NEONATAL DIABETES MELLITUS DUE TO INSULIN GENE MUTATION

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Introduction

- Diabetes mellitus is a heterogeneous group of metabolic diseases characterized by high blood glucose levels that can present at any age.
- Genetic factors play an important role in the development of diabetes. The identification of the underlying genetic defects has provided important insights into pancreatic development and the control of pancreatic cell function and improvements in diagnosis and treatment.
- Insulin (*INS*) mutations are an important cause of permanent neonatal diabetes mellitus (PNDM) change single protein building blocks in the protein sequence. These mutations are believed to disrupt the cleavage of the proinsulin chain or the binding of the A and B chains to form insulin, leading to impaired blood sugar control. At least 10 mutations in the *INS* gene have been identified in people with PNDM

Objectives:

To identify mutations of *INS gene* in patients with NDM; To describe clinical features and laboratory manifestations of patients with *INS* gene mutation and evaluate outcome of management

Methods:

- Descriptive study, case series study, collection of the symptoms and investigations, DNA was extracted from peripheral lymphocyte and analysed mutation using PCR and direct sequencing of *INS* gene.
- The patients include of 6 NDM patients with *INS* gene mutations are treated in National Hospital of Pediatrics

Results:

6 probands from 6 unrelated families were diagnosed NDM and were identified mutation in *INS* genes.

Demographics :

- Age of diagnosis was 129. 2 ±128.8 days of age (median 101.5 days)
- Gender: 3 males, 3 females
- Gestation age was 37.3 ± 3.0 weeks
- BW: 2816.6 ± 767.8 grams

Table 1. Genotype, phenotype correlation in INS gene mutation patients

Genotype-Phenotype		Case1	case2	Case 3	Case 4	Case 5	Case 6
Genotype		Het. Novel missense c.127T>A p.Cys43Ser exon 2	Het novel splising c.188-31 G>A P?, intron 2	Het novel splising c.188-31 G>A P?, intron2	Het. missense mutation .286T>C p.Cys96Arg Exon 3	Het. missense mutation c.265C>T p.Arg89Cys Exon 3	Het. Missense mutation c.265C>T p.Arg89Cys Exon 3
Phenotype	Clinical	Polydipsia, polyuria, fever, vommit, diarrhea, dehydration	Polydipsia, polyuria, fever, diarrhea, dehydration shock	Fever, vommit, lethargy	Fever, vommit, lethargy	Fever, cough	Fever, vommit, diarrhea, polydipsia, polyuria
	pH	6.8	6.9	7.14	7.23	7.35	6.83
	HCO^-_3 (mmol/l)	2.3	2.9	3.6	2	21	3
	BE (mmol/l)	---	-28.9	-23.2	-23	-3.3	---
	HbA1C (%)	8.3	12.8	8.55	11.4	3.9	13.6
	Glucose (mmol/l)	24	34.72	54	21	44.4	27.8
	Ketourine	++	+	+	+	-	+

Outcome: After 19.2 ± 13.4 months of insulin treatment

- 4/5 patients have normal development with DQ 80-100%, HbA1C of 6.85 ±0.49%, quite normal blood glucose levels.

-The case 1 with c.127T>A mutation treated with insulin for 14 years has physical development delay, poor blood glucose control with HbA1C of 11.4%.

Conclusions:

It is important to perform screening gene mutation for patients with diabetes diagnosed before 12 months of age to control blood glucose and follow up the patients

References:

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