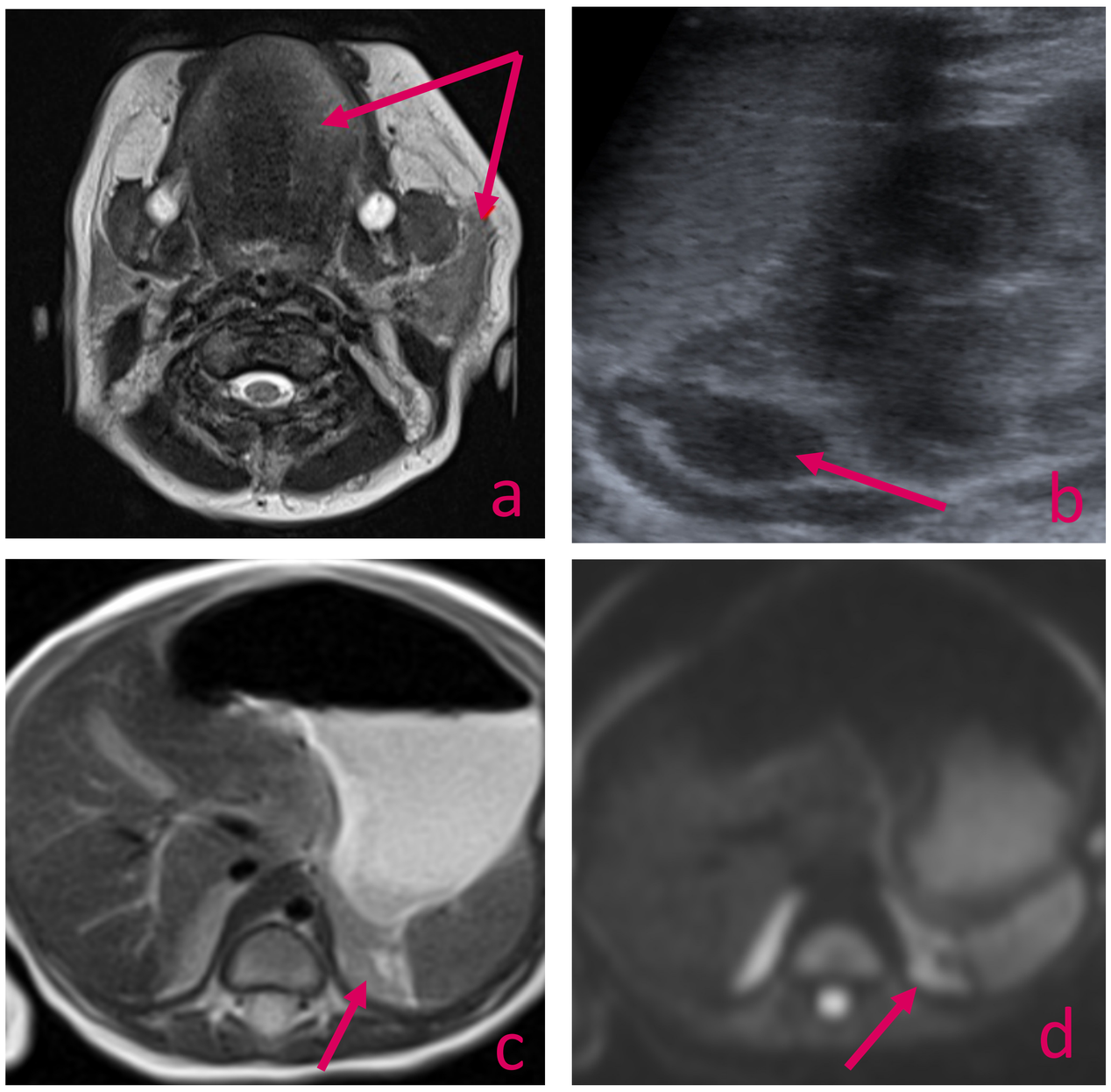
Fernandez B[1], Perrin A[1], Ghinescu C[1], Papangelopoulou D[1], Laurent M[2], Bajwa N[1]

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**.

Contact : Benjamin.Fernandez@hcuge.ch