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Case Report

Beckwith-Wiedemann Syndrome: A Case Report

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ABSTRACT

It is a congenital overgrowth disorder affecting male and female equally with an approximate incidence of one in13, 700-15,000 live births. Most of the cases,>85% are sporadic and <15% are familial. Diagnosis is mainly from clinical pictures, some of the cases are related to partial duplication of chromosome 11 (11p15). Baby conceived through in vitro fertilisation (IVF) have a 3 to 4 fold increased risk to develop this syndrome. Here we report a case of a one day old female baby presented with macrosomia, birth wt 4.210 kg, with feeding difficulty due to large tongue (macroglossia) with hemi hypertrophy of the body.

Key words: Beckwith-Wiedemann, macrosomia, macroglossia, hemi hypertrophy.

INTRODUCTION

In the 1960s, Dr. John Bruce Beckwith, an American pathologist and Dr. Hans-Rudolf Wiedemann, a German paediatrician, independently reported cases of a proposed new syndrome, Beckwith Wiedemann syndrome. [1,2] Previously it was known as EMG (exomphalos, macroglossia, and gigantism) syndrome. Beckwith-Wiedemann syndrome is the most common overgrowth syndrome in infancy. [3] It has an estimated incidence of one in 13,700. [4] It has been shown to specifically involve problems with a defined region on the short arm of chromosome 11 referred to as 11p15, that leads to over activity of the IGF-2 gene (growth factor) and/or no active copy of CDKN1C (inhibitor of cell proliferation). At least 20% of sporadic cases manifest paternal uniparental disomy (UPD) for band 11p15.5, resulting from postzygotic mitotic recombination and mosaic paternal isodisomy. [5,6] Children conceived through In vitro fertilization have a three to fourfold increased chance of developing Beckwith-Wiedemann syndrome. Generally the diagnosis is made by combination of clinical features and molecular testing. Given th- variation among individuals with BWS and the lack of a simple diagnostic test, identifying BWS can be difficult. In an attempt to standardize the classification of BWS, DeBaun et al. have defined a child as having BWS if the child has been diagnosed by a physician as having BWS and if the child has at least two of the five common features associated with BWS (macroglossia, macrosomia, midline abdominal wall defects, ear crease/ear pits, and neonatal hypoglycemia). [7] Another definition presented by Elliot et al. includes the presence of three major features (anterior abdominal wall defect, macroglossia, or pre postnatal overgrowth) or two major plus three minor findings (ear pits, nevus flammeus, neonatal hypoglycemia, nephromegaly, or hemi hyperplasia). [8]

