The utility of Alpha-Fetoprotein screening in Beckwith-Wiedemann syndrome (2017)

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Background

Historically, all patients with Beckwith-Wiedemann syndrome (BWS) were recommended to receive tumor screening to detect development of tumors, most commonly Wilms tumor and hepatoblastoma. Although the frequency and age intervals varied between some groups, all tumor screening protocols included abdominal/renal ultrasonography and serial alpha-fetoprotein (AFP) measurements. With the advancements of genetic testing, it was identified that some molecular subtypes of BWS have higher tumor risks compared to others. As a result, some groups in Europe began recommending tumor screening to only the molecular subtypes at higher risks and did not recommend screening molecular subgroups with lower tumor risks, mainly patients with BWS due to loss of methylation at imprinting control region 2 (IC2 LOM). The use of AFP screening was also not recommended by some groups in Europe due to the invasiveness of the screening and the difficulty in interpreting AFP results.

Purpose

This invited commentary discusses the usefulness of AFP screening for hepatoblastoma detection as well as tumor screening in patients with BWS due to IC2 LOM.

Findings

While patients with IC2 LOM are at an overall lower tumor risk compared to other groups, hepatoblastoma is the most common tumor to develop in these patients. The majority of patients with BWS who develop hepatoblastoma are affected by IC2 LOM or paternal uniparental disomy of chromosome 11p15 (pUPD). As a result, the IC2 region may play a role in the mechanism of hepatoblastoma development, as both patients with IC2 LOM and pUPD have altered methylation at the IC2 region. Hepatoblastoma occurs in similar relative frequencies in patients with IC2 LOM and pUPD, although patients with pUPD can also develop Wilms tumor. Even though IC2 LOM patients have an overall lower tumor incidence and risk, if they do develop a tumor, it is most commonly a hepatoblastoma.

Patients with BWS due to IC2 LOM may have additional risk factors for hepatoblastoma that other molecular groups of BWS do not:

- ART – The majority of patients with BWS conceived through assisted reproductive techniques (ART) have IC2 LOM. Research suggests that in the general pediatric population, patients conceived by ART may have a higher risk to develop hepatoblastoma than patients who were conceived naturally.
- Prematurity – More than three-quarters of premature births observed in BWS are in infants with IC2 LOM. In the general pediatric population, hepatoblastoma is more common in patients born premature than patients who were born full term.
- Low birth weight – While most patients with BWS are not small for gestational age, patients with BWS IC2 LOM are less likely to be large for gestational age (i.e. they have a lower birth weight) compared to other BWS groups. In the general pediatric population, hepatoblastoma occurs more frequently in patients with low birth weights.

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Early detection of hepatoblastoma improves outcome, as patients with tumors detected earlier at a lower stage have better surgical outcomes and often require less treatment. While ultrasound can detect hepatoblastoma, AFP can detect it sooner and at a lower stage.

Key Points

- The tumor risk for patients with BWS varies by subgroup; however, all subgroups are at some risk.
- Patients with IC2 LOM may have additional risk factors for hepatoblastoma compared to other BWS molecular groups.
- AFP screening helps with early detection.

Reference

Duffy KA, Deardorff MA, Kalish JM. The utility of alpha-fetoprotein screening in Beckwith-Wiedemann syndrome. *Am J Med Genet A*. 2017;173(3): 581-584. PubMed PMID: 28160403