Use of Long-Acting Somatostatin Analogue (Lanreotide) in three children with Focal Forms of Congenital Hyperinsulinaemic Hypoglycaemia

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- ✓ Long-Acting Somatostatin Analogue (Lanreotide) is effective in the management of patients with Congenital Hyperinsulinaemic Hypoglycaemia (CHI) unresponsive to Diazoxide.
- ✓ To date there are no publications regarding the effect of Lanreotide in CHI patients with focal pancreatic lesions.

Case 1

- One-month-old boy diagnosed with CHI
- Genetics: paternally inherited heterozygous *ABCC8* gene mutation
- 18F-DOPA-PET/CT scan: focal lesion in the pancreatic head
- Treatment:
  - diazoxide-unresponsive
  - Partially responsive to octreotide sc inj
- Surgical removal of the lesion was unsuccessful.
- At 11 months of age his treatment was switched to Lanreotide 30mg monthly, which has stabilised his blood glucose for the last 12 months.

Case 2

- One-month-old boy diagnosed with CHI
- Genetics: paternal heterozygous *KCNJ11* gene mutation
- 18F-DOPA-PET/CT scan: focal lesion in the pancreatic head
- Treatment:
  - diazoxide-unresponsive
  - partially responsive to Octreotide
- Over 6 months, he underwent three lesionectomies.
- After the third surgery, responded to Octreotide
- At 9 months of age, his treatment was switched to Lanreotide 30mg monthly.
- Currently:3years, glycaemia, improved fasting tolerance.

Case 3

- Three–week-old girl diagnosed with CHI
- Genetics: paternal heterozygous *ABCC8* gene mutation
- 18F-DOPA-PET/CT scan: focal lesion in the pancreatic head.
- Treatment:
  - diazoxide-unresponsive
  - Responded to octreotide and parents preferred a conservative approach due to the high risk of complications associated with pancreatic surgery.
- At the age of 20 months she was switched to Lanreotide 30mg monthly.
- Currently, she is 27 months old, with euglycaemia and improved fasting tolerance.

