

SIROLIMUS THERAPY IN INFANT WITH HYPERINSULINEMIC HYPOGLYCEMIA UNRESPONSIVE TO DIAZOXIDE



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Background:

Hyperinsulinemic hypoglycemia is the most common cause of severe and persistent neonatal hypoglycemia. The treatment of diffuse forms unresponsive to diazoxide and octreotide is near total pancreatectomy.

Objective

To describe the clinical characterization of a newborn with congenital hyperinsulinemic hypoglycemia due to a diffuse pancreas lesion and unresponsive to diazoxide.

Clinical case

Preterm term male of 33 weeks, LGA . Apgar: 8 - 9 a 5 min. after 5 hours of life: blood glucose level it was **20mg/dl**, concomitant insulin was increased (**36uU/ml**) and ketone bodies are negative, Hyperinsulinemic Hypoglycemia was suspect. He was treated with iv glucose infusion (up to 19mg/kg/minute and a and sc glucagon up to 8 ug/kg/ hour). At day 3 of life was started on diazoxide (with hydrochlorothiazide) at 10 mg/kg per day and then increased to 20 mg/kg per day but continued requirement of high glucose load and glucagon to maintain normal glucose levels. At day 10 of life sc octreotide was started at the dose of 5ug/k/per day and was increased to 25 ug/kg per day, with a good response. Sequence analysis for the ABCC8 and KCNJ11 gene showed no mutation and PET/CT with 68Ga-DOTATATE, shows a diffuse compromise of the pancreas (fig 1)

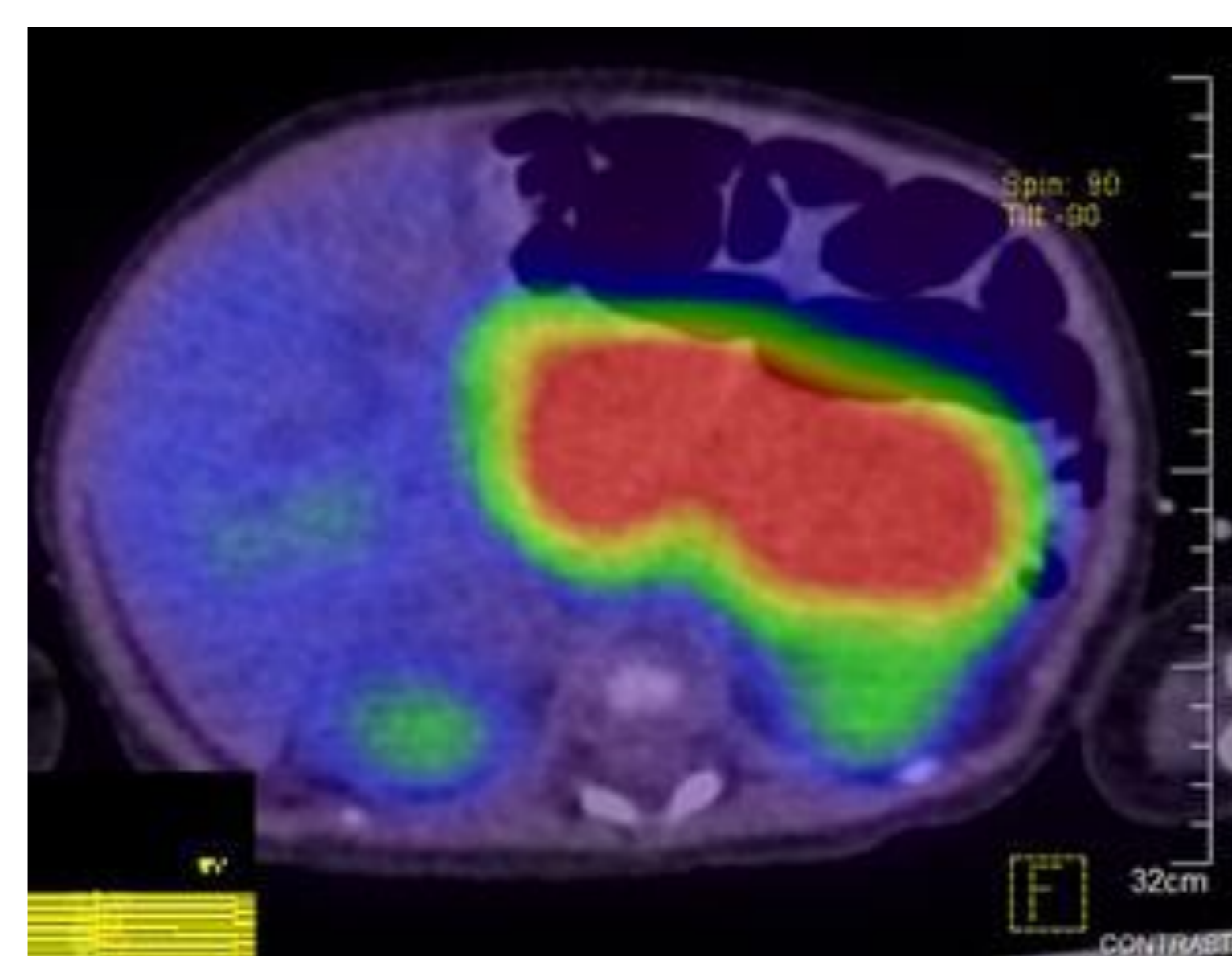


Figure 1.

Figure 1 and 2 shows pancreas with increase size and intense metabolic activity.

