THE MISSING LINK IN NEONATAL DIABETES

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BACKGROUND

Neonatal diabetes mellitus (NDM) has an incidence of 400,000/live births. It presents within 6months of life, is either permanent (PDM) or transient (TND). Monogenic causes accounts for the majority of cases. We describe the case of what appears to be a familiar NDM with no current known cause

CASE REPORT

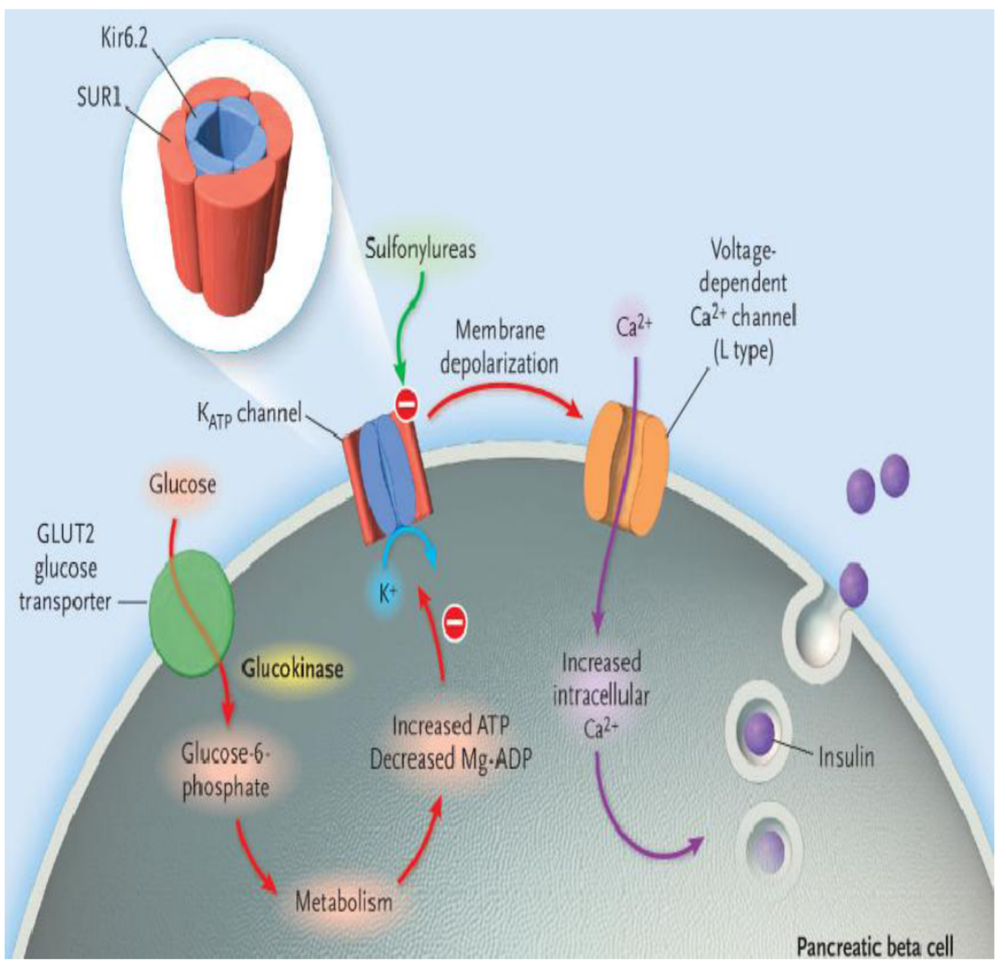
EM presented at 3 weeks old. She was born at term, IUGR (2.3kg) with one day history of diarrhoea, vomiting and anorexia. There was no history of polyuria, polydipsia or weight loss. The blood test showed severe ketosis and metabolic acidosis (**Table 1**). She commenced on Actrapid insulin 0.05units/kg/hr and transferred to PICU where she was started on CSII.

Her paternal uncle had NDM presenting aged 4 weeks, requiring insulin from onset. He went into remission aged 2 years old, and represented at 15 years in DKA and has remained on insulin henceforth. There is no other family history of diabetes.

EM's initial results showed HbA1c: 7.6%, C-peptide: 145pmol/L(370-1470), insulin: 114pmol/L (18-173) and negative diabetes antibodies (Anti-GAD, Islet, insulin autoantibodies). Sequence analysis of 6q TND, and KCNJ11, ABCC8 and INS genes for PND did not identify a pathogenic mutation. Mutation analysis of all known NDM genes have been undertaken in both EM and her uncle and so far have not identified any mutations. Analysis for whole genome sequencing is being undertaken. She is doing well on CSII (0.25units/kg/day), HbA1c:7.2%.

Glycemia	**37 mmol/L**
Blood ketones	**4.5 mmol/L**
PH	**6.8**
PCO2	3.4 Kpa
Bicarbonate	0.6 mmol/L
BXS	-30 mmol/L

Table 1



(Fig 1) Gloyn, A.L. et al. Activating mutations in the gene encoding the ATP-sensitive potassium-channel subunit Kir6.2 and permanent neonatal diabetes. N. Engl. J. Med. 2004; (350): 1838-1849.

CONCLUSION

Most commonly monogenic NDM is due to heterozygous activating mutations in *KCNJ11* and *ABCC8* genes encoding the Kir6.2 and SUR1 subunits of the K_{ATP} channel **(fig 1)**. Mutations in the *INS* gene are reported as the second most common cause. So far all these mutations were excluded. We present the case of what appears to be a familiar cause of NDM which remains under investigation.

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