Permanent Neonatal Diabetes Mellitus in Beckwith-Wiedemann Syndrome: An unusual co-occurence

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INTRODUCTION

Beckwith Wiedemann Syndrome was first described in 1960s by Dr John Beckwith and Dr Hans-Rudolf Wiedemann

It is rare disorder, with estimated incidence of 1 in 13700 cases per year world wide

It is characterized by omphalocoele/exomphalos, macroglossia, macrossomia, earlobe creases and neonatal hypoglycaemia

Diabetes mellitus is not characteristic of Beckwith Wiedemann Syndrome

An association between permanent neonatal diabetes and Beckwith-Wiedemann Syndrome have never been reported in English literature(Pubmed)

OBJECTIVES

To report on a 17 years old boy with Beckwith-Wiedeman Syndrome who was diagnosed with permanent neonatal diabetes mellitus since 4 months of age

To determine the molecular genetics study which maybe associated with diabetes and Beckwith Wiedeman Syndrome

METHODS

An adoloscent, now aged 17 years, Born full term by emergency lower segment caesarian section for cephalo-pelvic disproportion, Birth weigh of 5.25 kg, Apgar scores, 9^{1}, $10^{5.}$

He was noted to have omphalocoele, macroglossia and earlobe crease. Surgical consult was made and surgical repair of the omphalocoele was undertaken immediately after birth. There were no peri-operative or post-operative complications. His blood glucose dropped low time and again and he was maintained on intravenous dextrose

He stayed in hospital for 2 months post operation and he was discharged home. He suffered recurrent hypoglycaemias post discharge, which required multiple admissions for IV dextrose treatment.

At 4 months of age, following treatment for one of the hypoglycaemic attack with IV dextrose, his blood glucose remained persistently elevated and he was treated with insulin.

Molecular genetics studies were done, looking for the presence of the common mutations associated with neonatal diabetes. He was tested for DNA methylation at the imprinted KCNQ1OT1/H19 loci and PLAGL1 locus. He had sequence analysis of coding and flanking intronic regions of the ABCC8 and KCNJ11 gene.

RESULTS

His DNA showed complete hypomethylation at KCNQ1OT1. His DNA methylation was normal at H19 and the TND locus. There was no mutations detected in the KCNJ11 and KIR6.2 genes

The complete hypomethylation at KCNQ1OT1 is consistent with a diagnosis of BWS. The normal methylation at H19 is inconsistent with paternal uniparental disomy at chromosome 11. The absence of KCNJ11 and KIR6.2 is inconsistent with a diagnosis of neonatal diabetes

CONCLUSIONS

The combination of clinical signs with molecular genetic studies confirms the diagnosis of BWS in our patient.

However, the mutational analysis of the K-ATP channels fails to confirm the cause of diabetes mellitus.

The co-occurrence of Permanent Neonatal Diabetes Mellitus and Beckwith Wiedemann Syndrome is very rare

The future studies should aim to identify possible genetic linkages between neonatal diabetes and Beckwith Wiedemann Syndrome.

References

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