Beckwith-Wiedemann syndrome

Beckwith-Wiedemann syndrome is a genetic overgrowth condition that is characterized by large body size and an increased chance of tumor development. It is caused by mutations in genes in a particular region of chromosome 11.

Characteristics of Beckwith-Wiedemann syndrome

Beckwith-Wiedemann syndrome (BWS) is a genetic condition that is typically associated with increased growth in childhood along with other clinical features. The increased growth can present as macrosomia, which refers to a larger height and weight than might be expected for the particular family. However, BWS is not usually associated with obesity, and adult heights are typically in the normal range. Increased growth related to BWS can also involve the tongue (macroglossia) and/or lead to asymmetry in the size of the limb(s) or other regions of the body (hemihyperplasia). Children with BWS have an increased risk to develop tumors in early childhood and this risk is estimated to be approximately 7%; studies indicate a range of risks for tumor development from 4 – 21% and this is likely influenced by the underlying genetic alteration. The tumors most frequently seen in BWS include Wilms tumor (involving the kidney(s)) and hepatoblastoma (involving the liver), but other tumors have also been reported. The risk for tumor development occurs primarily in the first 8 years of life.

Individuals with BWS may have other clinical findings including but not limited to: abdominal wall defects (e.g. omphalocele which occurs when the abdomen does not close properly during fetal life; umbilical hernia which is a protruding belly button, which is also seen relatively frequently in the general population), ear creases (on the ear lobes) and/or ear pits (very small depressions found on the back of the ear), low blood sugar (hypoglycemia) in the newborn period, and findings involving the abdominal organs (such as enlarged organs, structural changes, etc.). Development is typically normal unless there is a chromosome abnormality or undetected and untreated hypoglycemia.

Diagnosis/Testing

The diagnosis of BWS can be based upon clinical findings alone. Genetic testing is valuable for confirming the diagnosis and for providing genetic counseling. Approximately 80% of individuals with BWS have an alteration in one or more of the genes on chromosome 11p15.5. These genes are thought to be important in growth and development during pregnancy and in early childhood. These alterations may involve chemical changes called methylation in the KCNQ1OT1 and/or H19 genes. This means a chemical called a methyl group (a carbon atom and three hydrogen atoms) attaches to specific regions that control when and where certain genes are read [turned on] or not read [turned off].

BWS can also be caused by paternal uniparental disomy (i.e., when both copies of chromosome 11 is received from the father instead of one copy from each parent) or by a change or mutation in the CDKN1C gene. Infrequently, children with BWS may have a chromosome change involving a larger region of chromosome 11.

Management/Surveillance

Even if genetic testing is negative, children diagnosed with BWS or clinically suspected of having BWS, should be followed on a tumor surveillance protocol. It is generally recommended that children with BWS have abdominal ultrasounds every 3 months to the age of 8 years, and blood testing for alpha fetoprotein (AFP) every 2 – 3 months to the age of 3 – 4 years to monitor for tumor development. Macroglossia can occasionally lead to problems with sleep apnea, feeding and/or speech articulation and appropriate evaluation should be undertaken for such concerns. Management of
Mode of inheritance

BWS occurs in all populations around the world and affects girls and boys equally. Most cases of BWS (85%) are sporadic, meaning that there are no other family members with BWS. Approximately 15% of individuals with BWS have a family history of the condition.

Risk to family members

The chance for parents of a child with BWS to have another affected child depends on the genetic cause. This is also true for the chance for an individual with BWS to have a child with BWS. Isolated methylation alterations (that is with no underlying microdeletion (i.e., small missing piece) or microduplication (i.e., small extra piece) in the chromosome 11p15.5 region) are currently thought to have a low chance to happen again. The chance for parents of a child with BWS to have another affected child may be increased when the child with BWS has a microdeletion, microduplication, mutation in the CDKN1C gene, chromosome duplication or translocation involving the chromosome 11p15.5 region. The specific risk depends on whether this is a new change (de novo) or whether it has been passed down from one of the parents and if so, whether the parent is the mother or the father.

Special considerations

There is a higher than expected number of identical (monozygotic) twins in whom one twin has a clinical diagnosis of BWS and the other twin does not; most of these twin pairs are females. Tumor surveillance is recommended for both twins even if there are no BWS-related clinical/molecular findings in one of the twins. Although most children with BWS are born to parents who have not had any problems conceiving, there is an increased rate of BWS when there are fertility issues and when assisted reproductive technologies have been used. The reasons for this are not well understood at this time.

Resources

Beckwith-Wiedemann Children’s Foundation  
http://www.beckwith-wiedemannsyndrome.org

Beckwith-Wiedemann Support Group  
http://www.bws-support.org.uk/

Genetics Home Reference: Beckwith-Wiedemann syndrome  

References


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