Cases of Beckwith-Wiedman Syndrome

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MJAFI 2009; 65 : 182-183

Key Words: Macrosomia; Macroglossia; Omphalocele; Hypoglycemia

Introduction

Beckwith-Wiedman syndrome (BWS), also called Exomphalos-Macroglossia-Gigantism Syndrome is classified as an overgrowth syndrome. Major clinical features include increased birth weight, postnatal gigantism, macroglossia (large tongue), craniofacial anomalies, umbilical anomalies (hernia, omphalocele), earlobe anomalies, capillary facial flame nevus, hypoglycemia and cardiac defects. Occasional features include hepatomegaly, hemihypertrophy and certain embryonal tumours [1-3].

It is caused by excess availability of IGF-II encoded by the gene *Igf 2* and its incidence is 1:13,700 births [4]. Three cases of BWS are reported with a view to highlight the importance of the possibility of undiagnosed untreated hypoglycemia in these patients which may result in long term developmental difficulties [5] and the need for such children to be followed up for embryonal tumors.

Case Report

Case 1

Full term male neonate, only product of nonconsanguineous marriage was born to an unbooked 20 year old primigravida. Baby was detected to have omphalocele and macroglossia (Fig. 1). Birth weight was 4.2 kg (90-95th centile) and length 52cms (75-90th). BWS was suspected due to these features and hence regular blood glucose monitoring was done. Asymptomatic hypoglycemia (blood glucose 32 mg/dl) was detected at 36 hours of life and managed with dextrose infusion. Omphalocele was operated on Day 2 of life. Postoperative recovery was uneventful and dextrose infusion was slowly tapered off. Baby was on regular follow-up till nine months of age and showed normal developmental milestones.

Case 2

Full term female neonate, first product of nonconsanguineous marriage was born to a 24 year old primigravida. Antenatal ultrasonography (USG) revealed a

large baby. Birth weight was 4.5 kg. Baby had macroglossia and hypertrophy of the right side of the body. During routine blood sugar monitoring, she was found to have asymptomatic hypoglycemia (blood glucose 36 mg/dl) which was managed with dextrose infusion, tapered off by Day 3. At two months of age, she had a solitary generalized tonic-clonic seizure and 15 days later, she was admitted with status epilepticus which was controlled with intravenous antiepileptics. Blood sugar, electroencephalograph, computed tomography and magnetic resonance imaging of brain were normal. She is now seizure free on long-term antiepileptic drugs. Presently she is three years old, weighs 17 kg (90-95th centile) with a height of 98cms (75-90th). Her developmental milestones are normal and she undergoes six monthly abdominal USG to screen for tumours.

Case 3

A 5 year 3 month old boy, first product of a 3rd degree consanguineous marriage presented with complaints of a large tongue since birth. He was being treated with eltroxin (L-thyroxin) due to a clinical suspicion of hypothyroidism, however no documents were available. Birth weight was unknown though the parents remember him to be a large baby with no history suggestive of hypoglycemia. On examination, weight was 25kg (95-97th centile) and height

Fig. 1 : Macroglossia seen in BWS

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118cm (95th centile). He had significant macroglossia, hemihypertrophy of left side of body, palpable liver and normal intelligence. Eltroxin was discontinued and thyroid function tests done after a month were normal. He is on regular follow up including USG screening.

Discussion

In 1964, Beckwith and associates described a syndrome characterized by omphalocele, macroglossia and visceromegaly. Wiedman almost simultaneously described a similar clinical picture in three siblings [2].

Macroglossia was present in all our cases. Hypothyroidism, an important differential diagnosis was ruled out by presence of other characteristic features of BWS and a normal thyroid profile. However, there are reports of the two conditions coexisting in some patients [6]. Hypoglycemia (noted in the first two cases) is associated with hyperinsulinemia (due to diffuse islet cell hyperplasia) [4]. Blood glucose must be monitored frequently during the first 72 hours of life in all neonates showing the clinical features of this disorder [2].

Hypoglycemia in a majority of cases is asymptomatic and will respond to frequent feeding. However if this cannot maintain normal glucose levels or if the baby becomes symptomatic, a bolus of 2ml/kg of 10% dextrose is given over a minute followed by dextrose infusion starting @ 8 mg/kg/hr with frequent blood sugar monitoring [7]. If blood glucose does not normalize with dextrose, a number of agents which reduce the excess insulin secretion such as glucocorticoids, glucagon and diazoxide have been employed [2]. Less than 5 % of cases have hypoglycemia beyond the neonatal period requiring either continuous feeding or a partial pancreatectomy [8]. The prognosis is poor if symptomatic hypoglycemia is severe [4].

Majority of cases of BWS are sporadic while familial forms occur in 15% cases. None of our cases had any family history suggestive of this disorder.

BWS occurs due to perturbations of the normal dosage balance of a number of genes clustered at 11p15 (organized in 2 separate domains). Domain 1 contains paternally expressed insulin like growth factor (IGF2) as well as genes and transcripts that control expression of IGF2. Domain 2 contains several imprinted genes including CDKN1C and KCNQ10T1 (L1T1) [1].

As with other dysmorphic syndromes, the diagnosis of BWS depends upon a characteristic clinical picture rather than any specific diagnostic test. Demonstration of the underlying genetic abnormalities requires sophisticated methodology beyond the scope of a standard clinical or genetics lab [2].

Some cases may acquire embryonal tumours (frequency of 6.5%) including Wilms tumour, hepatoblastoma, neuroblastoma and rhabdomyosarcoma [4]. Obtaining USG and alfa-feto protein (AFP) levels every six months to rule out Wilms tumour and hepatoblastoma respectively are warranted. AFP levels are to be compared with normal curves established specifically for BWS [9]. Antenatal diagnosis is possible as maternal USG showing polyhydramnios. Accelerated growth beginning between 25-36 weeks gestation, even without omphalocele should alert the physician to the possibility of this syndrome [10]. At birth there is a relatively high incidence of prematurity. Apart from hypoglycemia other problems with neonatal adaptation may occur including apnea, cyanosis and polycythemia. Infant mortality rate is estimated to be as high as 21 %. Fortunately, affected individuals who survive infancy generally are healthy. Mental capacity may be normal though some cases show mild to moderate mental deficiency [1].

Conflicts of Interest

None identified

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