CASE PRESENTATION

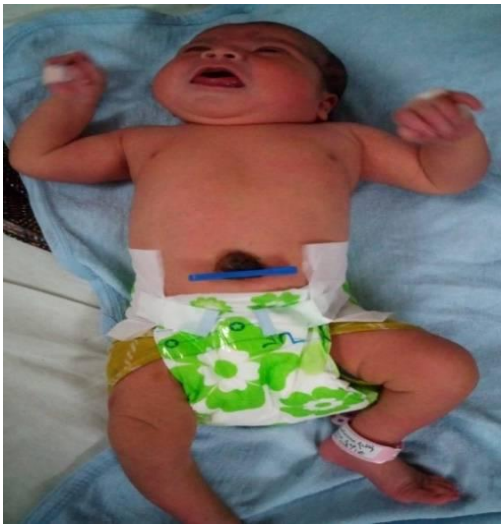

Fig. 1 macrosomia

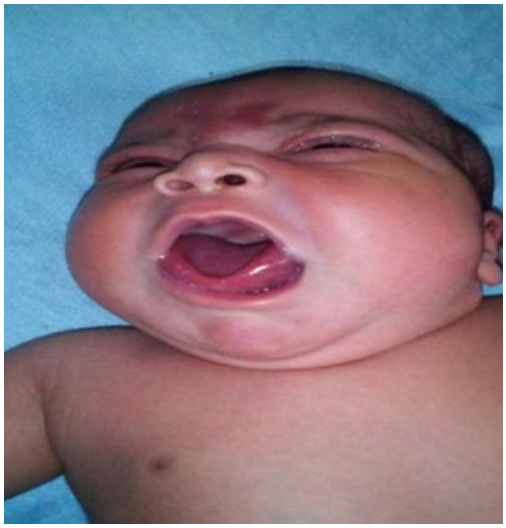

Fig. 2 macroglossia

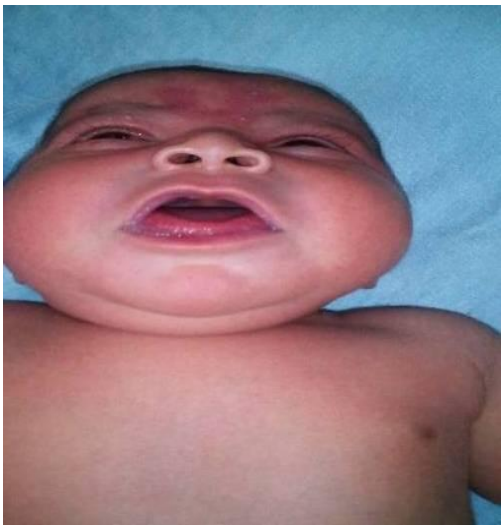

Fig. 3 nevus flammeus over forehead

Fig. 4 ear lobe crease

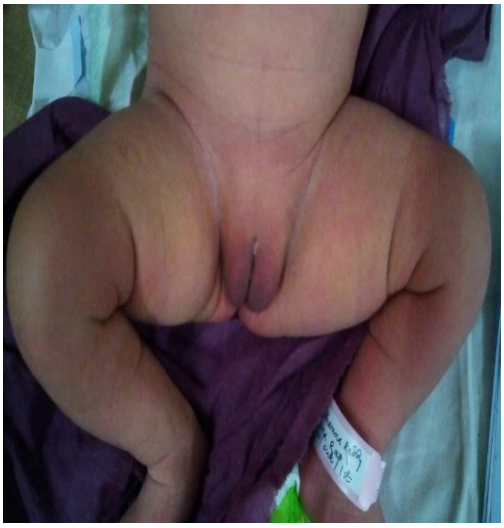

Fig. 5 hemi hypertrophy of left thigh

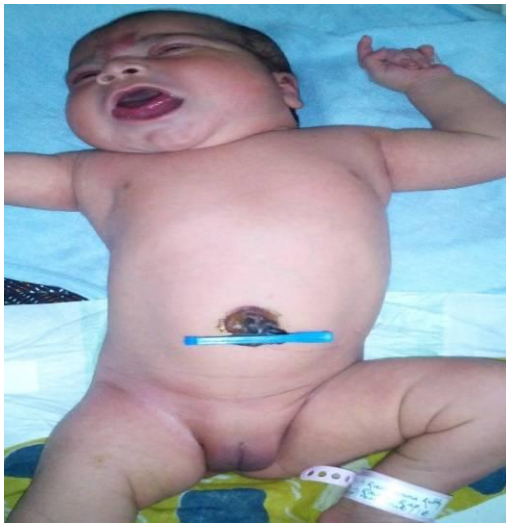

Fig. 6 left hemi hypertrophy of body

One day old female baby, born by NVD, presented to our SNCU with feeding difficulty and excessive cry. There was no history of birth asphyxia. No IVF. Another sibling is 2 yrs of age whose birth wt. was 2.7 kg and had no significant post-natal events and normal physical, neurological development. On examination of this baby wt. was 4.5 kgs, (macrosomia) (fig.1), length 54 cms, head circumference 35 cms. Cry, reflex, tone, activity was good. On head to toe examination, macroglossia (fig.2), nevus flammeus (fig.3), ear lobe crease (fig.4) and left sided hemi hypertrophy of the body (fig 5, 6), left MUAC 12.5cms comparisons to right 11cms, left thigh 17cms in comparisons to right15 cms. On investigation blood sugar was low 35 mg/dl and child was admitted and treated for hypoglycemia. Complete blood count, serum electrolyte, renal function test, liver function test was normal. On USG, liver and both kidneys ware enlarged, echocardiography and, karyotyping being normal.

DISCUSSION

BWS syndrome in genetic disorder is characterised by overgrowth, tumour predisposition and congenital malformation. Although incidence is around every 15000 births, but presentation may vary from child to child, thus difficult to diagnose.

Common features used to define BWS are [9]

- Macroglossia (large tongue),
- Macrosomia (above average birth weight and length), above 95% centile
- Midline abdominal wall defects (omphalocele/exomphalos, umbilical hernia, diastasis recti),
- Ear creases or ear pits,
- Neonatal hypoglycemia (low blood sugar after birth).
- Hepatoblastoma

This baby having two major features like macrosomia and macroglossia and also having minor findings like hypoglycemia, hemi hyperplasia, nephromegaly, nevus flammeus, ear pits.

