Fellow's Column: An Extremely Premature Infant with Atypical Physical Characteristics

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Case Report:

A premature infant born at 25 weeks and 6 days via urgent cesarean-section secondary to premature rupture of membranes and chorioamnionitis. Prenatal history was significant for poor prenatal care and perinatal ultrasound consistent with protruding abdominal wall mass suspecting omphalocele. At the time of delivery, resuscitation was required secondary to prematurity. Initial APGAR scores of 1, 5, 7 at 1, 5, and 10 minutes of life were given. After initial stabilization, including intubation and surfactant administration, he was admitted to the Neonatal Intensive Care Unit (NICU), and standard treatment was provided. Initial physical examination was significant for large for gestational age at 96.6% for weight (1.230 kilograms) head circumference at 81% for age (25.5cm), presence of small bilateral preauricular pits and 4-cm omphalocele with intact viable bowel. Omphalocele was surgically corrected. Infant continued to grow, and by 1 month of age, he was noted to have facial coarsening and macroglossia (protruding and prominent tongue). A renal ultrasound (US) was obtained secondary to oliguria, which revealed bilateral prominent hydronephrosis.

Final Diagnosis:

Due to omphalocele, macroglossia, and bilateral hydronephrosis genetic testing for Beckwith-Wiedemann (BWS) obtained via molecular analysis. Results were consistent with diagnosis of BWS showing hypomethylation of cyclin-dependent kinase inhibitor IC2 -LIT1 on chromosome 11p15.

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Hospital Course:

The infant remained under the care of neonatology for 136 days. His course was complicated by multiple surgical procedures for corrections of omphalocele, bowel atresia with small bowel resection, and interventional drainage of an abdominal abscess. Other complications included large PDA with ibuprofen treatment, anemia requiring multiple transfusions, retinopathy of prematurity stage 3, microcolon and intraventricular hemorrhage grade 3 bilaterally. He was discharged on enteral feeds via gastrostomy tube feeds and on room air. The infant has since undergone multiple keyhole tongue reduction procedures. His last ultrasound showed normal liver and hyperechoic kidneys. He follows with pediatric gastroenterology, hematology, OMFS, and developmental clinic.

