A 4 MONTH-OLD BOY WITH BECKWITH WIEDEMANN SYNDROME (BWS)

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No conflict of interests.

Background

Beckwith-Wiedemann syndrome (BWS), an overgrowth and tumor predisposition syndrome is clinically heterogeneous. It is characterized by macroglossia, macroglossia, hypoglycemia, macroglossia, hypoglycemia, and macroglossia-like tumors (hematoma tumor, hepatoblastoma, nephroblastoma, and malformations (medial diaphragmatic, nephroblastoma, medullary tumor kidney, and nephroblastoma)) [1]. Growth rate slows around age seven to eight years. Hypoglycemia may affect abdominal body regions or select organs and tissues. Early death may occur from complications of hypoglycemia, hypoglycemia, and macroglossia-like tumors. Prenatally reported mortality of 20% is likely an overestimate due to enhanced treatment options and better recognition of the disorder.

Case Report

- A 4-month-old boy with overgrowth and longitudinal hemihypertrophy of tongue and left cheek delivered with (ELSC) Elective Section Caesarean due to low macroglossia.
- Birth weight was 400g (43.5 SD), 86.6th percentile and birth length 53cm (49.5 SD), 90th percentile.
- Anthropometric parameters: height 5.5 kg (43.5 SD), and height; 46cm (43.5 SD) 6 months, both at 95th percentile, at 20 months; 17kg (39.5 SD), 95th percentile, and 88 cm (53.5 SD) and DMR 21.56 kg (43.5 SD).
- There is a difference of tonsilar circumference between his left and right leg, but not in their length or in area.
- The behavior, intelligence and development were also normal.

Abstract

Background: Beckwith-Wiedemann Syndrome (BWS) is an overgrowth disorder with variable phenotype/hemihypertrophy, macroglossia, visceromegaly, malformations, hypoglycemia in 35-50% and predisposition to tumors, during the second part of pregnancy and first few years of life.

Aims and objectives: Molecular characterization of a patient with BWS was performed to ensure adequate clinical management. The analysis revealed the most common form of BWS due to loss of methylation in KDMR1 in presence of a normal H19-DMR methylation.

Methods: We present a 4-month-old boy with overgrowth and longitudinal hemihypertrophy of tongue and left cheek delivered with (ELSC) Elective Section Caesarean due to low macroglossia. His birth weight was 400g (43.5 SD), 86.6th percentile and birth length 53cm (43.5 SD), 90th percentile. The boy had 5.5 kg (43.5 SD) and height; 46cm (43.5 SD) 6 months, both at 95th percentile. There was a difference of tonsilar circumference between his left and right leg, but not in their length or in area. Diagnostic assessment was achieved according to clinical features, ultrasound survey, biochemical and molecular analysis.

Results: Prolonged tongue, cardiac, abdominal and renal ultrasound scans (US) showed longitudinal hemihypertrophy of tongue tissue, round heart shape with mild aortal valve sclerosis, mild hypothyroidism and low and moderate hypothyroidism of kidneys, especially left one. A renal ultrasound was uneventful, but on MRI were prominent both frontal(particularly subependymal nodules more than 5mm. Karyotype was normal male, 46 XY.

Biochemical and hormonal analyses: no evidence of hypoglycemia, others in normal range for his age and sex.

Molecular genetic deletion/duplication analyses of BWS/SDS critical region 11p15.5 (NLPA2):
- hypomethylation of KDMR1 (LIT1) in chromosome 11p15 region;
- normal methylation pattern for H19-DMR with estimated tumor risk of 1-5%

Discussion

- No consensus diagnostic criteria for Beckwith-Wiedemann syndrome (BWS) exist, although the presence of several findings (three major or two major and one minor) is often used to render a clinical or provisional diagnosis.
- Beckwith-Wiedemann syndrome is associated with abnormal regulation of gene transcription in the imprinted domain on chromosome 11p15.5. Many individuals with BWS are reported to have normal chromosomal studies or cytogenetics.
- Most BWS cases are sporadic, 85% have no family history of it and result from loss of maternal methylation at imprinting center 2 (IC2), part of maternal methylation at imprinting center 1 (IC1) or paternal uniparental disomy (UPD)(4).
- Nearly 10-15% have a familial history consistent with subchromosomal domain translocations of BWS (3).
- Treatment of manifestations: tongue reduction surgery for macroglossia in infancy or early childhood, ophthalmo-surgical benefit patients with fetal hypoglossia, recombinase should be treated using adequate pediatric oncology protocols (2).
- Prevention of secondary complications: Annual renal ultrasonic examination for affected children between age eight years and mild adenopathy to identify those with nephropathosis or radiolucent subependymal kidney disease (3).
- Surveillance: Monitor for hypoglycemia, especially in the neonatal period, screens for subependymal tumors by abdominal ultrasonic examination every three months until age eight years; monitor serum alpha-fetoprotein (AFP) concentration every two to three months in the first four years of life; early detection of hepatoblastoma (6).
- Prenatal screening: 16-22 weeks: possible by chromosome analysis for fetuses with an inherited chromosome abnormality or by molecular genetic testing for families in which the molecular mechanism of BWS has been defined.

Conclusions

Determination of insulin in a patient with an overgrowth and confirmed molecular diagnosis is crucial for establishing the correct diagnosis and clinical management.

We present a patient with BWS phenotype associated with molecular confirmation of loss of function in specific gene in the imprinting center and low risk of endocrine tumors. The overall evaluation will predict his clinical management.

References


Ultrasound scan (US) survey:
- Tongue – longitudinal left hemihypertrophy of tongue tissue,
- Cardiac – round heart shape with mild aortal valve sclerosis,
- Abdominal – mild hypertrophy of liver,
- Kidney – moderate hypertrophy of kidneys, especially left one;
- Brain – uneventful.

Brain MRI: prominent both frontoparietal subependymal nodules more than 5mm.

Karyotype: normal male, 46 XY.

Biochemical and hormonal analyses: no evidence of hypoglycemia, others in normal range for his age and sex.

Molecular genetic deletion/duplication analyses of BWS/SDS critical region 11p15.5 (NLPA2):
- hypomethylation of KDMR1 (LIT1) in chromosome 11p15 region;
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