TRANSIENT NEONATAL DIABETES MELLITUS DUE TO NOT DESCRIBED MUTATION IN ABCC8 GEN WITH DIFFERENT BEHAVIOR IN AFFECTED FAMILY MEMBERS

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Background

Neonatal diabetes (ND), occurs in 1/200,000 live births. It is characterized by hyperglycemia in the first 6 months of life and needs insulin treatment at least 2 weeks. There is no autoinmmune base. In 50% cases of TND, remission presents within the first year of life, only to relapse later before puberty in 50% of cases.The most frequent cause is mutation of the 6q24 gene accompanied by mutations in heterozygosis of ABCC8 gene (which codifies SUR 1 subunit).
The majority of mutations in this gene are in novo, due to autosomal recessive inheritance (40%).There are described families with the same mutation with different clinical presentations. Epigenetic factors can influence in this physiopathology. Such cases respond to treatment with sulfonylurea (SU).We present a case of TND that motivated the change of diagnosis in both (mother and baby)

Material and Method

A term male infant was born at 38 weeks'gestation, weighing 2660gr(10-25th centile),length:48cm(40th centile).Presented isolated hyperglycemia in the first 48 hours, with true hyperglycemia on the 4th day, requiring treatment with Actrapid0.2 UI/KG/D.One month later the insulin requirements were0.2-0.3UI / kg/d.
FH:Non-Consanguinean parents.Type 1 DM mother at 9 years old,onset with hyperglycemia, requiring insulin treatment.Maternal grandmother at 38 years old, was diagnosed with Type I Diabetes requiring insulin treatment.
Evolution:A glycaemic control and study of pancreatic reserve (prior to the transition from insulin treatment to Sulfonylureas), were assessed 2 months after the change and 6 months after and the medication was removed 15 days before.
Results
Evolution HBA1c:4.7-5%.
Previous glucagon test:C-Peptide: 0': 0.22, 6: 0.82ng/dl.At 2 months: 0.42. 6´;0.91ng/ ml.Six months: 0': 0.27.6':0.37ng/ml
His mother had HBA1c:6.5% wich decreased to 6% following commencement on sulfonyilureas.His grandmother had HBA1c:10% wich similarly reduced to 6% following sulfonylureas treatment.

		Basal	2 months	6 months(and finish)
GLIBENCLAMIDE mg/kg/d	Infant	0,2	0,1	0,08
INSULIN UI/kg/d	Infant	0,2-0,3	Transition into SU in 1 day	

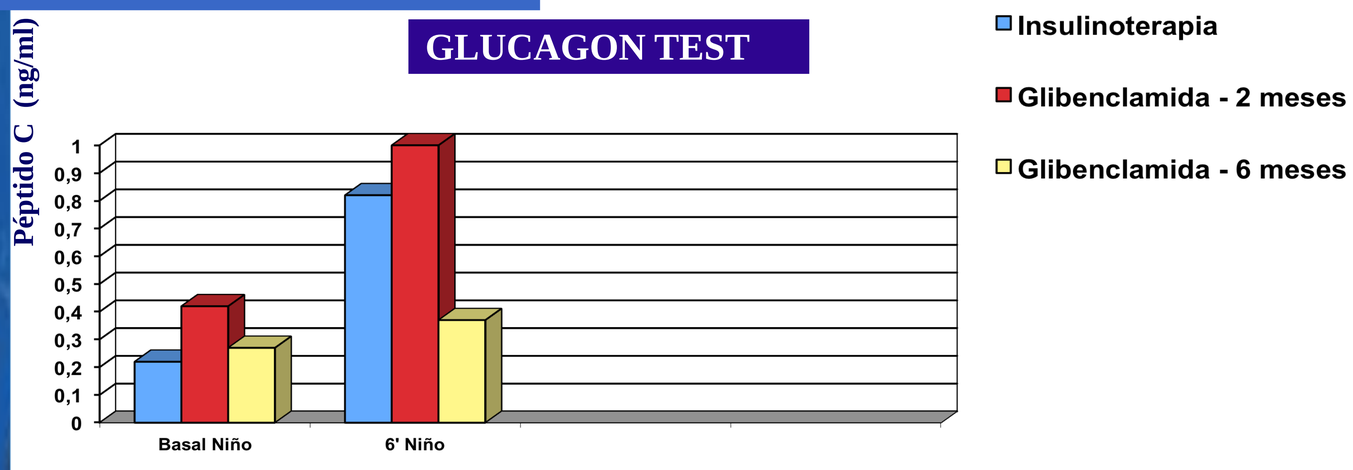
LABORATORY TESTS:

