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A case report of Beckwith Wiedemann Syndrome with prolonged hypoglycaemia and requiring hemi-glossectomy

Authors
Dr Mansoor KP[1*], Dr Ravikiran S R[2]
[1]Junior Resident, [2]Associate Professor,
Dept. of Paediatrics, KMC Mangalore, Manipal University, Pin 575001
*Corresponding Author
Dr Mansoor KP
Junior resident, Dept. of Paediatrics, KMC Mangalore, Manipal University, Pin 575001, India
Mobile: 9846630980, Email: *mansoor.kp47@gmail.com*

Abstract
Beckwith Wiedemann Syndrome (BWS) is a congenital condition characterised by overgrowth of different body parts which is usually manifested at birth. It is a rare condition where there may be asymmetric body growth or hemi hyperplasia, omphalocele or other abdominal wall defects, hypoglycaemia in neonatal period, macroglossia, intra abdominal organomegally, ear skin creases or pits, and renal abnormalities. They have high risk to develop tumours; especially Wilms tumour, hepatoblastoma, rhabdomyosarcoma. Degree of clinical manifestations vary from person to person as some may have all features while some may have only one symptom.
Keywords: *Beckwith Wiedemann syndrome, macroglossia, hypoglycaemia, glossectomy.*

Introduction

Beckwith Weidmann Syndrome (BWS) was initially put forward by two doctors in1960s separately, Dr. John Bruce Beckwith, an American pathologist and Dr. Hans-Rudolf Wiedemann, a German pediatrician [1][2] . Iinitially it was termed EMG (*exomphalos*, *macroglossia*, and *gigantism*) syndrome which later known as Beckwith Wiedemann syndrome. Estimated incidence of BWS is about one in 13,700. Importance are gaining more for BWS following recent increase in incidence of BWS among babies born using Assisted Reproductive Techniques than general population [3][4] .

Clinically, BWS manifest in different forms, it's most common features being macroglossia (97-100%) which can be asymmetric, abdominal wall defects (77-80%) most commonly omphalocele, hypoglycemia in neonatal period (63%) and macrosomy (68%). Affected child may have asymmetric body growth of one side or hemi hyperplasia, Other presentations includes microcephaly, other midline abdominal wall defects (umbilical hernia, diastasis recti), ear creases or posterior helix pits, cleft palate, renal alterations, visceromegaly, refractory hyperinsulinemia, polydactyly. Neurologic complications are rare[6]. These children have a higher risk to develop tumours during childhood,

peculiarly Wilms tumour, hepatoblastoma, rhabdomyosarcoma. Genetically BWS is related with an alteration of the gene expression at the short arm of chromosome 11 (11p15) causing IGF-2 gene over activity (growth factor) and/or no active copy of CDKN1C (inhibitor of cell proliferation gene). BWS can occur most commonly sporadically (85%) or inherited (15%) or because of chromosomal abnormalities (1%). Some of affected children have rearrangements of maternal chromosomal 11p15 while others may have paternal uniparental disomy (UPD) of chromosome 11 (that is, an additional paternal copy of this chromosome replaces maternal copy of this chromosome). Many have altered DNA methylation in multiple areas of 11p15, causing normal epigenetic marks that regulate imprinted genes in this region are abnormal. Instead of two copies a few have single gene copy at 11p15 [5]. Thus there are no specific molecular tests to detect a specific cause for BWS. This fact shows why BWS remains a clinical diagnosis, rather than genetic.

Recognizing BWS is difficult due to difference in manifestations among children with BWS and unavailability of a simple diagnostic test. Thus in a venture to standardize the diagnosis of BWS, DeBaun et al. have designated a child as having BWS if at least two of the five common features associated with BWS (macroglossia, macrosomia, midline abdominal wall defects, ear creases, neonatal hypoglycemia) are present [7].

