Mortality in children with monogenic diabetes
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RESULTS

Among 106 children with monogenic diabetes 9 patients died to date (8.5%). Eight of them (88.8%) had NDM. We found 3 patients with autoimmune monogenic diabetes mellitus (ADM) with mutations in AIRE, FOXP3 and LRBA, two of whom had NDM (hemizygous FOXP3 p.R347H and homozygous LRBA p.Glu946Ter). 2 children with ADM/NDM died before age 1 year, and the patient with AIRE p.Cys311fs/p.Arg257Ter died at 15 years. He was admitted to ECU with hyperparathyroidism and died due to severe dyselectrolytemia (Ca 1.2 mmol/l), ischemic stroke and myocardial infarction. The patients with FOXP3 and LRBA died due to respiratory insufficiency and intestinal gangrene respectively. In both NDM cases results of genetic testing were obtained after death.

The patient with a homozygous IFI1 c.1A>G mutation, was diagnosed with NDM at the age of 6 days and died at 6 months due to cytolysis syndrome, cholestatic hepatitis, sepsis and systemic multiple organ failure.

The patient with INSR p.Tyr94*/p.Arg1020* was diagnosed with NDM at the age of 1 month and died at age 4 months and 13 days due to systemic multiple organ failure.

Two NDM patients with EIF2AK3 (p.D164fs/p.E421fs and homozygous p.G1010V) died at an early age. The patient with EIF2AK3 p.D164fs/p.E421fs was diagnosed with diabetes at the age of 13 weeks and died at 3 months due to cerebral edema. The patient with EIF2AK3 p.G1010V had multiple inpatient admissions due to cytolysis syndrome and died at age 2y 2 months due to systemic multiple organ failure.

Two siblings with NDM and ABCB8 p.I49F died at the age 5 and 9 y.o., where 5 y.o. girl died because of pneumonia (had also severe rickets and curvature of the chest) and her 9 y.o. brother died within 1 day after admission to the ECU because of hypertermia, cytolysis syndrome and systemic multiple organ failure.

CONCLUSIONS

Whilst ADM, EIF2AK3 and INSR are described as a well known cause of death in patients with monogenic diabetes, the cause of death in patients with IFI1 and ABCB8 has not yet been widely described.

REFERENCES


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INTRODUCTION

In this study we investigated mortality in children with monogenic diabetes (NDM) and MODY.

METHOD

Within the Ukrainian Pediatric Diabetes Register (UPDR) the number of children 0-17 y.o. in 2019 with:
DM1 was 9860 (1 in 769),
DM2 - 36 (1 in 210,547),
NDM - 65 (1 in 115,000),
MODY - 40 cases (1 in 114,844).

We used targeted next generation sequencing (tNGS) of all known NDM genes in any child diagnosed in the first 9 months of life and all known MODY genes in those who was diagnosed after 9 months of life.

Fig.1. Distribution of children with NDM according to the Register