Children's Hospital of Philadelphia
RESEARCH INSTITUTE

Diagnosis of Beckwith-Wiedemann Syndrome in children presenting with Wilms Tumor (2018)

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Background

Beckwith-Wiedemann syndrome (BWS) is an overgrowth and cancer predisposition syndrome that is caused by molecular changes on chromosome 11p15. BWS was redefined as Beckwith- Wiedemann spectrum (BWSp) to include classic BWS, as well as patients with molecular changes on 11p15 without classic presentation of BWS. Patients with BWSp are at an increased risk for tumors, and Wilms tumor (WT) is the most common tumor to develop. As a result, at the time of diagnosis, tumor screening is recommended for patients with BWSp until the 7th birthday. In some cases, WT may be the first feature that leads to the diagnosis of BWSp.

Purpose

This study describes 12 patients who first presented with Wilms tumors (WT) and were subsequently diagnosed with BWSp.

Findings

Between January 2014 and July 2017, 12/183 patients (6.5%) were diagnosed with BWSp or isolated lateralized overgrowth (ILO) after first presenting with WT. All patients had some degree of lateralized overgrowth (hemihypertrophy). Four patients were large for gestational age at birth, two patients had ear creases/pits, and one patient had a history of transient hypoglycemia at birth. One patient additionally had a history of mild macroglossia and umbilical hernia, however BWSp was not suspected until the patient was diagnosed with WT.

All patients were found to have a molecular change consistent with BWSp in their tumor sample: half were diagnosed with paternal uniparental isodisomy of chromosome 11p15 (pUPD11) and half were diagnosed with gain of methylation at imprinting control region 1 (IC1 GOM). In addition to their tumor samples, four patients were found to have positive genetic testing on adjacent normal kidney samples (all IC1 GOM) and one patient was found to have IC1 GOM in a skin biopsy sample, displaying varying degrees of mosaicism (the amount of cells that have genetic changes compared to the amount of normal cells in a sample). All blood samples that were tested were negative. The positive genetic testing in one or more tissues from each patient demonstrated that all patients were part of the Beckwith-Wiedemann Spectrum. Using the BWSp consensus scoring system, the final clinical diagnosis was BWSp in 8 patients and ILO in 4 patients.

Conclusion

Wilms tumor can be the presenting sign of Beckwith-Wiedemann spectrum in some patients. A detailed clinical history and exam should be performed in all patients presenting with a kidney mass, as treatment recommendations differ for patients with an underlying cancer predisposition syndrome. In patients with suspected cancer predisposition syndromes, nephron-sparing surgery should be performed to preserve kidney tissue and function. Testing multiple available tissues (such as kidney tumor samples, adjacent normal kidney samples, and skin biopsy samples) can help confirm the suspected diagnosis and inform tumor risk.

Key Points

- Patients with BWSp may present with WT before a BWS diagnosis is made.
- Patients diagnosed with a kidney mass should be carefully evaluated for BWSp.
- Testing kidney tumor tissue and other available samples can help confirm a suspected BWSp diagnosis.

Reference

MacFarland SP et al. Diagnosis of Beckwith–Wiedemann syndrome in children presenting with Wilms tumor. *Pediatric Blood & Cancer.* 2018;65(10): e27296. PubMed PMID: 29932284