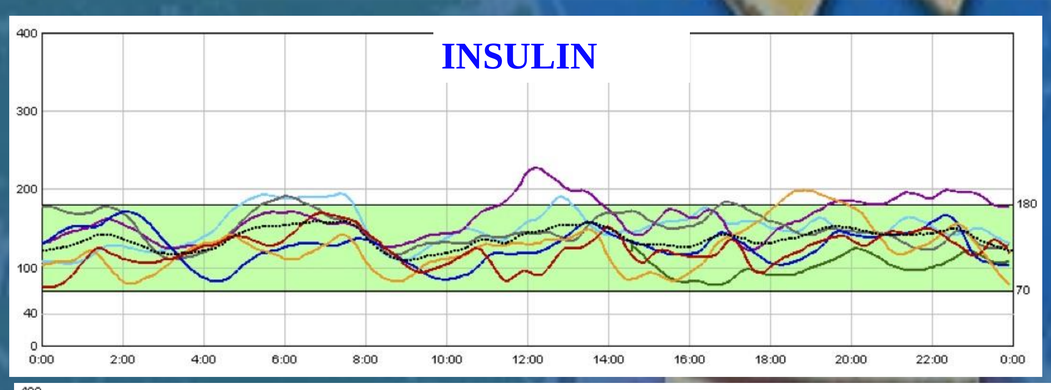
Glucose:300mg/dl,HBA1c 4.7%, no ketonuria, C-Peptide;0.58ng/dl,

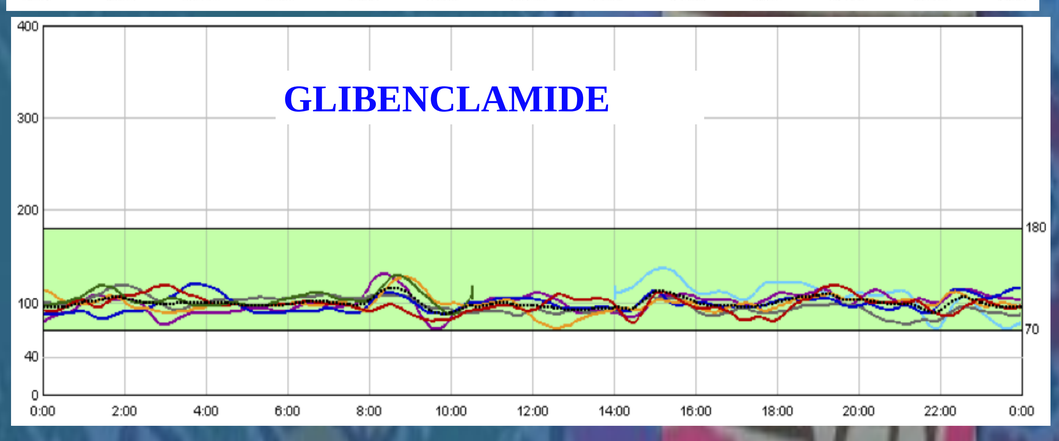
Fasting insulin:0.6mUI/ml.Negative diabetes antibodies (Anti-GAD, Islet, insulin autoantibodies) in mother and neonate.Genetic study of both:mutation in heterozygosis of exon 21 of the ABBC8 gene(p.C24982G>C,Gly.833G>Ala), associated with PND.

	MOTHER	GRANDMOTHER
GLUCAGON TEST C-PEPTIDE ng/ml Previous	2.03	1.97
HBA1c %Previous	7	10
GLUCAGON TEST C-PEPTIDE Ng/ml At 6 months	3.64	3.82
HBA1c %After	6.3	6
Glibencamide dose (mg/Kg/day)	0.3	0.1

EVOLUTION:







OGTT	Insulin Therapy		Glibenclamide 2months		Without Glibenclamide 6months	
	0'	120'	0'	120'	0'	120'
GLUCOSE (mg/dl)	230	298	80	238	66	127
INSULIN (mUI/ml)	4	5,4	1,5	9	3	2,8

HBA1c EVOLUTION: 4,7 – 5%

Conclusion

Clinical onset of diabetes in patients with mutations in ABCC8 gene in the first month of life are well documented. However, clinical picture can be different even with the same mutation as the case we present in the 3 family generations. In this case, the mutation was not previously described before and associated with (PND), being developed in our patient initially as(TND).Treatment with sulfonylureas improves the pancreatic reserve and metabolic control in all cases.Clinical follow-up of these patients is important,due to the risk of recurrence in 50% cases of DNT.