



Hearing reduction of a child with Beckwith-Wiedemann syndrome

Clinical case



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Introduction

The American pathologist John Bruce Beckwith in 1963 and the German pediatrician Hans-Rudolf Wiedemann in 1964 independently reported Beckwith-Wiedemann syndrome (BWS), which is the most common overgrowth syndrome.

Beckwith-Wiedemann syndrome (BWS) is a rare genetic disorder. It affects 1 in 15,000 newborns (5, 6). Genetic testing and family history are important for the diagnosis of the syndrome. If genetic test results are negative, the diagnosis can be made based on the clinical signs. Beckwith-Wiedemann syndrome is the result of a mutation in genes that control body growth.

Etiologically, this syndrome is caused by genetic and epigenetic changes affecting the regulation of genes in a specific region of chromosome 11p15, resulting in overactivity of the IGF-2 gene (growth factor) and/or lack of an active copy of CDKN1C (cell proliferation inhibitor gene) (11). According to Mendoza Paulo A. Borjas et al., approximately 80–90% of patients exhibit a known molecular aberration that affects the regulation of a group of imprinted genes involved in cell cycle progression and somatic growth control, located within chromosome 11p15.5. (5) Normally, a person inherits one copy of this chromosome from each parent. Genes within chromosome 11 are expressed by the copies from both parents – genomic imprinting. Genomic imprinting is an epigenetically regulated process by which only one copy of a gene is expressed depending on the sex of the parent carrying the allele. Less than half of all cases of Beckwith-Wiedemann syndrome are the result of

changes in a process called methylation (silencing of gene expression). Typically, methylation occurs on the paternal allele at IC1 and the maternal allele at IC2. (11).

According to Dimitrov S, about 20% of cases of Beckwith-Wiedemann syndrome are caused by a genetic alteration known as paternal disomy, where people have two active copies of genes inherited from the father, instead of one active copy from the father and one inactive copy from the mother. In Beckwith-Wiedemann syndrome, paternal disomy usually occurs early in the development of the embryo and affects only one part of the body's cells. This is called mosaicism. Mosaic paternal disomy leads to an imbalance in the expression of paternal and maternal genes on chromosome 11, which is the basis of the signs and symptoms characterizing the syndrome. More rarely, mutations in the *CDKN1C* gene cause Beckwith-Wiedemann syndrome. About 1% of all people with Beckwith-Wiedemann have chromosomal abnormality known as translocation – an exchange of terminal sections of the arms of two non-homologous chromosomes, abnormal copying (duplication) or loss (deletion) of genetic material from chromosome 11 (3).

BWS is usually sporadic (85%) with familial transmission occurring in approximately 15% of cases. (5, 8, 11). In some reported cases of BWS, mutations are identified outside the region of chromosome 11p15.5, thus expanding the ability to diagnose individuals and families with Beckwith-Wiedemann syndrome (1).

According to studies, the molecular defects that may be observed in Beckwith-Wiedemann syndrome are:

- Loss of methylation at IC2 of the maternal allele in 50 to 60% of cases.
- Uniparental isodisomy of 11p15 on the paternal side in 20 to 25% of cases.
- Increased methylation at IC1 of the maternal allele in 5 to 10% of cases.
- Autosomal dominant maternal point mutations in CDKN1C (regulated by IC2).
- Chromosomal rearrangements (duplications, translocations, deletions or inversions) in fewer than 1% of cases.
- Unknown molecular defect in 10 to 15% of cases (5, 6, 8).

According to Duffy A Kelly and al, BWS cases can be divided further into three patient subgroups: those with classic characteristics, isolated lateralized overgrowth (ILO), and atypical BWS (2).

Characteristic symptoms of Beckwith-Wiedemann syndrome in early childhood vary in severity and include macroglossia, abdominal wall defects, lateral overgrowth, cardiac and renal malformations, enlarged abdominal organs, and an increased risk of developing embryonic tumors. Suspicions of Beckwith-Wiedemann syndrome arise in utero and after birth. Although most individuals with BWS show rapid growth during the late fetal development stage and in early childhood, growth usually slows by the age of seven to eight. Newborns often have features characteristic of the syndrome, which allows for the diagnosis to be made. Adult height is usually within normal ranges.(8, 11)

Abdominal wall defects are common in newborns with Beckwith-Wiedemann syndrome. These defects can range in severity from omphalocele to umbilical hernia and diastasis recti. Omphalocele is a congenital malformation, a defect of the anterior abdominal wall, umbilical hernia where the newborn's intestines, and sometimes other abdominal organs, protrude from the abdomen through the umbilicus.(11)

Neonatal hypoglycemia, low blood glucose during the first month of life, occurs in about half of infants (8). Hypoglycemia is reported in 30–50% of infants with BWS, caused by islet cell hyperplasia and hyperinsulinemia (5,11).

