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Case Series

Surgery Section

The Relevance of Follow-up after Primary Management of Omphalocele in Beckwith-Wiedemann Syndrome: A Series of Five Cases

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ABSTRACT

Omphalocoele, also called exomphalos, though a large disease by itself, can just be one part of association of much broader growth disorder of Beckwith-Wiedemann Syndrome (BWS), which one needs to be familiar with primarily. The omphalocoele is amenable to primary surgical correction in neonatal period. With the successful treatment of omphalocoele in the spectrum of BWS does not conclude the management, as the literature suggests the follow-up is imperative as there is increased incidence of visceral malignancy and blood cancers in these patients over the years of life. Present series is of five cases of BWS treated at birth for omphalocoele by surgery successfully, kept on regular follow-up, with one child developing leukaemia and loss of life due to the disease. The emphasis thus is on the need identification of the syndrome of BWS in a case of omphalocoele and also elaborating on their follow-up, long enough after surgery because of the risk of development of various malignancies.

Keywords: Exomphalos macroglossia gigantism syndrome, Leukaemia, Neonatal period, Omphalocoele management

INTRODUCTION

The BWS is a rare syndrome, but is most often seen congenital overgrowth syndrome [1,2]. BWS has high morbidity and mortality rate (32% in newborns) [3]. Omphalocoele, in this context, is a part of BWS; but as an isolated anomaly itself, omphalocoele is a major condition necessitating early and appropriate management to prevent sepsis and mortality during the neonatal period [3,4]. The case series focuses on the management of omphalocoele major with BWS in neonates, detailing single-stage surgery, its results and mid-term follow-up with respect to development of visceral malignancies and blood cancers.

This case series included newborns with omphalocoele major with BWS or Exomphalos, Macroglossia, Gigantism (EMG) syndrome, presenting before day 2 of life and of either sex. Fifteen cases of major omphalocoele with associated anomalies in neonates were studied. Five of these patients had BWS and were included in this case series. Only cases with atleast minimal follow-up period of five years were included. The details of each case are as follows:

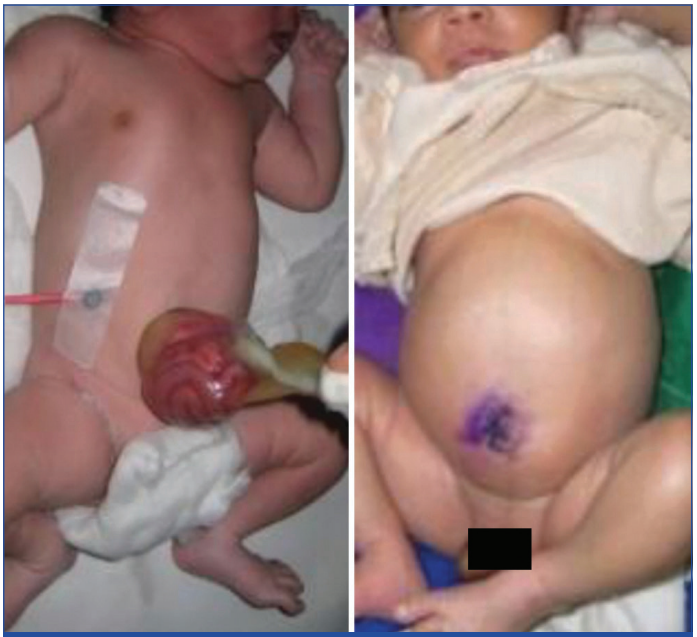
CASE SERIES

Case 1

The male baby born by caesarean section at 37 weeks of gestation to a gravida 2 mother, weighing 4.1 kg. He presented with swelling at umbilicus, with herniated bowel and liver (omphalocoele), ear pits, and low-set ears. Antenatally, this foetus was diagnosed in late third trimester as omphalocoele major without other obvious associated anomalies and he was referred to this centre for delivery. On presentation, the infant was lethargic had mottling due to hypoglycaemia.

The baby was diagnosed to have BWS on presence of three major criteria: macrosomia, macroglossia and abdominal wall defects, and two minor criteria of hypoglycaemia episodes and post-helical ear pits [Table/Fig-1]. Complete blood counts were normal, hypoglycaemia was stabilised, and he was taken for surgery for the omphalocoele.

