Beckwith Weidemann Syndrome

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Introduction

Since first described in 1963, Beckwith Weidemann Syndrome is increasingly being recognised as an important genetic overgrowth disorder. With the characteristic diagnostic triad of exomphalos, macroglossia and gigantism, its early recognition is necessary because of the associated risk of hypoglycaemia in the neonatal period, embryonal neoplasms in childhood and for the purpose of genetic counselling. We report one such classical case.

Case Report

A male infant was born to a young 4th gravida by a vaginal delivery at 34 weeks gestation. The mother had suffered three previous pregnancy losses due to prematurity. In view of the bad obstetrical history and observed macrosomia, the baby was transferred to our centre. Anthropometric

examination revealed a weight of 4.5 kg, head circumference - 35 cm, chest circumference - 46 cm and length of 56 cm. Dysmorphic features observed were mongoloid slant of eyes, naevus flammeus over forehead, low set ears, macroglossia and a horizontal groove over ear lobes with a linear indentation over the antihelix (Fig 1). The abdomen was protuberant with diversification of recti and a umbilical hernia (Fig 2). Abdominal examination revealed a liver span of 6 cm, spleen palpable 2 cm below costal margin and bilaterally palpable kidneys. The external genitalia was male and there was bilateral cryptorchidism. The neonate suffered three episodes of asymptomatic hypoglycaemia and one episode of symptomatic hypoglycaemia while in hospital which responded to dextrose supplementation.

Investigations revealed normal blood counts and calcium levels. X-ray chest excluded cardiomegaly and diaphragmatic eventration. X-ray wrist was suggestive of an advanced bone age of 30 months. 2D ECHO study was normal and excluded a hypertrophic cardiomyopathy. Abdominal ultrasound

Fig. 1 : Profile of the neonate showing low set ears, a horizontal groove over the ear lobe with a linear indentation over the antihelix

Fig. 2 : Neonate's abdomen is protuberant with rectal diversification, a umbilical hernia and bilateral cryptorchidism

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examination showed bilateral hydronephrosis with megaureters. Both testes were visualised in the inguinal canal. Adrenals were of normal size. Micturating cystourethrogram delineated a normal sized bladder and excluded urethral obstruction and vesicoureteric reflux. DTPA scan showed a normal total and differential glomerular filtration rate and a type 2 excretory curve. Karyotyping revealed duplication of the short arm of chromosome 11, confirming the diagnosis of Beckwith Weidemann Syndrome.

The neonate was discharged with the advice of nursing in the prone position, frequent feeding and three monthly follow up to exclude the development of embryonal neoplasms with clinical ultra sound and tumour marker screening. At 6 monthly follow up, the infant had developed hemihypertrophy, macroglossia had partially regressed, he was clinically and radiologically free of tumours and the renal functions were normal

Discussion

An association between adrenal cytomegaly, hemihypertrophy, macroglossia, omphalocele and pancreatic islet hyperplasia was described by Beatty and Hawes in 1955 [1]. However, it was first recognised as a syndrome complex by Beckwith in 1963 and Weidemann a year later, who recognised its familial nature as also the association with hypoglycaemia and macrosomia [2]. It is estimated that this condition has an incidence of 1 in 14,000 births with an equal sex distribution. The true incidence however, may be underestimated as the less severe cases may go unreported. Although most cases appear to be sporadic (85%), the etiology is believed to be genetic in nature [3]. Present evidence supports an autosomal dominant mode of inheritance with reduced penetrance and variable expressivity that may relate to the effects of genomic printing [4]. Cytogenetic studies have revealed the gene for Beckwith Weidemann Syndrome to be located on the chromosome 11(11p15.5) in close proximation to the insulin like growth factor 2 gene. Prenatal ultrasound demonstrating foetal omphalocele, macrosomia, or renal/hepatic/kidney enlargement suggests the possibility of Beckwith Weidemann syndrome which could be further substantiated by the presence of polyhydramnios, a large and thickened placenta and a long cord. Perinatal risk factors are those associated with prematurity, birth trauma due to large foetal size and hypoglycaemia. Prematurity contributes to the high infant mortality, the cause of death being congestive heart failure, apnoea due to macroglossia and hyaline membrane disease. Growth rate is normal but at or above the 95th percentile. Asymmetric overgrowth results in hemihypertrophy, seen in almost 13% of the cases [5]. Puberty occurs at normal age at which time the overgrowth diminishes so that these children achieve an average height.

Distinctive associated craniofacial features are earlobe transverse creases and pits, facial nevus flammeus, prominent eyes with infraorbital ridges and macroglossia. Besides causing respiratory and feeding difficulties, macrosomia can lead to orthodontic abnormalities, a prognathic appearance and speech difficulties. However, the problems with macroglossia improve with age and these children appear to grow into their large tongues. Abdominal wall defects are common occurring in almost 75% of cases. The other associated gastrointestinal abnormalities are pyloric and ileal stenosis, colon atresia, imperforate anus, malrotation and diaphragmatic hernias/eventration. Organs affected with visceromegaly are kidneys, spleen, pancreas and less commonly heart. A significant complication of this syndrome is the increased risk of developing malignant tumours. The reported incidence ranges from 7-10% [6]. Association with hemihypertrophy as in our case, increases the risk of malignancy to 40% [7]. The common associated neoplasms reported are Wilm's tumour (59%), adrenocortical carcinoma and hepatoblastoma. Prognosis for long term survival with normal cognition is favourable if neonatal complications are promptly addressed. The dysmorphic features regress with age. In view of the increased risk of malignancy, particularly when associated with hemihypertrophy, a screening protocol is recommended which includes (i) base line CT scan of abdomen at 6 months (ii) detailed abdominal clinical and ultrasound examination and (iii) tumour marker screening, to be carried out 3 monthly till 7 years and 6 monthly till completion of skeletal growth [8]. We are monitoring our case on the above lines. He is presently aged 8 months and as yet free of neoplasia.

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