Macroglossia and macrosomia are usually present at birth but may also be present after birth. Growth rate slows down around 7–8 years of age (8). Macroglossia, enlarged tongue, is a very common (> 90%) feature of the syndrome. Children with macroglossia usually cannot close their mouths completely, have impaired breathing, swallowing, and are at risk for obstructive sleep apnea. Such children have increased interdental spaces, may have a cleft palate, and may exhibit prognathism. In some children with Beckwith-Wiedemann syndrome, certain parts of the body may become abnormally large, resulting in an asymmetrical appearance – hemihyperplasia. Hemihyperplasia usually becomes less noticeable over time (2, 6)

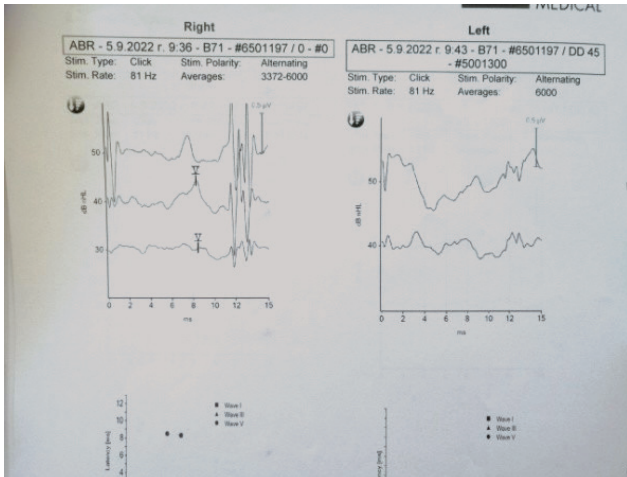
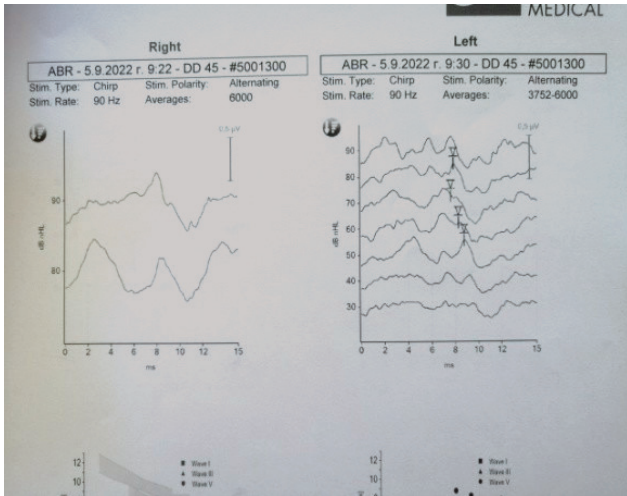
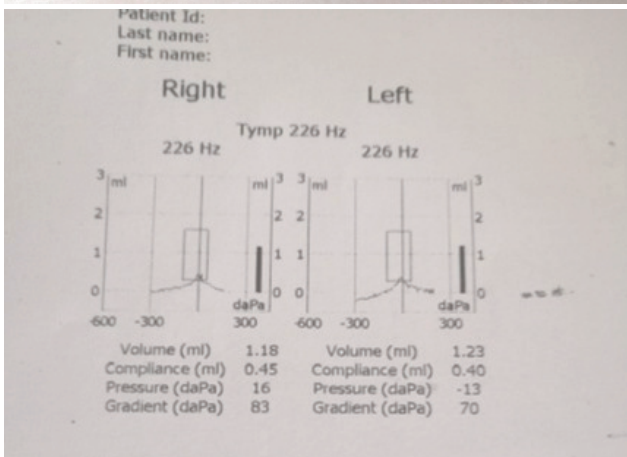
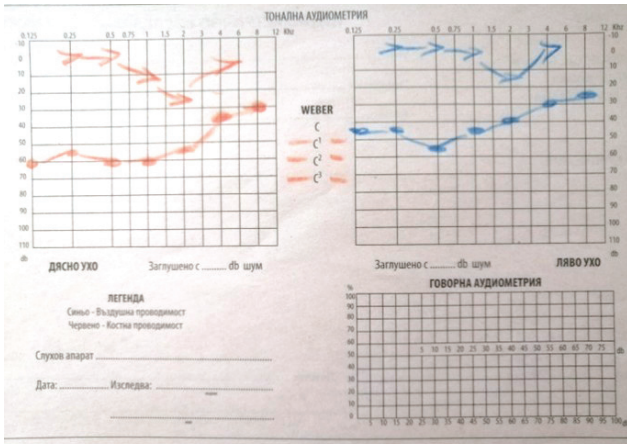
Children with Beckwith-Wiedemann syndrome are at increased risk of developing malignant and benign tumors. Wilms tumor, hepatoblastoma, neuroblastoma, and rhabdomyosarcoma may occur (8, 11).

Early recognition of the condition in the prenatal or neonatal period is important for diagnosis and early treatment of complications (4). Most children and adults with Beckwith-Wiedemann syndrome do not have any serious medical issues. Life expectancy is usually normal.