The child was put on ventilator support and weaned off it gradually weaned off over four days. The baby recovered and was discharged with full feeds on postoperative day 16 [Table/Fig-2]. The baby was on continuous surveillance with USG abdomen and blood investigations. However, he developed precursor B-cell Acute Lymphoblastic Leukaemia (ALL) at 10 years of age. Genetic studies revealed a t(9;22) Philadelphia translocation (Ph). This was explained here due to negative regulation of haematopoiesis and the transforming growth factor beta pathway, depending on up-regulation of CDKN1C. He was placed on augmented Berlin-Frankfurt-Munster (a-BFM) protocol and imatinib, responded initially to induction chemotherapy, but succumbed later due to severe bleeding diathesis.



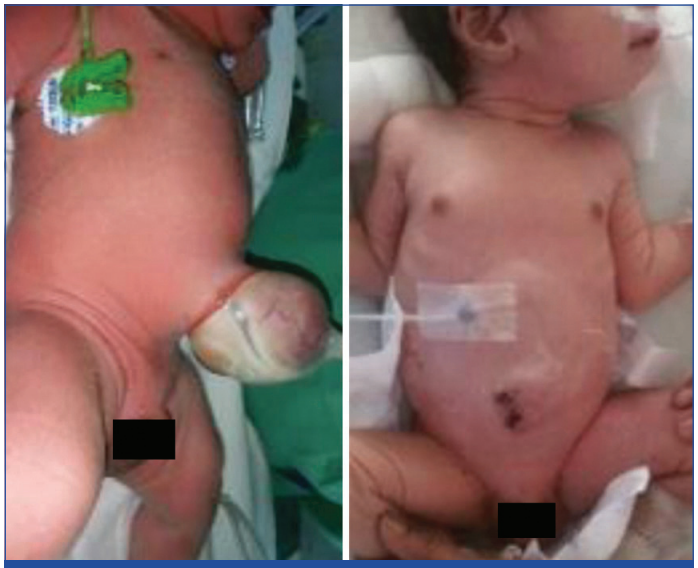
[Table/Fig-1]: Omphalocoele in a first case of BWS.
[Table/Fig-2]: Postoperative appearance of first case of BWS. (Images from left to right)

Case 2

The male baby was born by caesarean section at 36 weeks of gestation to a gravida 2 mother and was referred on day 1 of life

with umbilical swelling, herniation of liver and bowel and a birth weight of 4.1 kg with no history or notes of antenatal USG. Upon presentation, there was no significant family history on presentation, umbilical swelling with herniated bowel and liver, had macrosomia, was lethargy and mottling due to hypoglycaemia.

The baby was diagnosed to have BWS on presence of three major criteria: macrosomia, macroglossia and abdominal wall defect (omphalocoele), and two minor criteria of hypoglycaemia episodes and post-helical pits. Neonate underwent resuscitation and was prepared for surgery. The baby had umbilical swelling with herniated bowel and liver, posterior helical pits, low-set ears, hepatomegaly, and hypoglycaemia [Table/Fig-3]. The neonate underwent surgery, and had no other associated intestinal atresia or other anomalies were found. Surgery was by single stage omphalocoele surgery and shifted to Neonatal Intensive Care Unit (NICU) with ventilator support, from which he eventually recovered. The baby was weaned off the ventilator over five days, started on feeds and was discharged on postoperative day 15 [Table/Fig-4]. The child is doing well in the follow-up period of eight years.



[Table/Fig-3]: Omphalocoele in a second case of BWS.
[Table/Fig-4]: Postoperative appearance in second case of BWS. (Images from left to right)