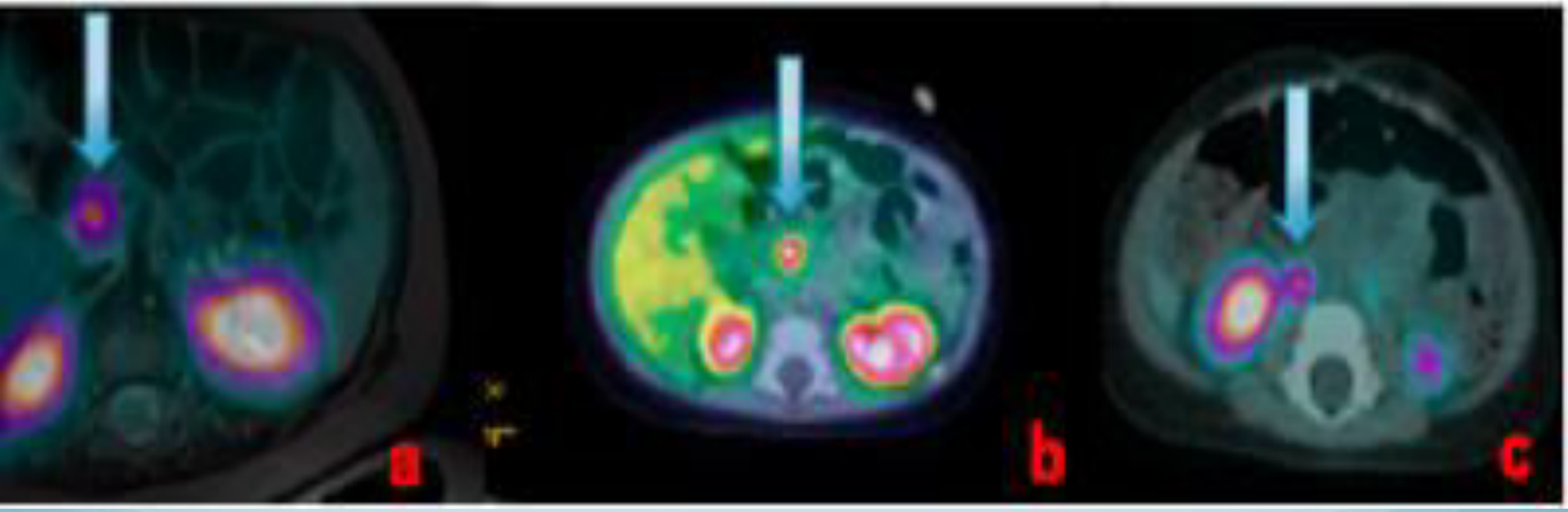
	Case 1	Case 2	Case 3
Age at diagnosis	1st month of life	1st month of life	1st month of life
Genetic results	Heterozygous nonsense *ABCC8* (c.2464C>T, p.Gln822Ter)	Heterozygous missense *KCNJ11* (c.119G>A, p.G40D)	Heterozygous missense *ABCC8* (p.G1401R)
PET scan results	Pancreatic head focal lesion	Pancreatic head focal lesion	Pancreatic head focal lesion
Surgery	None	Three lesionectomies	None
Diazoxide maximal dose (mg/kg/day)	20	15	20
Octreotide maximal dose(mcg/kg/day)	40	40	35
Sirolimus maximal dose based on concentrations up to 15ng/ml ($mg/m^2/day$)	6	16	Not tried
Feeding plan prior to Lanreotide	Daytime 2 hourly PEG feeds Overnight PEG feeds	Day-time 3 hourly PEG feeds Overnight PEG feeds	3-4hourly oral feeds daytime and overnight
Age of commencement of Lanreotide	11 months	9 months	20 months
Initiation of Lanreotide dose	30mg/4 weeks	30mg/4 weeks	30mg/4 weeks
Age of last clinic review	23 months	3 years	27 months
Current weight	12.5 kg (+0.21 SDS)	14.15 kg (- 0.18 SDS)	10.75 kg (- 1.52 SDS)
Current height	84cm (-0.66 SDS)	90cm (-1.1 SDS)	84.7cm (+0.02 SDS)
Current height velocity	12cm/year (+1.16 SDS)	9cm/year (+0.48 SDS)	6.5cm/year (-1.9 SDS)
Current biochemistry (TFT, LFT, IGF1/IGFBP3)	Normal	Normal	Normal
Gallbladder USS	Normal	Normal	Small gallstones
Current feeding plan	3 hourly PEG feeds daytime Overnight PEG feeds(12% CHO)	4 hourly Neocate advance daytime and overnight PEG feeds	4-6 hourly feeds (food and Similac)
Current Lanreotide dose	30mg/4 weeks	30mg/5 weeks	30mg/4 weeks
Duration of fast while on Lanreotide	Up to 3 hours	Up to 8 hours	Up to 12 hours

^{18}F-DOPA-PET/CT scan: Focal lesion in the head of the pancreas

Patient 1 (Figure 1a)

Patient 2 (Figure 1b)

Patient 3 (Figure 1c)



Lanreotide

- Synthetic octapeptide analogue of somatostatin.
- Inhibitory hormone of GH, TSH, insulin and glucagon.
- High binding affinity for human somatostatin receptors (SSTR) 2,5. Reduced binding affinity for human SSTR 1, 3, 4.
- Longer half-life than somatostatin, with more prolonged effects
- Used for acromegaly (pituitary, non-pituitary GH-secreting tumours), neuroendocrine tumours, particularly carcinoid tumours and VIPomas. Activity against non-endocrine tumours.
- Three long-acting formulations, namely octreotide LAR, lanreotide acetate and an aqueous slow-release depot preparation (Autogel).
- Studies concluded that may be is a safe and effective alternative therapy in patients with diffuse forms of CHI, **offering an improved quality of life, as it is well tolerated and simplifies the medical care.**

Conclusion

- ✓ CHI patients with focal lesions in the pancreatic head are challenging, especially if not amenable to surgery
- ✓ Conservative treatment is preferable
- ✓ Lanreotide may be a novel and effective therapeutic option for CHI patients with inoperable focal lesions.
- ✓ The therapeutic impact of Lanreotide treatment in focal forms of CHI should be confirmed in prospective studies and the side effects must be monitored closely