Materials and methods:

We present a clinical case of a 6-year-old boy with confirmed Beckwith-Wiedemann syndrome – abnormal methylation in the KvDMR1 region. He was born with pronounced dysmorphism – coarse features, protruding eyes, poorly formed auricles, small pointed chin, short saddle-shaped nose, large tongue fitting into the oral cavity (after glossectomy at the age of one year), birthmark on the forehead and occipital region, coarse musculature, umbilical hernia, distended abdomen, manifestations of hypoglycemia and muscle hypotonia, bilateral cryptorchidism.

Due to complaints of hearing loss at the age of 6, an examination of ENT organs, pure-tone threshold audiometry, tympanometry, computed tomography of the brain and middle ear, air and bone scintigraphy were performed.



Results

No abnormalities were found during the examination of ENT organs. The performed tone threshold audiometry found bilateral conductive hearing loss. Tympanometry showed a type A curve with low amplitude. The scintigram did not show any abnormalities. The SSEP found bilateral conductive hearing loss.

According to Hopsu Erkki and all, Takahashi and all and Daugbjerg and all, Schick and all, patients with Beckwith-Wiedemann syndrome may develop progressive conductive hearing loss after birth. Hearing loss in connection with this syndrome is rare. It is caused by fixation of the stapes and/or fixation of the malleus in the epitympanum. Sometimes a discontinuity between the long process of the incus and the stapes is also found without bone erosion. Clinically, stapes fixation is identical to otosclerosis, but the typical family history of otosclerosis is absent. Stapedial fixations can be confirmed by tympanometry. Improved hearing is achieved using stapedoplasty. (4, 7, 9)

Conclusion

Diagnosing Beckwith-Wiedemann syndrome can be difficult. The absence of positive results from the genetic test should not exclude the diagnosis of BWS. What is significant are the numerous clinical features characteristic of the syndrome.

The presented case is of interest to every specialist. Our attention should be directed to the examination of hearing as a probable symptom of this disorder. Conductive hearing loss in patients with Beckwith-Wiedemann syndrome is a relatively rare finding. When diagnosing stapes plate fixation, as the most common cause, the treatment is surgical and leads to significant improvement in hearing.

Children with Beckwith-Wiedemann syndrome develop well and usually grow up without the syndromic features of childhood. The prognosis is good. Monitoring the condition of patients and early diagnosis of tumors are crucial.

References

1. Choufani Sanaa, Cheryl Shuman, Rosanna Weksberg Beckwith–Wiedemann syndrome American Journal of medical genetics 20 August 2010. <https://doi.org/10.1002/ajmg.c.30267>
2. Duffy A Kelly, Cielo M. Christopher, Coent L. Jennifer, et al Characterization of the Beckwith-Wiedemann spectrum: Diagnosis and management Am J Med Genet C Semin Med Genet. 2019 December; 181(4): 693–708. doi:10.1002/ajmg.c.31740
3. Dimitrov Stanislav Beckwith–Wiedemann syndrome Puls.bg 22 January 2019
4. Hopsu Erkki MD, PhD Aarnisalo Antti, MD, PhD; Pitkäranta Anne, MD, PhD Progressive Stapedial Fixation in Beckwith-Wiedemann Syndrome Arch Otolaryngol Head Neck Surg. 2003;129 (10):1131-1134. doi:10.1001/archotol.129.11.1165
5. Mendoza Paulo A. Borjas; Mendez D Magda. Beckwith Wiedemann Syndrome Last Update: March 15, 2022.
6. Prof.Cammarata-Scalisia Francisco, Prof. Avendanoa Andrea, Frances Stock, M.D.b, Michele Callea, M.D.and all Beckwith-Wiedemann syndrome. Clinical and etiopathogenic aspects of a model genomic imprinting entity Arch Argent Pediatr 2018;116 (5):368-373
7. Schick Bernhard, Brors Dominik, Presher Andreas, Wolfgang Draf Conductive hearing loss in Beckwith–Wiedemann syndrome [https://doi.org/10.1016/S0165-5876\(99\)00015-4](https://doi.org/10.1016/S0165-5876(99)00015-4)Get rights and content
8. Shuman C, Beckwith JB, Weksberg R Beckwith-Wiedemann Syndrome Book from University of Washington, Seattle, Seattle (WA), 11 Aug 2016 PMID: 20301568
9. Takahashi S, Shinoda H, Nakano Y Congenital stapedial fixation associated with Beckwith–Wiedemann syndrome: two cases of a woman and her brother. The American Journal of Otolaryngology, 01 Jan 1996, doi:10.1016/S0165-5876(96)00015-4 PMID: 8694112
10. Wang H. Kathleen H, Kupa Jonida, Duffy A Kelly and all. Diagnosis and Management of Beckwith-Wiedemann Syndrome Division of Human Genetics, Children’s Hospital of Philadelphia, Philadelphia, PA, United States, Department of Pediatrics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, United States
11. Weksberg Rosanna, Shuman Cheryl, Beckwith J Bruce Beckwith–Wiedemann syndrome European Journal of Human Genetics volume 18, pages 8–14 (2010) Cite this article



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