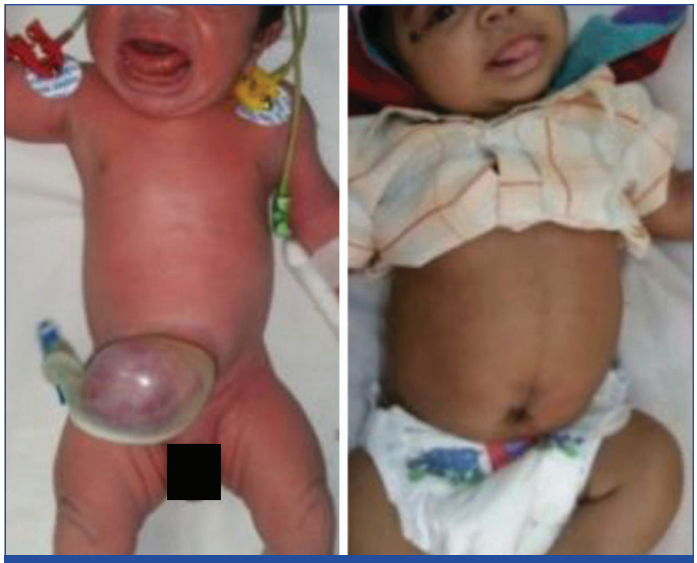
Case 3

A male baby was born by caesarean section at 35 completed weeks of gestation to a primigravida mother by caesarean section elsewhere. Baby presented on day one of life with lethargy, umbilical swelling, herniation of bowel and liver, macrosomia (weight of 4.3 kg), macroglossia, low-set ears and a preauricular sinus and lethargic. No significant family history. Upon examination, the baby had umbilical swelling with herniated bowel and liver [Table/Fig-5]. The newborn underwent routine investigations which were normal, except for hypoglycaemia. The diagnosis of BWS was made based on the presence of three major criteria: macrosomia, macroglossia, and abdominal wall defect (omphalocoele), along with two minor criteria of hypoglycaemia episodes and bilateral ear lobe creases.

Child underwent single-stage surgery for omphalocoele, did not have any associated anomalies like atresia of the gut. Postoperatively, he was shifted to NICU with ventilator support. The baby was weaned of ventilator over three days, started on feeds and was discharged on postoperative day 15 [Table/Fig-6]. The child is doing well during the follow-up period of seven years and four months.

Case 4

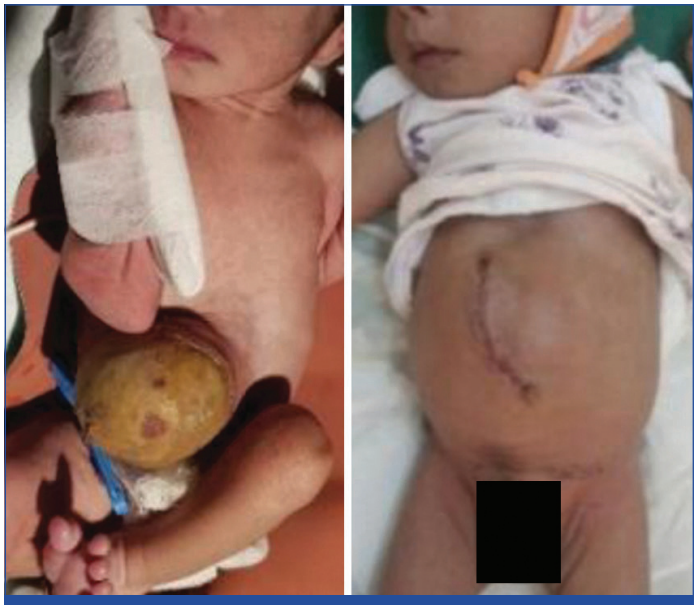
A male baby was born via caesarean section at 37 weeks of gestation to gravida 3 mother with late antenatal diagnosis of



[Table/Fig-5]: Macrosomia and omphalocoele in a third case of BWS.
[Table/Fig-6]: Postoperative appearance in third case of BWS. (Images from left to right)

omphalocoele. The neonate weighed 2.9 kg and had mottling and was having refusal to feeds. There was no significant family history. The baby on examination, the baby had umbilical swelling with herniated bowel and liver, preauricular sinus, low-set ears, hepatomegaly, hypoglycaemia and a cardiac murmur suggestive of congenital heart disease {Ventricular Septal Defect (VSD)} [Table/Fig-7]. The newborn underwent routine investigations, which were normal except for echocardiography showing muscular VSD and hypoglycaemia. The diagnosis of BWS was established based on the presence of three major criteria: visceromegaly, macroglossia, and abdominal wall defects (omphalocoele) and two minor criteria of hypoglycaemia episodes and cardiac anomaly of VSD.

The child underwent single-stage surgery for omphalocoele and did not have any associated anomalies like intestinal atresia. The neonate was shifted to NICU with ventilator support and exhibited features of cardiac failure but recovered with medical management. The baby was weaned of ventilator over six days, started on feeds and was discharged on postoperative day 17 [Table/Fig-8]. The child is doing well in the follow-up period of six years and 11 months, with minor strabismus and no amblyopia, treated conservatively.