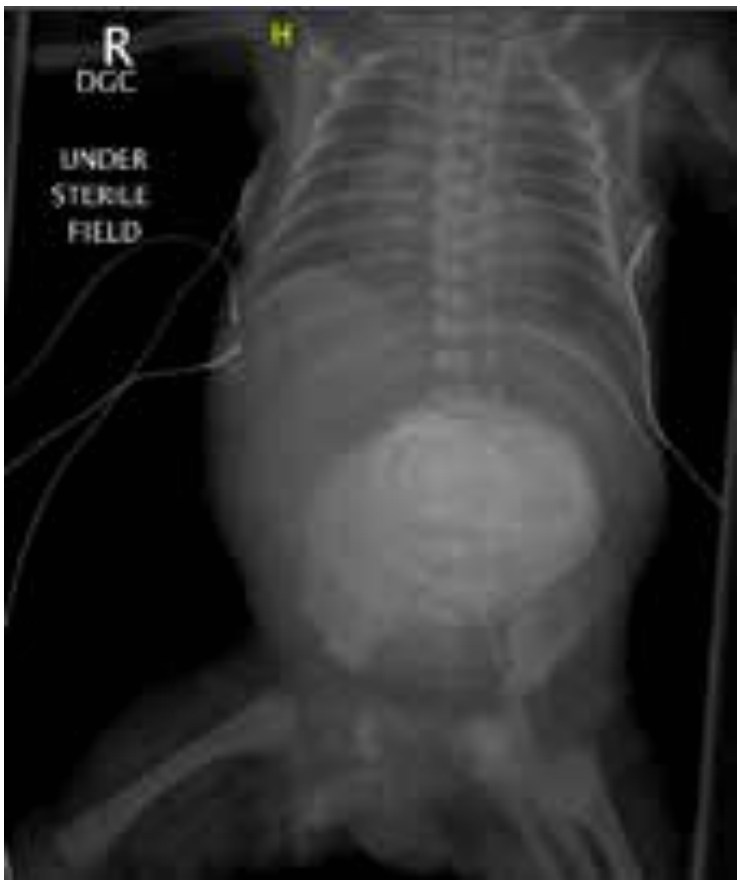

Figure 1 . Initial radiographic study of premature infant with ompahalocele

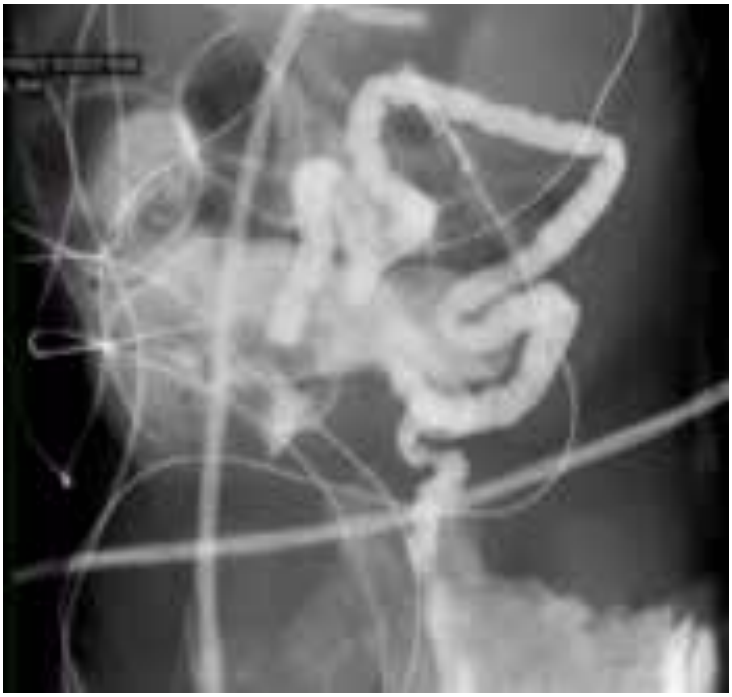

Figure 2. Image 2: Gastrointestinal study of our patient demonstrating microcolon

"Recognizing the classical findings can be a challenge when dealing with extremely premature infants. As demonstrated in this case report diagnosis may or may-not change acute management; however it is important to obtain genetic analysis due to the follow up medical care that is needed."

Discussion:

Beckwith-Wiedemann Syndrome is a rare pediatric genetic growth disorder associated with various physical and metabolic abnormalities. BWS individuals can display variability in clinical presentation. The classic physical findings include macrosomia, macroglossia, and hemihyperplasia 1. In the neonatal period, recurrent episodes of hypoglycemia and macroglossia are typically present 2. A literature review has a few documented cases of a neonatal diagnosis of BWS with no documented cases in extremely premature infants. Macroglossia and macrosomia are generally present at birth but may have postnatal onset 2,3. Our patient, unfortunately, born at 25-weeks gestation, the classical characteristics of BWS were initially masked. BWS leads to overgrowth stimulation due to epigenetic and genetic modifications in two regions of chromosome 11p15. The estimated prevalence of BWS is 1 in 13700, with an average of 300 children born per year.(1,4) The main areas affected include loss of methylation of maternal chromosome in imprinting center IC2, a gain of methylation on the maternal chromosome in imprinting center 1 (IC1) or paternal uniparental disomy for chromosome 11p15 (NCBI). These areas are involved in fetal growth and growth restriction via cyclin-dependent kinases. Cyclin-dependent kinases are involved in the regulation of cell cycle and require binding to cyclin to be active. (2,4-5) Inhibitors of these enzymes act to distort the binding leading to suppression of growth. In BWS, this regulation is lost, causing continued activation of kinase leading to the overgrowth phenomenon. The loss of inhibition also contributes to increased risk of developing tumors. Half of all affected individuals will have a loss of methylation at the IC2 region of the maternal chromosome, while up to 30% of patients have paternal uniparental disomy. (2,5-6) Another 5% of patients have a gain of methylation in the IC1 region of the maternal chromosome 5-8. Up to 85% of individuals with a diagnosis of BWS have no family history of this genetic disorder 8.

A clinical diagnosis of BWS can be made based on physical findings. However, it is recommended that patients undergo genetic testing to identify further the area affected. Treatment for BWS includes treating the manifestations when possible. Close monitoring for hypoglycemia, repairing the abdominal wall defects, and tongue reduction surgery to limit feeding and speech complications. (2) Surveillance for embryonic tumors via abdominal ultrasound is recommended every 3-6 months of age until 8 years of age. (2,9) A renal ultrasound should be performed at least once a year. Laboratory monitoring using alpha-fetoprotein (AFP) is recommended every 2-3 months until 4yrs of age aids in detecting hepatoblastomas. (2) Up to 8% of patients with BWS develop tumors during the first 8 years of life. (6,10) Genetic counseling should be offered to families of affected individuals.

Conclusion:

Diagnosis of BWS should be suspected when polyhydramnios, wall defects, and other organ anomalies are visualized on prenatal ultrasound or initial exam. (4,8) Recognizing the classical findings can be a challenge when dealing with extremely premature infants. As demonstrated in this case report diagnosis may or may-not change acute management; however it is important to obtain genetic analysis due to the follow up medical care that is needed.

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