Poster
LBP4

Sirolimus precipitating Diabetes in a patient with Congenital Hyperinsulinism due to autosomal dominant *ABCC8* mutation

Great Ormond Street Hospital for Children NHS Foundation Trust

Dastamani A[1], Güemes M[1,2], Shah P[1,2], Walker J [3], Hussain K [1,2]

1. Endocrinology Department, Great Ormond Street Hospital for Children, London
2. GGM Programme, GEHD section, Institute of Child Health, University College London
3. Department of Paediatrics, Portsmouth Hopsitals NHS Trust

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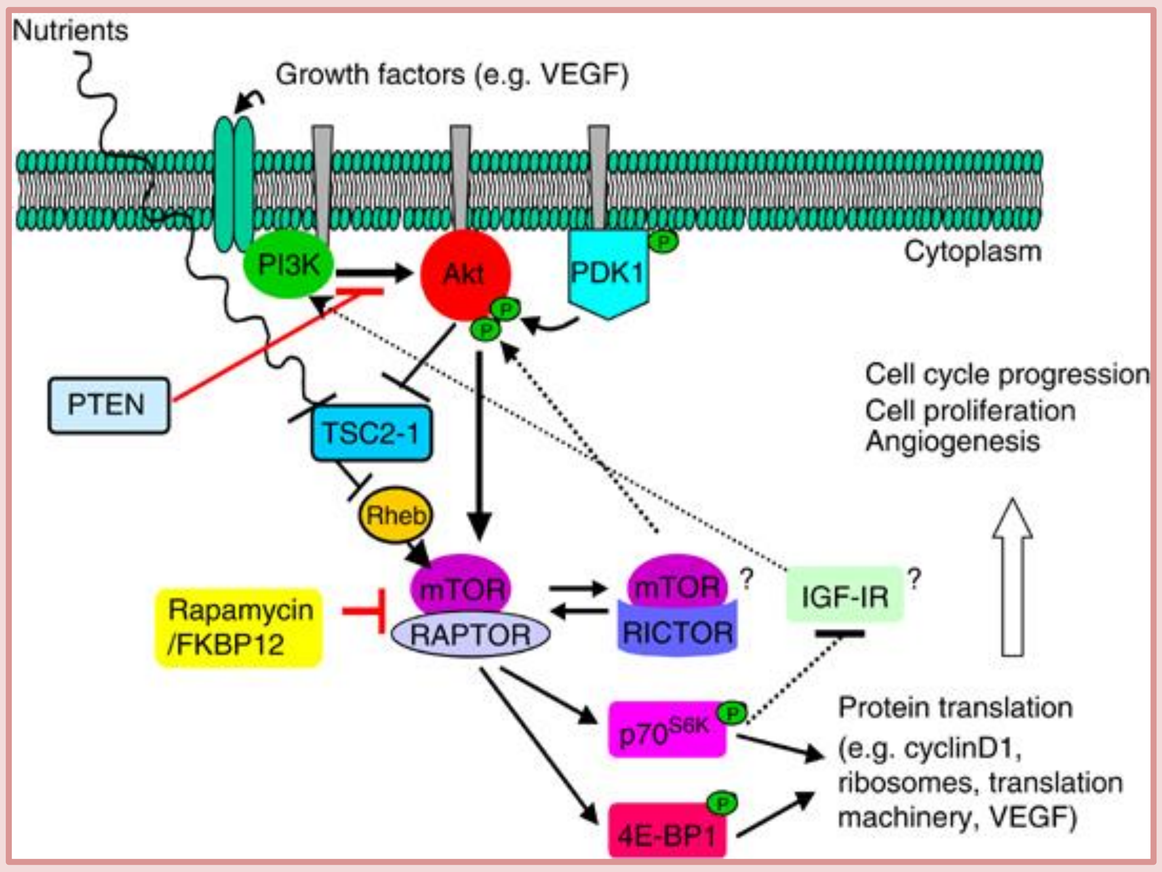
BACKGROUND

- **Sirolimus(Rapamycin) inhibits the mTOR pathway, potentially limiting the production of insulin from the beta-cells.**
- **It has been shown to be effective in the management of patients with Congenital Hyperinsulinism (CHI) (1).**
- **Studies in kidney transplant recipients (2) have suggested that sirolimus may be diabetogenic by possible mechanisms:**
  - **Impaired insulin**
  - **Suppression of hepatic glucose production**
  - **Insulin resistance from ectopic triglyceride deposition**
  - **Direct β-cell toxicity**
- **However, to date there are no publications regarding the diabetogenic effect of Sirolimus in CHI patients.**



OBJECTIVE

To report the first case of sirolimus precipitating diabetes in a CHI patient with known genetic mutation.

METHODS

Prospective follow up of patient with CHI who has a dominant *ABCC8* gene mutation.

CASE

- **A patient with CHI due to autosomal dominant *ABCC8* mutation on high dose (15mg/kg/day) of diazoxide was switched to sirolimus therapy (4.25 mg/m^2/day) at the age of 16.6 years, as she developed severe hypertrichosis.**
- **4 months later, whilst receiving concomitant treatment with clarithromycin for folliculitis, she was found to be hyperglycaemic.**
- **Despite reduction in the dose of sirolimus (and eventually stopping), investigations revealed:**
  - **persistent hyperglycaemia on the 24 hour blood glucose profile**

24hr Glucose Profile													
Time	14:00	16:00	18:00	20:00	22:00	24:00	02:00	04:00	06:00	08:00	10:00	12:00	14:00
BMs (mmol/L)	11.9	12.9	14.7	17.7	16.1	13.9	14.2	15.7	12.8	12.0	14.2	11.7	13.4

  - **increased HbA1c (70 mmol/mol)**
- **She was started on a sulphonylurea, with the plan to increase it to the maximum dose and if no response to introduce metformin and if still hyperglycaemic to consider introducing other insulin sensitising agents. In the long term it is possible that she may require subcutaneous insulin injections.**
- **Family background: Her mother carried the same mutation and spontaneously developed diabetes during adulthood (30 years).**

CONCLUSIONS

- ✓ **Dominant *ABCC8* mutations are prone to diabetes at a later stage in life, but the timing may be influenced by medications such as m-TOR inhibitors.**
- ✓ **The diabetogenic impact of Sirolimus treatment in CHI patients should be confirmed in prospective studies.**

REFERENCES

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(2)Olwyn Johnston, Caren L. Rose, Angela C. Webster, and John S. Gill Sirolimus Is Associated with New-Onset Diabetes in Kidney Transplant Recipients. 2008 by the American Society of Nephrology

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ANTONIA DASTAMANI

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