[Table/Fig-7]: Omphalocoele major in a fourth case of BWS.
[Table/Fig-8]: Postoperative appearance in forth case of BWS. (Images from left to right)

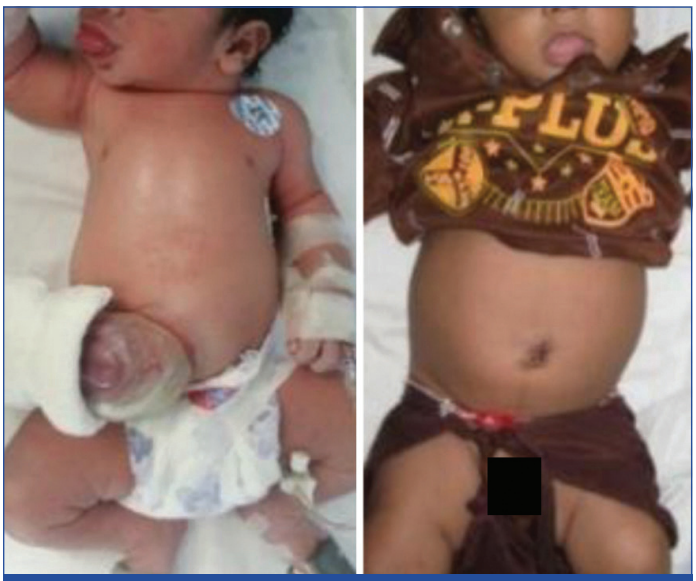
Case 5

The male baby was born by caesarean section at 34 weeks of gestation to a primigravida mother. Neonate had a late antenatal

diagnosis of omphalocoele. He presented on day one, weighing 2.2 kg, with mottling and refusal to feeds. There was no significant family history. The baby on examination had umbilical swelling with herniated bowel and liver, preauricular sinus (ear pits), low-set ears, hepatomegaly, hypoglycaemia, and a cardiac murmur suggestive of congenital heart disease {small Atrial Septal Defect (ASD)} [Table/Fig-9]. The routine investigations were normal except echocardiography showing muscular ASD and hypoglycaemia.

The diagnosis of BWS was made depending on presence of three major criteria: visceromegaly, macroglossia and abdominal wall defects of omphalocoele, and three minor criteria of hypoglycaemia episodes, cardiac anomaly (ASD), and post-helical ear pits. Child underwent single-stage surgery for omphalocoele and intraoperatively had no associated anomalies like intestinal atresia, etc. The neonate was shifted to NICU with ventilator support and exhibited features of cardiac failure but recovered with medical management. The baby was weaned of ventilator over six days, started on feeds, and was discharged on postoperative day 18 [Table/Fig-10]. The child is doing well in the follow-up period of six and half years.

The summary of all the cases is presented in [Table/Fig-11].



[Table/Fig-9]: Macrosomia, omphalocoele with macroglossia in a fifth case of BWS.
[Table/Fig-10]: Postoperative appearance fifth case of BWS. (Images from left to right)

DISCUSSION

The EMG syndrome was described by Dr. John Bruce Beckwith, a pathologist, in early 1963, and by Dr. Hans-Rudolf Weideman, a pediatrician, in 1964, who then coined the term EMG syndrome [1,2]. BWS has an incidence of 1 in 1 0,000 to 13,700 live births with most cases being sporadic (85%) [3]. EMG later became known as BWS and is diagnosed based on the presence of major criteria, including macroglossia (90-97%), macrosomia (birth weight and length >90th percentile) (45-88%), abdominal wall defects (omphalocoele, umbilical hernia, or diastasis recti) (44-80%), hemi hyperplasia (24-65%), and visceromegaly (59%) [4-6].

The minor findings include neonatal hypoglycaemia (30-63%), placentomegaly, pregnancy-related polyhydramnios (53%), vascular lesions (62%), structural cardiac anomalies (13%), and bilateral or unilateral earlobe creases or post-helical pits (6.5-63%) [3,4,7]. Three major criteria or two major and a minor criteria are required to label as EMG/BWS Syndrome [4,6]. Literature showed that patients with BWS may exhibit features of prematurity, polyhydramnios, and foetal macrosomia in as high as 50%, with most minor criteria involving hypoglycaemia, antenatal diagnosis of polyhydramnios, premature birth, earlobe creases/post-helical pits (unilaterally or bilaterally), and cardiac anomaly [3,6-8].

