SIX CASES OF CONGENITAL HYPERINSULINISM CAUSED BY MUTATIONS IN MODY GENES

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INTRODUCTION

Congenital hyperinsulinism (HI) is the most common cause of persistent hypoglycemia in infants and children (1).
Recently, mutations in genes usually involved in MODY 1 and 3 have been described in HI (2). We present here 6 cases of hyperinsulinism associated with MODY1 (1 case) and MODY3 (4 cases) and 1 case of HI associated with MODY5 mutation.

CASES REPORT

	CASE 1	CASE 2	CASE 3	CASE 4	CASE 5	CASE 6
Sex (year)	GIRL (2011)	BOY (2013)	GIRL (2012)	BOY (2015)	BOY (2004)	GIRL
Gestational age (wks)	35+5	41	38+1	39+2	34+3	39
Birth weight (g) Birth length (cm) Head circumference (cm)	3350 47,5 33	3670	2610 41 34	2990 50 35,5	1570 39	normal
Diagnosis of hypoglycemia and HI due to MODY mutation	Neonatal	Neonatal Transient hyperinsulinism	Neonatal	Neonatal	4,7 years Hypoglycemia seizure with ketonuria	5 years Hypoglycemia seizure with ketonuria
Mutation	exon 2 of **HNF4a gene** Heteroz. c.131G>C p.Arg44Pro	exon 1-9 of **HNF1b gene** Wide duplication Heteroz. c.1-?-1674+?dup p. ?	Exon 3 of **HNF1a gene** Heteroz. c.598 C>T p.Arg200Trp	Exon 3 of **HNF1a gene** Heteroz. c.598 C>T p.Arg200Trp	**HNF1a gene** c.502 C>T	**HNF1a gene** c.77 T>C
Family history	Mother : MODY1 with insulin (same mutation)	Mother and maternal grand-mother : MODY5 with same mutation, no insulin	Father and brother (case 4) : same mutation	Father and sister (case 3): same mutation	Father ans sister: same mutation Father : history of loss of consciousness in childhood Sister : no sign or symptom	Mother : MODY 3 with same mutation
Treatment	Diazoxide-responsive for 3 years	Diazoxide-responsive for 10 days	Diazoxide-responsive for one month	No treatment	Still requiring diazoxide treatment 5 years later	Still requiring diazoxide treatment after 1.5 years.
Molecular study	ABCC8-, KCNJ11-, GCK-	ABCC8-, KCNJ11-, GCK-, HNF4a-, HNF1a-	ABCC8-, KCNJ11-, GCK-, HNF4a-, HNF1a-		ABCC8-, KCNJ11-, GCK-, HNF4a-	
Other clinical signs	Developmental delay (6 months) Hyperglycemia on CGMS at the age of 2,5 years	Diffuse angioma Developmental delay (1 year)	Hypoglycemia with diarrhea			Neonatal hypoglycemia and hypotonia Growth delay (4,5 years)

CONCLUSION

We report the first case of HI associated with HNF1b mutation.
HNF4a and HNF1a are recently described causes of HI.
Our cases showed that the clinical presentation can be variable, from transient neonatal HI to persistent HI discovered during childhood.

REFERENCES

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