The most common tumour associated with this syndrome are Wilms tumour (kidney tumour; about 40% of cases) Hepatoblastoma (liver tumour) Adrenocortical carcinoma (about 20% of cases) Neuroblastoma, Rhabdomyosarcoma. Most children (>80%) with BWS do not develop cancer; however, children with BWS are much more likely (~600 times more) than other children to develop certain childhood cancers, particularly Wilms' tumour (nephroblastoma), pancreato-blastoma and hepatoblastoma. [9] Individuals with BWS appear to only be at increased risk for cancer during childhood (especially before age four) and do not have an increased risk of developing cancer in adulthood. [9] Diagnosis mainly clinical correlation along with molecular testing, molecular testing confirm the diagnosis but it does not rule out BWS. Ante natal USG can detect major abdominal defect, chorionic villous sampling and amniocentesis can detect genetics changes. Supportive medical care and corrective surgery is mainstay of treatment.

Neonatal hypoglycemia, low blood glucose in the first month of life, occurs in about half of children with BWS. [10] Usually this hypoglycemia can easily be treated with more frequent feedings or medical doses of glucose. Rarely (<5%) children with BWS will continue to have hypoglycemia after the neonatal period and require more intensive treatment. [11]

For abdominal wall problem, corrective surgery required only in case of omphalocele, umbilical hernia, diastasis recti may resolve spontaneously.

Macroglossia, Macroglossia in BWS becomes less noticeable with age and often requires no treatment; but it does cause problems for some children with BWS. In severe cases, macroglossia can cause respiratory, feeding, and speech difficulties may require surgery. The best time to perform surgery for a large tongue is not known. Some surgeons recommend performing the surgery between 3 and 6 months of age. Surgery for macroglossia

involves removing a small part of the tongue so that it fits within the mouth to allow for proper jaw and tooth development.

Nevus flammeus (port-wine stain) is a flat, red birthmark caused by a capillary (small blood vessel) malformation. Children with BWS often have nevus flammeus on their forehead or the back of their neck. Nevus flammeus is benign and commonly does not require any treatment.

Ear Lobe Creases, these are sometimes found in conjunction with indentations behind the upper rim of the ear.

Wilms Tumours; tumours of the kidney. Around 7.5% of BWS children will develop Wilms Tumour. Because of the aggressiveness of these tumours, abdominal ultrasound scans should take place every three months up to the age of 7 or 8 years. A baseline MRI scan may also be performed. The susceptibility to these tumours diminishes and is not usually a problem after the age of 8. Please note that not all children with BWS are at risk of Wilms tumour and therefore do not require USG scan. Sometimes this will require surgery to remove the affected kidney and possibly chemotherapy and radiotherapy.

Visceromegaly, Enlarged abdominal organs, usually the kidneys, liver, spleen, adrenals and pancreas.

Hemi hypertrophy, May require orthopaedic surgery though is often treated with a shoe lift.

Isolated hemi hypertrophy is associated with a higher risk for cancer. [12] The types of cancer and age of the cancers are similar to children with BWS. As a result, children with hemi hypertrophy should follow the general cancer screening protocol for BWS

Hepatoblastoma, the risk of these diminishes after the age of 3 years. They can also be detected by abdominal ultrasound but, as not all the liver can be viewed, AFP (alpha-feta-protein) levels in the blood may also be monitored 3 monthly. As the risk of these tumours is so low, this test is not usually carried out in the UK.

Cardiomegaly or Structural Cardiac Abnormalities

Enlarged heart or heart defects. These are relatively uncommon and may resolve without treatment.

PROGNOSIS

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. Advances in treating neonatal complications and premature infants in the last twenty years have significantly improved the true infant mortality rate associated with BWS. In a review of pregnancies that resulted in 304 children with BWS, not a single neonatal death was reported. [13] This is compared to a previously reported mortality rate of 20%. [14] The data from the former was not an exclusion criterion to join the registry. This suggests that while infants with BWS are likely to have a higher than normal infant mortality risk, it may not be as high as 20%.

CONCLUSION

Though BWS is rare but it can be diagnosed by proper clinical examination, because presentation may vary, may present with milder form. Any child having macrosomia and macroglossia, always look for this syndrome because early detection and treatment can improve the outcome of the child.

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