The disease affects both sexes equally and the incidence of BWS increases by tenfolds in babies born to parents with use of artificial reproductive techniques. Genomic alteration leading to abnormal methylation at 11p15.5 or variant in CDKN1C are usually found, which leads to abnormal cell cycle progression and somatic growth [7]. Patients have 1,000-fold increased risk of developing embryonal tumours with incidence of development of ALL as a type of malignancy in these cases is rare, one case in this series developed ALL with Philadelphia chromosome-positive (ph+) [9]. Neonatal mortality in cases of BWS is as high as 20%. Undetected or untreated hypoglycaemia may result in cerebral dysfunction and mental retardation [9,10].

Most important issue at birth is closure of exomphalos, which has many techniques. In this case, it was achieved with single-stage surgery, which was done with relative ease without raising intra-abdominal pressure and causing any respiratory incompliance [11-13]. These children need regular follow-up to detect development of intra-abdominal malignancies or blood cancers every three months up to eight years, as they have 600 times more risk of developing these malignancies [4-6]. Highest chance is in early age up to four years then reduces significantly by eight years, and reduces much

S. No.	Diagnosis/sex	Antenatal diagnosis	Presentation at birth	Criteria for diagnosis	Surgery	Complications and follow-up
1	BWS with omphalocoele/ Male	Omphalocoele, diagnosed in late IIIrd trimester	Swelling at umbilicus with herniated bowel and liver, (omphalocoele) ear pits and low set ears	3 major criteria of macrosomia, macroglossia and abdominal wall defects and two minor criteria of hypoglycaemia episodes and posthelical ear pits	Single stage repair with umbilicoplasty	Pre-ALL (Leukaemia) after 9 years, expired during maintenance chemotherapy
2	BWS with omphalocoele/ male	No history available	Umbilical swelling with herniated bowel and liver covered by sac	3 major criteria of macrosomia, macroglossia and omphalocoele and two minor criteria of hypoglycaemia episodes and posthelical ear pits	Single stage repair with umbilicoplasty	Doing well in follow-up period of 8 years
3	BWS with omphalocoele/ Male	Diagnosed at 8 1/2 mnth on ultrasonogram	Umbilical swelling with herniated bowel and liver covered by sac, ear creases and lethargy	3 major criteria of macrosomia, macroglossia and omphalocoele and two minor criteria of hypoglycaemia episodes and bilateral ear lobe creases	Single stage repair with umbilicoplasty	Redo surgery. Neurodevelopmental delay+, follow-up of 7 years
4	BWS with omphalocoele with CHD/ Male	No history available	Umbilical swelling with herniated bowel and liver covered by sac with respiratory distress	3 major criteria of visceromegaly, macroglossia and omphaloceole and two minor criteria of hypoglycaemia episodes and cardiac anomaly of VSD	Single stage repair with umbilicoplasty and observation for VSD	Doing well in follow-up period of 6 years and 11 months
5	BWS with omphalocoele/ Male	Diagnosed at 8th month scan antenatally	Umbilical swelling with herniated bowel and liver covered by sac, cardiac murmur	3 major criteria of visceromegaly, macroglossia and omphalocoele, and three minor criteria of hypoglycaemia episodes, cardiac anomaly (ASD) and posthelical ear pits	Single stage repair with umbilicoplasty and observation for ASD	Doing well in follow-up period of 6 years and 6 months

[Table/Fig-11]: Summary of cases.
CHD: Congenital heart disease; VSD: Ventricular septal defect; ASD: Atrial septal defect; ALL: Acute lymphoblastic leukaemia

more in later years [8-10]. This makes screening less needed in later years, emphasising the importance of regular and vigorous screening and examination in follow-ups in early age i.e., at least for a decade after surgery for omphalocoele in BWS children [3,6,7].

CONCLUSION(S)

Omphalocoele, which is an important component of BWS, warrants early repair in neonates and this procedure is feasible, producing acceptable surgical results of this surgery but the management does not end here but begins. As one needs to be vigilant with cases with birth defects where quality of life and neurodevelopmental issues may persist. Those with BWS are at risk of developing malignancies in early or intermediate age group. Long-term follow-up has shown that children with BWS have shown to have normal growth, with an average life expectancy in those who surviving the two storms, one of neonatal surgical repair of omphalocoele and second of malignant potential with proper follow-up in the early years, hence recommending continuous surveillance, tumour screening and early diagnosis contribute to good long-term cancer-free outcomes.

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