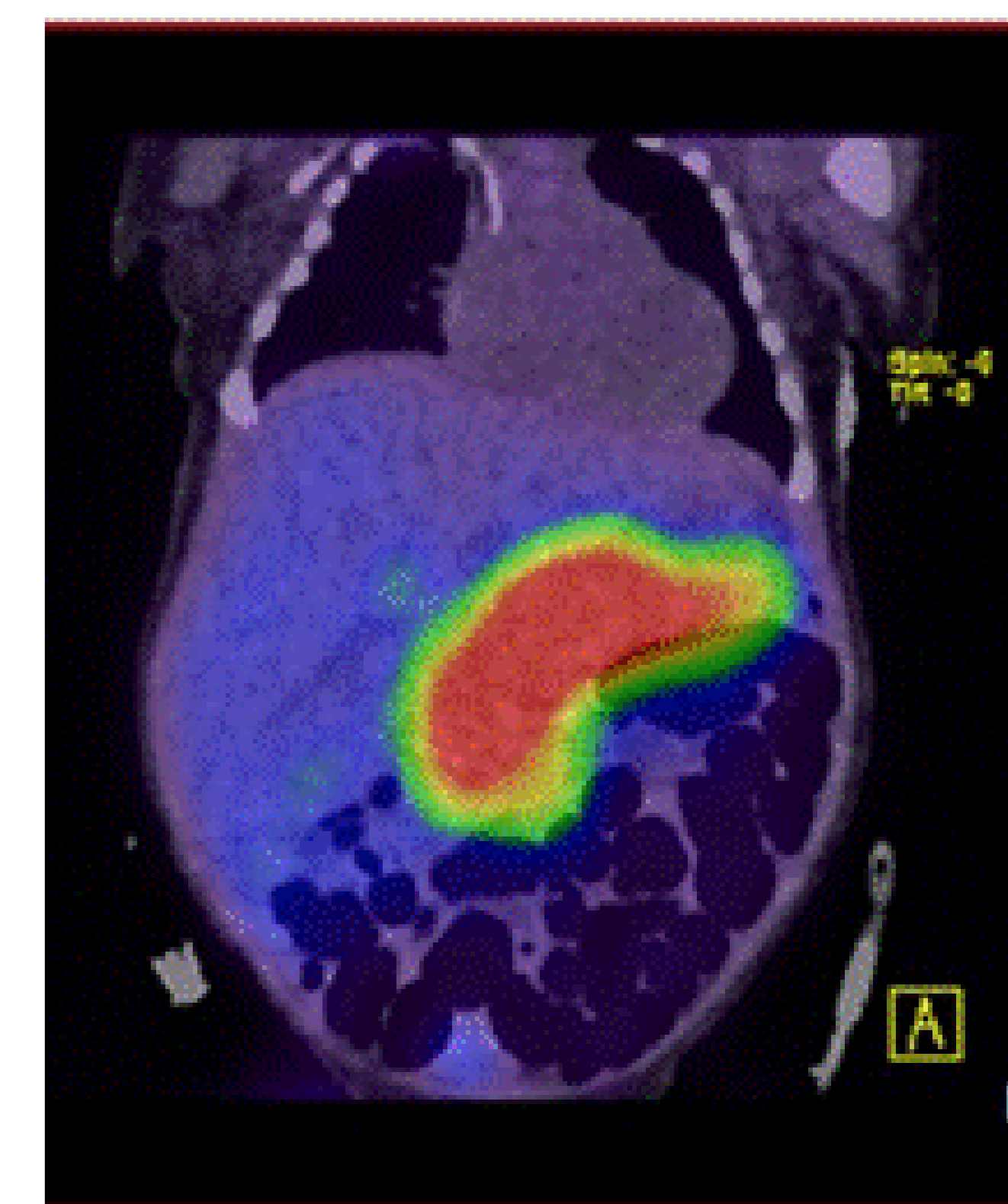


Figure 2.

Day 30 of life : the patient present and acute cholecystitis.

Suspension of octreotide was decided. Glucose load and glucagon must be recommence.

So the patient failed to respond to maximal dose of diazoxide and have major side effect with octreotide.

2 month age: before to decide surgery of near total pancreatectomy, we decide treatment with **Sirolimus** an mtor pathway inhibitor at of 0.5 mg per square meter of body-surface area per day orally.

The dose was gradually increased with the goal of reaching a serum trough level of 5 to 15 ng/ml. Over a period of 1 month the patient maintained stable blood glucose levels. Glucose infusion and glucagon were then gradually discontinued.

3 month age: The patient discharge, with enteric feeding every four hours, without hypoglycemia and Sirolimus doses of 1mg/m²

Sirolimus therapy (days)	0	7	15	20	30 discharge	18 months
Age (days)	66	73	81	86	96	20 months
Glucose Load (mg/kg/min)	16	9	6	0	0	0
Glucagon dose (ug/kg/h)	7	6	6	5	0	0
Sirolimus dose (mg/m ²)	0,45	0,45	0,6	0,6	0,5	0,3-0,2
Sirolimus Plasma levels(ng/ml) (nv 5-15)		4,3		6,3	5,5	
Plasma glucose (mg/dl)	80-100	110-140	140-180		90-150	90-130

There was not adverse effect of therapy during 18 months follow up.

At 18 month of therapy normal glycemie control persist despite low dose of sirolimus.

At 20 month of age Sirolimus is suspend.

We present a clinical case of a newborn with transient Hyperinsulinemic Hypoglycemia with resistant to diazoxide that respond satisfactory to Sirolimus therapy.