Case Report

2.5month old female child presented in our paediatric emergency department with seizures. Neonatal history suggestive of she was born out of third degree consanguineous marriage to a 19 year old mother and 22 year old father with normal antenatal period at 36weeks +6days LGA (birth weight 3.6kg) by caesarean section (PPROM, failed induction), cried soon after birth was admitted in NICU on day 1 due to mild respiratory distress, hypoglycaemia and mild macroglossia. Child had microcephaly and visceromegally at birth (hepatosplenomegally). Child was managed as per protocol of symptoms and discharged once stable to keep under follow up, but did not reviewed by parents. Now child presented with subtle seizure cause consistent with hypoglycaemia requiring GIR 15mg/kg/min and was prolonged for more than 2weeks. Clinically child had microcephaly, low set ears, flat nose, significant macroglossia (figure1 and 2) more on left side, micrognathia, haemangioma on right forehead, mild hepatosplenomegally, appears macrosomia no focal neurological deficit, had mild respiratory distress with variation to position related with macroglossia and feeding difficulties, cardiac examination was normal.. Sepsis screen, TORCH screening was negative. MRI Brain showed mild diffuse cerebral atrophy with T2 flair hyper intensities in bilateral parietal white matter. Thyroid function normal. Child was clinically diagnosed as a case of BWS as fits 3 criterias (macroglossia, hypoglycaemia, macrosomia, visceromegally).

Fig1

Fig 2

(figures reproduced with permission from parents)

Hypoglycemia critical sample showed hyperinsulinemia, normal cortisol. Hypoglycaemia managed as per protocol requiring prolonged hydrocortisone for 7 days and glucose infusion. Diazoxide was not used due to non availability. Seizure was controlled along with hypoglycaemia control and also requiring 2 antiepileptics. As child have mild respiratory distress and difficult feeding due to macroglossia (tongue size have increased after neonatal period), child undergone left sided partial glossectomy. Gradually full feeding orally was established and glucose levels were in normal levels. Screening (USG abdomen and Alpha feto protein level) was also done to look for any tumour possibilities which were negative and child was discharged with follow up. Genetic testing deferred due to financial constrains. During 3 month follow up child had no seizures or hypoglycaemia episodes, was on formula feed regular basis, had developmental quotient 70%. As EEG was normal anti epileptics were gradually stopped and planned for long term follow up including neuro developmental follow up and screening for possible malignancies in future.

Discussion

BWS is diagnosed clinically, but genetic testing is better advised in suspected familial cases. Management includes initially management of complications as per usual protocols of isolated presentations of these conditions and then follow up. Management of complications includes as follows:

- Abdominal wall defects- *omphalocele* require emergency surgery to place the abdominal contents back into the abdomen, *umbilical hernia* wait and watch up to 2to 4 years and then surgery if not resolve its own, *Diastasis recti* requires no treatment usually.
- Neonatal hypoglycaemia- to be managed according to usual protocol for hypoglycaemia in neonates. Rarely (<5%) children with BWS will continue to have hypoglycaemia after the neonatal period and require more intensive treatment like tube feedings, oral hyperglycaemic medicines, or a partial pancreatectomy.
- Macroglossia-often tongue protrudes out. Macroglossia in BWS becomes less noticeable with age and often requires no treatment. In severe cases, macroglossia can cause respiratory, feeding, or speech difficulties which may require partial glossectomy involving cranio fascial surgery team. Definite time for this procedure is not established.
- Nevus flammeus (port-wine stain) is benign and commonly does not require any treatment.
- Hemihypertrophy (hemihyperplasia) usually warrants follow-up for tumours in future.
- Neoplasms: children with BWS are much more likely (~600 times more) than other children to develop certain childhood cancers, particularly Wilms' tumor (nephroblastoma), pancreatoblastoma and hepatoblastoma. but not during adulthood. Also case reports of developing ganglioneuroma, adrenocortical carcinoma, acute lymphoid leukemia, liver sarcoma, thyroid

carcinoma, melanoma, rhabdomyosarcoma, and mesoblastic nephroma. Are there.[8] Given the importance of early diagnosis, all children with BWS should receive cancer screening.[9] USG abdomen every 3 months until at least eight years of age and blood alpha-fetoprotein (AFP) estimation every 6 weeks until at least four years of age is recommended by some authorities.[10]

In general, the prognosis is very good. Children with BWS usually do very well and grow up to become the heights expected based on their parents' heights. While children with BWS are at increased risk of childhood cancer, most children with BWS do not develop cancer and the vast majority of children who do develop cancer can be treated successfully. Children with BWS for the most part had no significant delays when compared to their siblings. However, some children with BWS do have speech problems that could be related to macroglossia or hearing loss. Severe hypoglycaemia if occurs can otherwise cause developmental delay or seizure

Conclusion

BWS if followed as per protocol have good prognosis.

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Conflicts of interests: none.

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