Children's Hospital of Philadelphia
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Management of adrenal masses in patients with Beckwith-Wiedemann syndrome (2017)

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Background

Patients with Beckwith-Wiedemann syndrome (BWS) are at an increased risk to develop tumors. As a result, patients receive routine tumor surveillance, which includes ultrasonography, to monitor for tumor development. While Wilms tumor and hepatoblastoma are the most common tumors to develop in patients with BWS, patients can develop adrenocortical carcinoma, a malignant adrenal tumor. Other malignant and nonmalignant adrenal masses have been reported in patients with BWS. No recommendations for adrenal evaluation in patients with BWS exist.

Purpose

This study proposes guidelines for evaluating adrenal masses detected in patients with BWS. A literature search was performed to identify all reported cases of patients with BWS and adrenal findings and reviewed in patients with BWS and adrenal findings treated at Children's Hospital of Philadelphia (CHOP).

Findings

Three broad categories of common adrenal findings in patients with BWS were found: adrenal hyperplasia and cysts; adrenal adenoma; and neuroendocrine tumors. Additionally, adrenal calcification and adrenal carcinoma were also reported. The majority of the reported findings occurred before the first 8 years of life and were detected by routine ultrasound imaging. Most patients with the adrenal findings had hemihypertrophy (now referred to as lateralized overgrowth).

Several genes that can be altered in BWS may explain the genetic mechanism leading to adrenal masses in patients with BWS. Changes in the expression of insulin like growth factor 2 (IGF2) and cyclin dependent kinase inhibitor 1C (CDKN1C), two proteins encoded in the BWS region, can lead to abnormal adrenal development in the fetus. IGF2 overexpression is seen in the majority of adrenal tumors, but an increase in IGF2 alone is not cancer causing. In mouse models, decreased expression of CDKN1C has been shown to cause adrenal overgrowth as well. Further research is needed to better understand why patients with BWS can develop adrenal masses.

The approach for managing adrenal findings depends on the nature of the mass (cystic or solid), whether high-risk features are present, and the age of the patient. Regardless of age, patients with high-risk features should be further evaluated to determine if the mass is malignant. This includes monitoring for the overproduction of hormones from the adrenal glands. Cystic masses should be observed with ultrasound imaging every three months. Adrenal masses in patients less than six months old are less likely to be cancerous or require surgery. Patients over six months of age should be more thoroughly evaluated.

Conclusion

This study outlines steps for clinically evaluating adrenal masses detected in patients with Beckwith-Wiedemann syndrome. Evaluation should be guided by the patient's age, type of mass and presence of high risk features.

Key Points

- Increased IGF2 expression and decreased CDKN1C expression in patients with BWS is a possible explanation for adrenal abnormalities.
- Management should be guided by the type of the mass, the presence of high-risk features, and the age of the patient.

Reference

MacFarland SP et al. Management of adrenal masses in patients with Beckwith- Wiedemann syndrome. *Pediatr Blood Cancer.* 2017; 64(8). PubMed PMID: 28066990

Special Note:

This study was conducted prior to the development of the Beckwith-Wiedemann Spectrum scoring system by the International BWS Consensus Meeting. The pathology finding adrenal cortex cytomegaly is now considered a "cardinal feature" of BWS.